

De circadiane klok en insuline resistentie

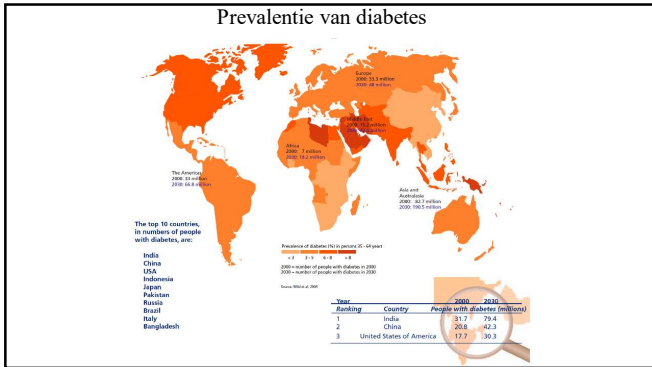
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Metabolic Research Unit Maastricht (MRUM)

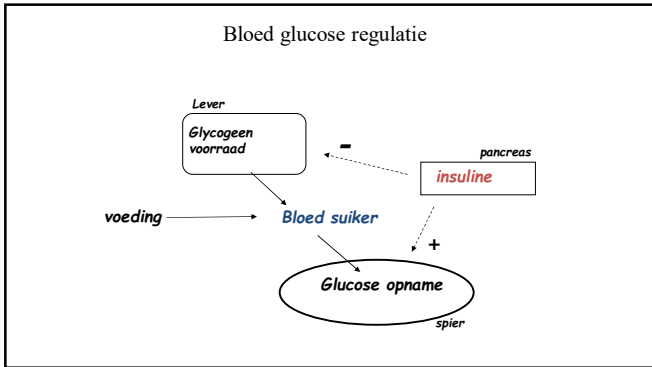
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**Domino effect:
diabetes verhoogt risico op complicaties**

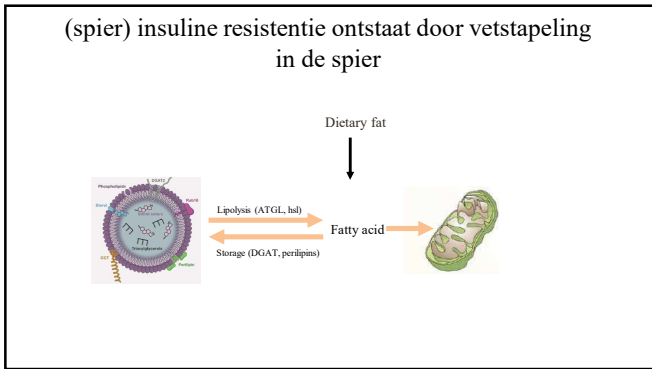
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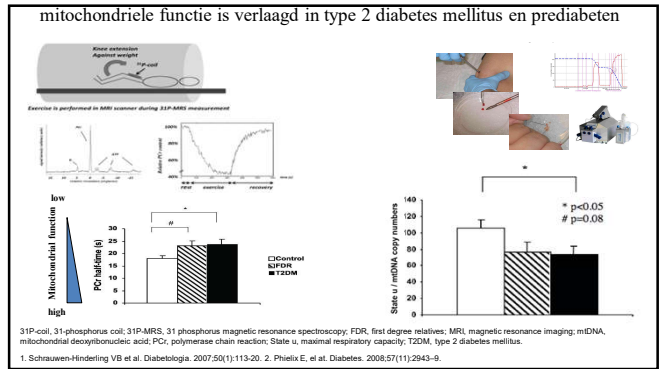
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Focus op insuline resistentie

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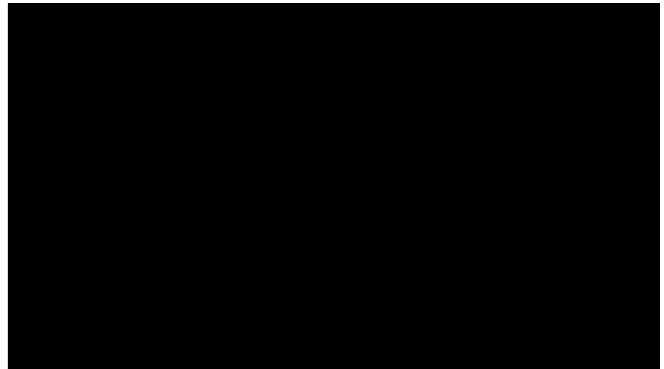
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Waarom?

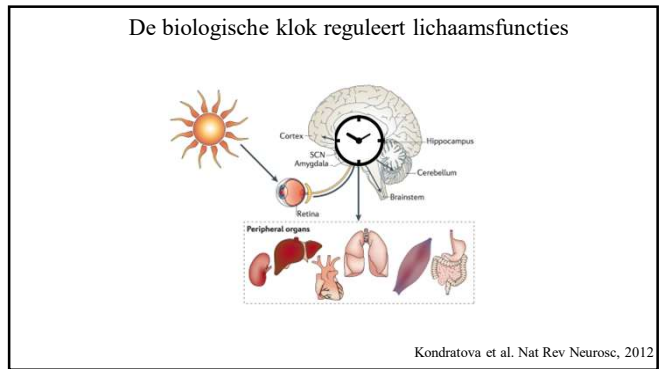
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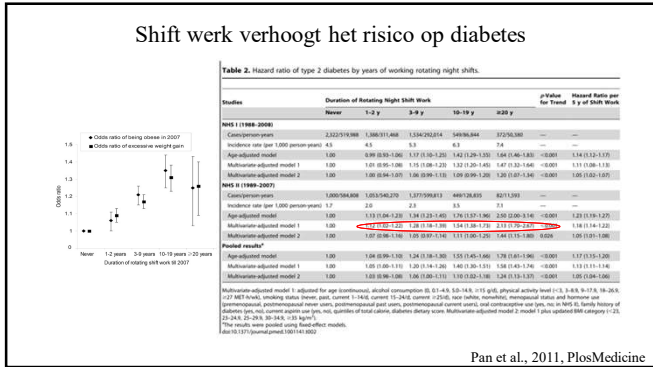
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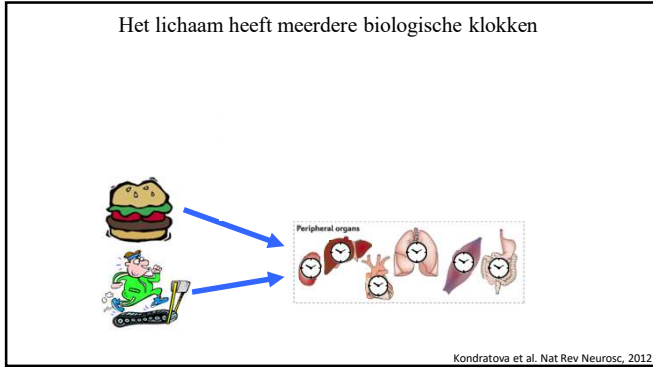
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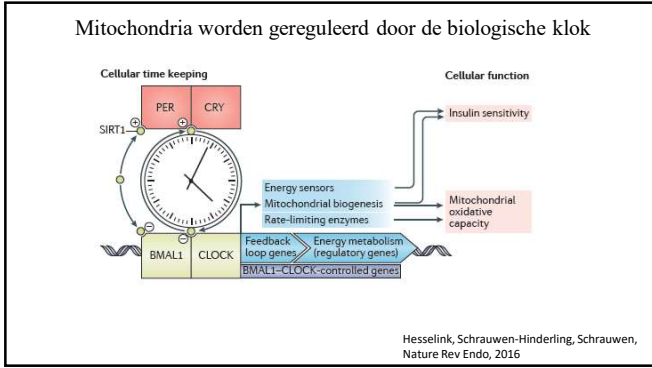
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Wat is de rol van de biologische klok in de etiologie van type 2 diabetes ?

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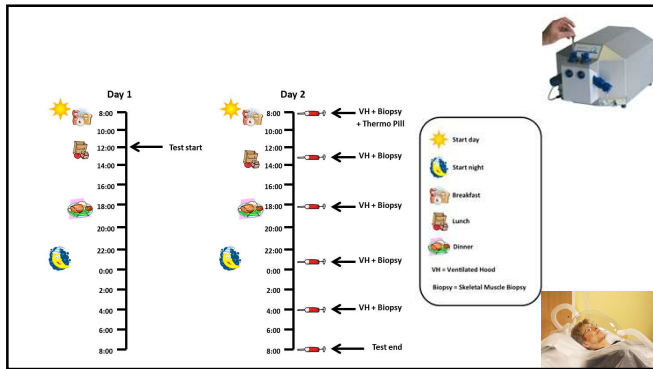
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Q: Is het (mitochondrieel) metabolisme van de spier ritmisch bij de mens?

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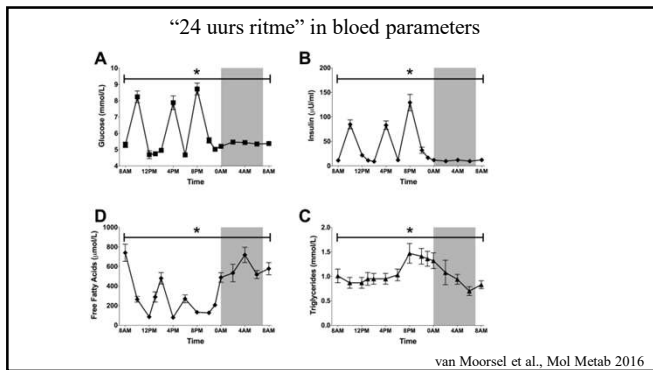


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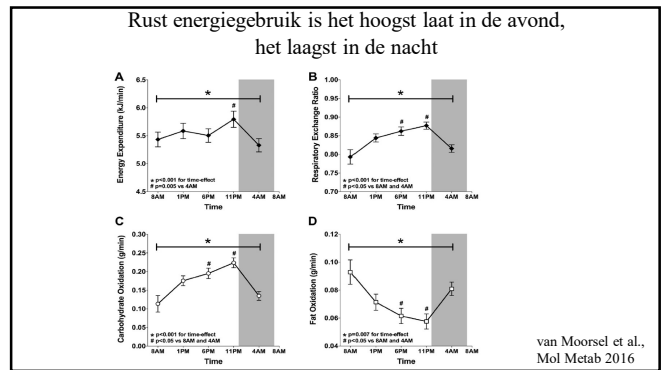
Proefpersoon karakteristieken

- Gezonde mannen
- 18-35 jaar
- Normaal slaap patroon
- Sedentaire leefstijl

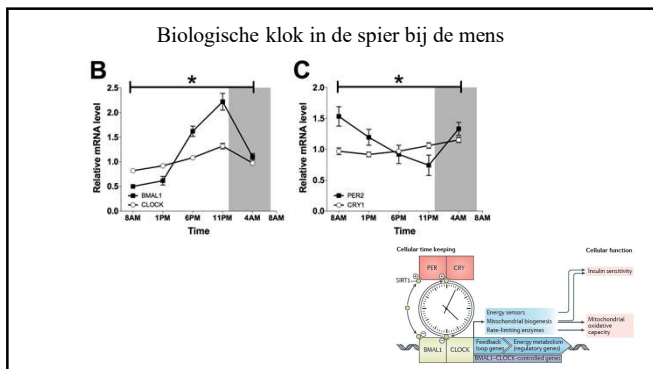
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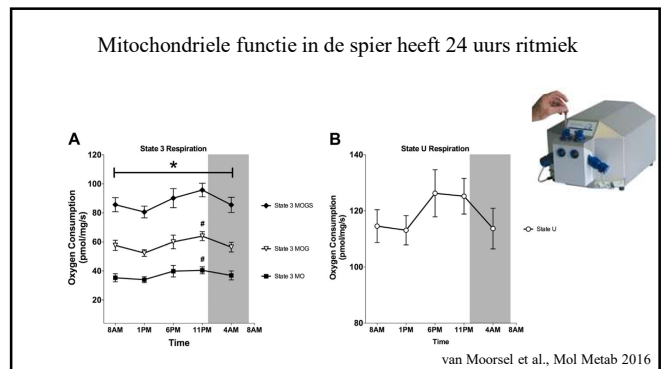
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Q: Is het spier metabolisme verstoord in mensen met verhoogd risico op diabetes?

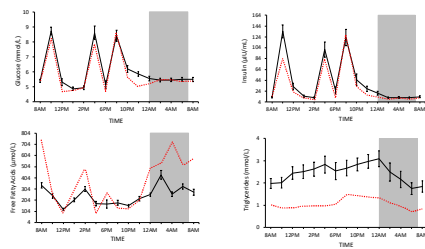
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Proefpersoon karakteristieken

Parameter	Mean ± SD
Age (years)	65 ± 9
Height (m)	1.78 ± 0.05
Body weight (kg)	96 ± 12
BMI (kg/m ²)	30.3 ± 2.7
Body fat (%)	33 ± 4
Fasting plasma glucose (mmol/L)	5.7 ± 0.4
Fasting plasma insulin (μU/mL)	13.8 ± 8.5
2-h plasma glucose (mmol/L)	7.3 ± 1.5
HbA _{1c} (%)	5.3 ± 0.5
Glucose clearance (ml/kg/min)	327 ± 38

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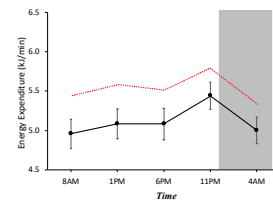
24 uur ritme in bloed parameters is verstoord in 'prediabetes'



Wefers et al., Mol Metab 2020

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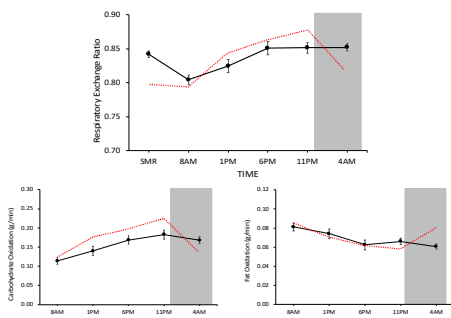
Rust energiegebruik is identiek



Held et al., Mol Metab 2020

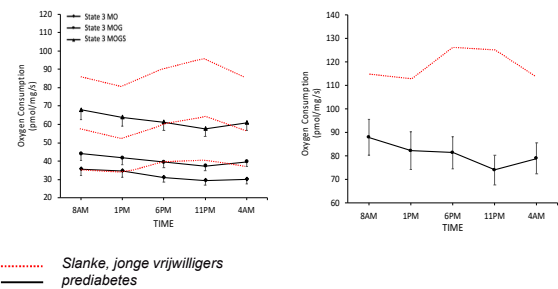
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24h ritme in substraat metabolisme is verstoord in 'prediabetes'



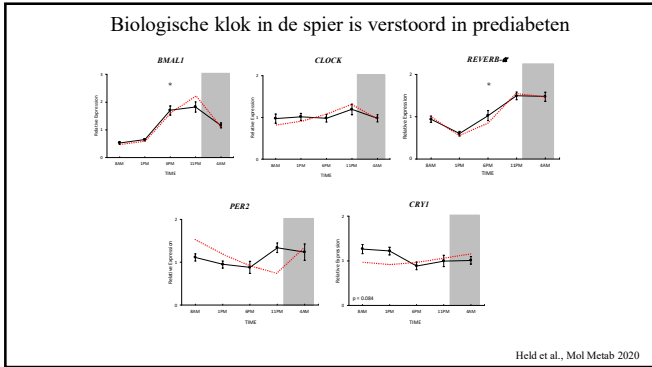
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Mitochondriële functie is NIET ritmisch in prediabetes



Held et al., Mol Metab 2020

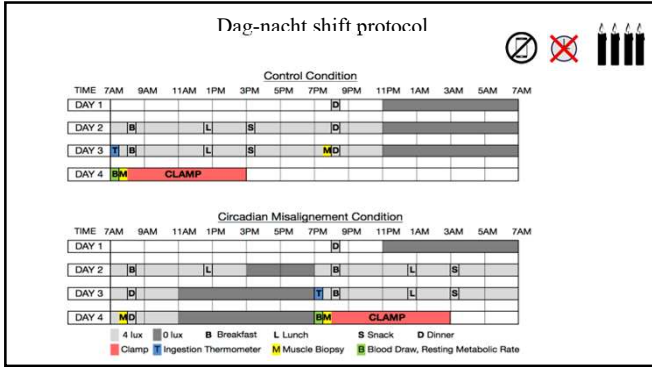
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Q: leidt een verstoring van de biologische klok tot insuline resistentie in gezonde, jonge mannen?

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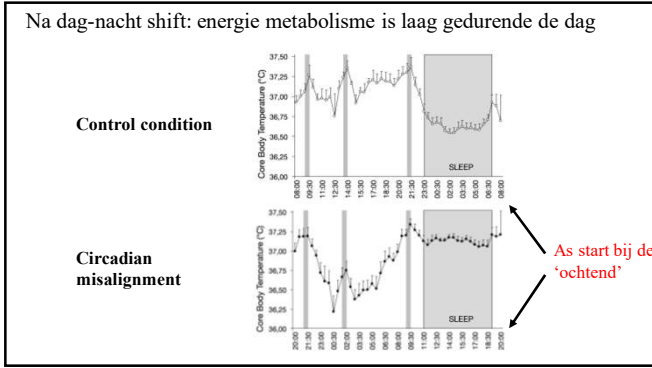


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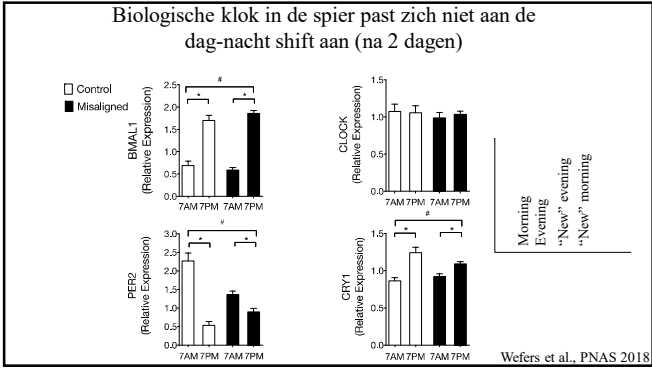
Proefpersoon karakteristieken

	Mean (n=14)	±SD
Age (years)	22.4	2.8
Height (meter)	1.82	0.08
Weight (kg)	74.5	11.1
BMI (kg/m ²)	22.3	2.1
Score MEQ	53.8	6.8

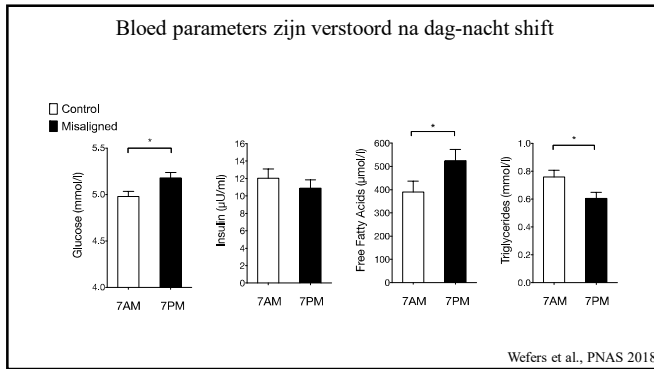
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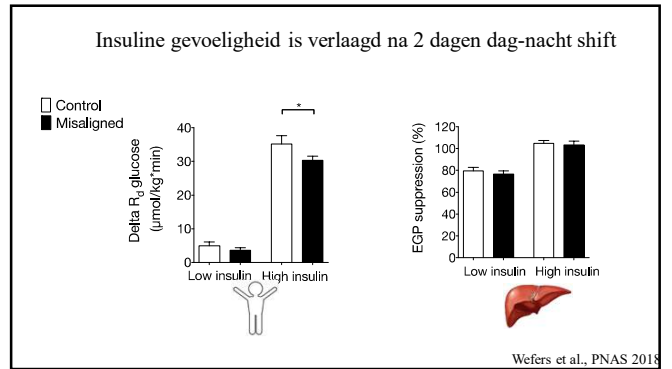
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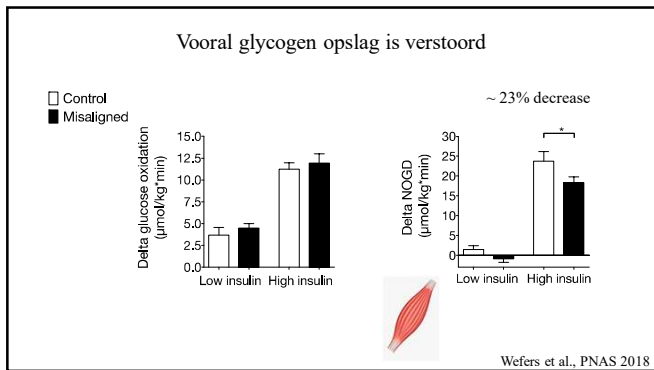
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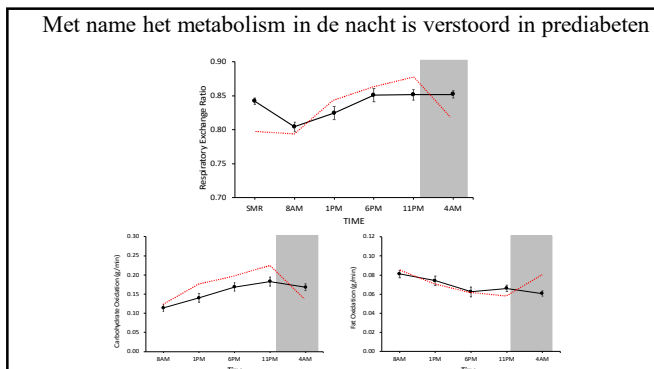
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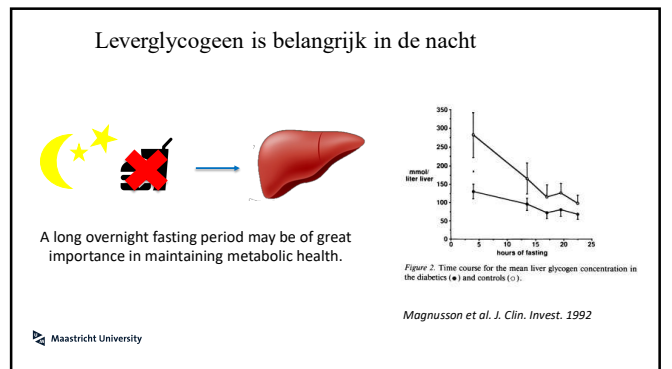
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Q: Kunnen we de biologische klok 'gebruiken' om gezondheid te verbeteren?

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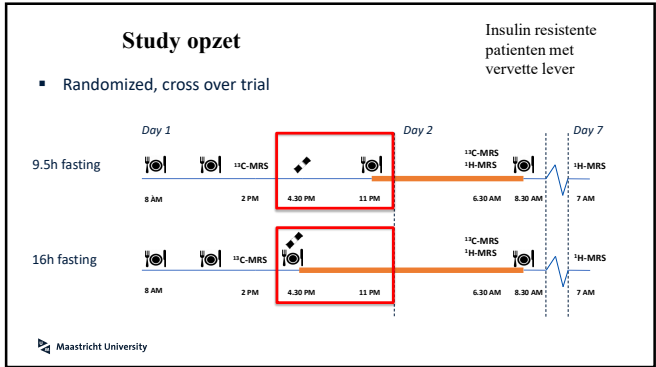
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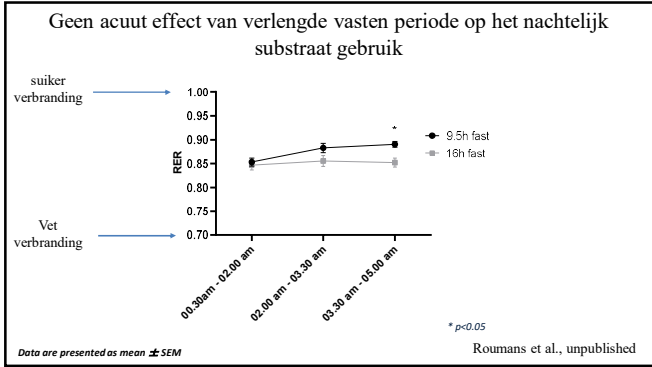
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Q: kunnen we het metabolisme verbeteren door de vastentijd binnen een dag te verlengen?

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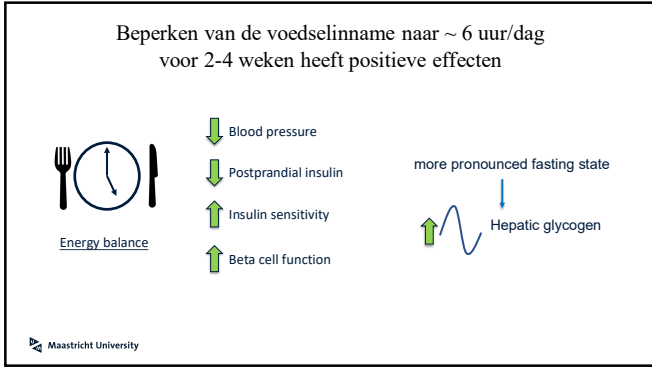
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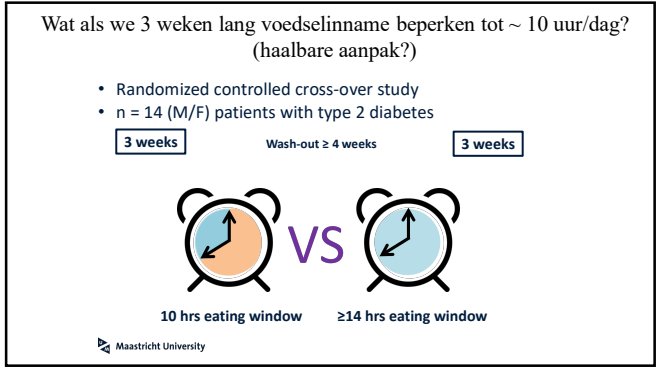
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Q: wat zijn de langere termijn effecten van 'time restricted eating'?

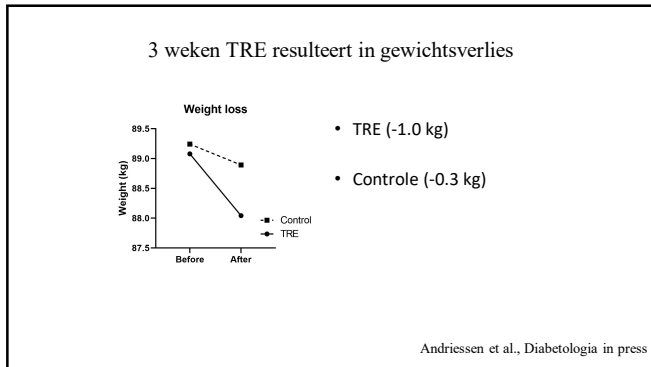
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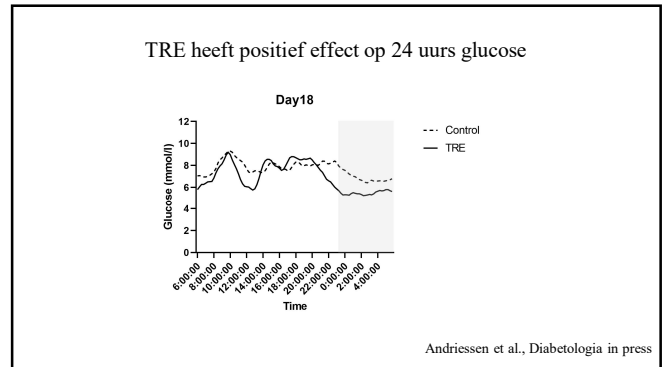
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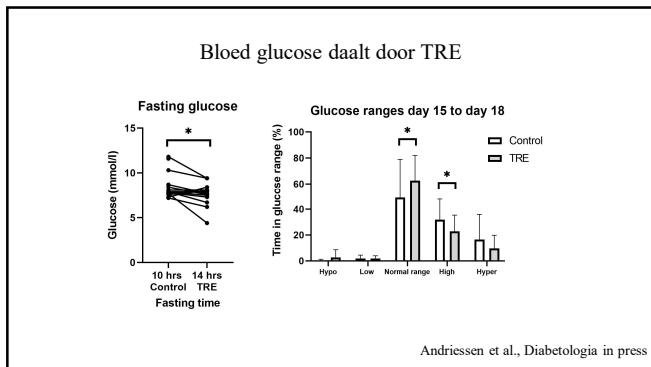
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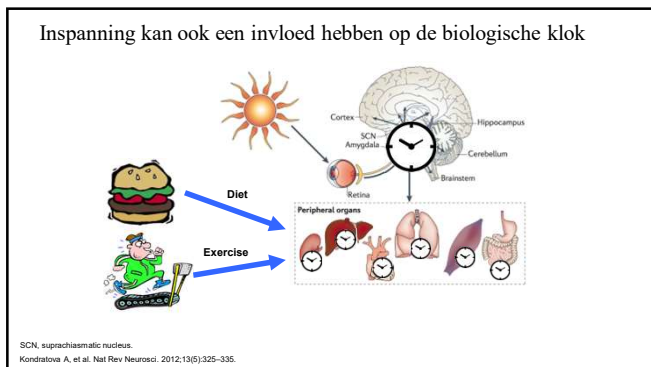


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Conclusie

- Drie weken beperken van de voedselinname tot 10 uur /dag is effectief in het verlagen van bloedsuikerspiegel in type 2 diabetes patiënten
- TRE leidt tot gewichtsverlies
- De interventie was haalbaar voor alle deelnemers

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Q: is er een verschil in de effecten van trainen in de ochtend versus de middag?

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- Twaalf weken training programma, combinatie van duur en kracht training
 - 32 mannen met BMI > 26 kg/m²
 - 12 deelnemers trainden tussen 08:00 en 10:00 (AM groep)
 - 20 deelnemers trainden tussen 15:00 en 18:00 (PM groep)
 - Compliantie ~ 98%.
- Mancilla et al., *Physiol Rep* 2020

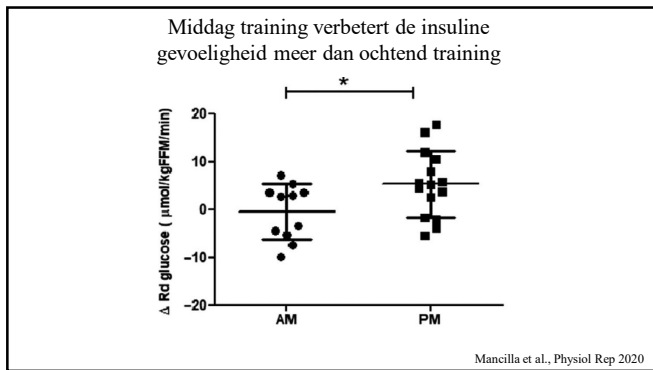
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Geen verschillen vóór training

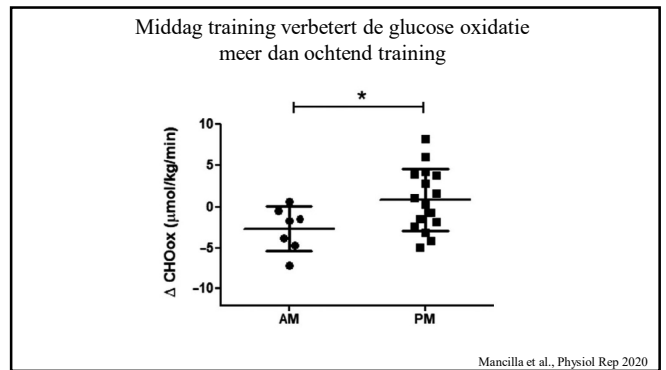
	AM	PM
Sample size	12	20
T2D subjects	4	8
NAFL subjects	3	6
Healthy obese subjects	5	6
Age (year)	61 ± 5	57 ± 7
Body weight (kg)	94.7 ± 11.7	98.1 ± 10
BMI (kg/m ²)	30.3 ± 2.6	29.8 ± 2.3
Fat mass (kg)	27.4 ± 4.3	28.8 ± 5.6
Fat percentage (%)	28.6 ± 2.3	29 ± 3.2
Trunk fat mass (kg)	16.0 ± 2.5	16.2 ± 3.4
Fat-free mass (kg)	65.4 ± 7.2	67.1 ± 5.1
VO _{2max} (ml/kg/min)	26 ± 4.0	26.5 ± 4.5
W _{max} (W/kg)	1.9 ± 0.4	2.0 ± 0.3
Fasting glucose (mmol/l)	6.7 ± 2.1	6.8 ± 2.1
Fasting-free fatty acids (μmol/l)	566 ± 171	615 ± 169

Mancilla et al., *Physiol Rep* 2020

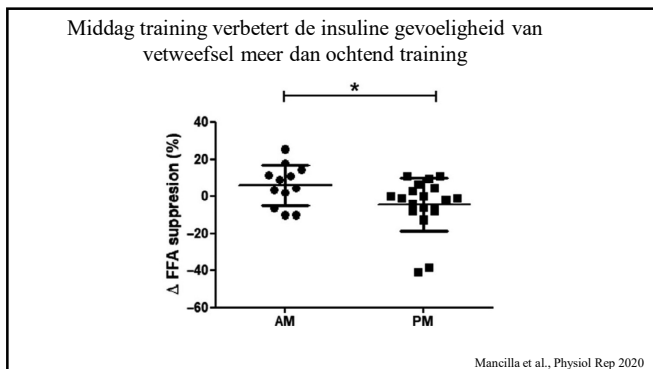
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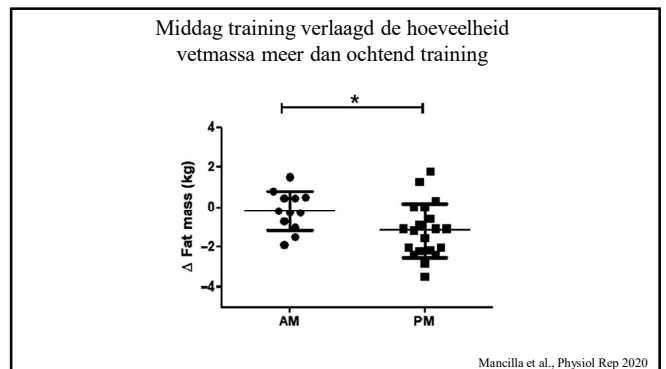
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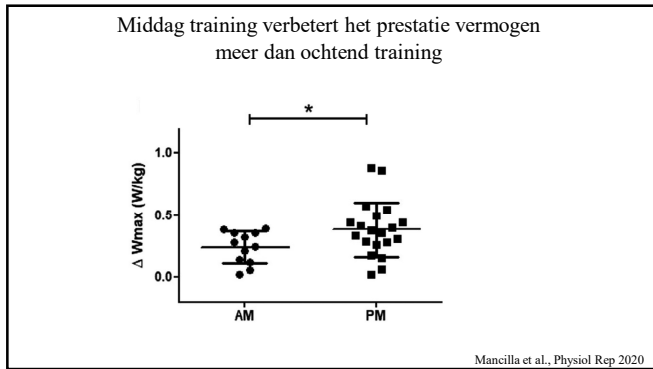
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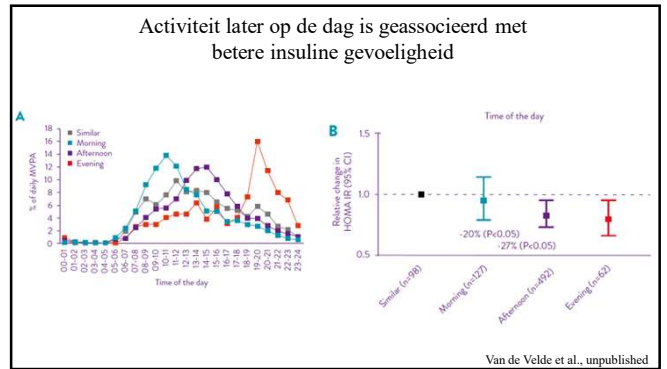
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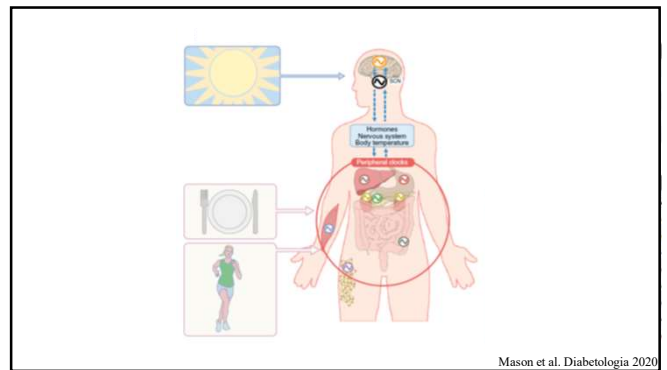
PHYS ED

The Best Time of Day to Exercise

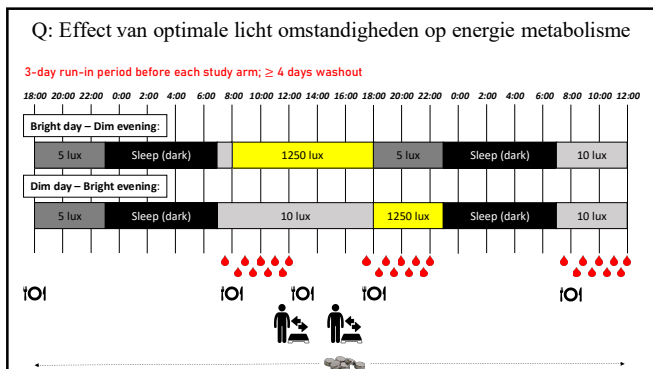
Men at risk for diabetes had greater blood sugar control and lost more belly fat when they exercised in the afternoon than in the morning.

Mancilla et al., *Physiol Rep* 2020

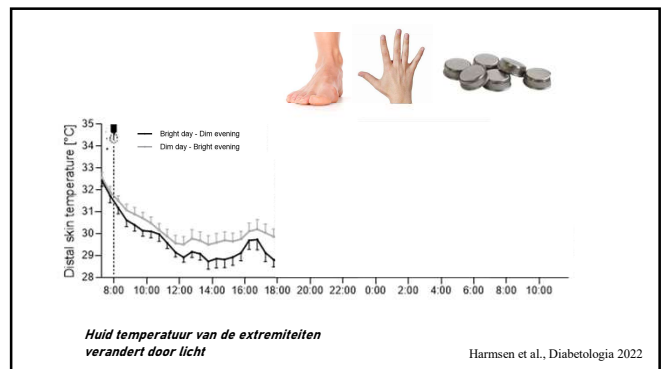
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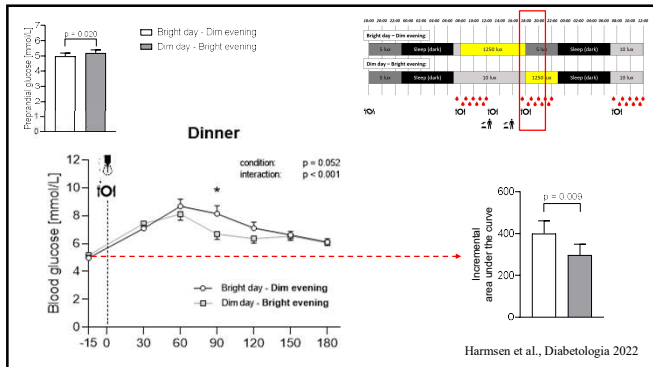
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Conclusions

- Mitochondriële functie en substrate metabolisme vertonen 24 uurs ritme in gezonde, maar niet in pre-diabete volwassenen
- Een snelle dag-nacht shift (jet lag/ night shift) resulteert in insuline resistentie
- Beperken van de voedselinname tot ~ 10 uur/dag heeft gunstige effecten op bloedsuikerspiegel in type 2 diabetes
- Inspanning in de middag/avond verbetert het metabolisme meer dan inspanning in de ochtend
- Blootstelling aan licht heeft een invloed op onze stofwisseling

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