Delivery of short chain fatty acids into the human colon to evaluate their impact on the host



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Mechanisms

Activation of G-Protein Coupled receptors









Systemic effects of SCFA on lipid and glucose metabolism



Nature Reviews | Endocrinology

Systemic effects of SCFA: gut-brain axis



Fraction of SCFA that reach systemic circulation in humans is largely unknown



Strategy



Systemic avaibility of SCFA



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Systemic availability of SCFA



$$Cl\left(\frac{L}{h}\right) = \frac{\text{Infusion rate }^{2}\text{H}-\text{SCFA}}{\text{Steady state }^{2}\text{H}-\text{SCFA concentration}}$$



Cross-feeding in the colon









Incorporation of ¹³C-propionate in glucose



5.9%

n = 12

Incorporation of ¹³C-acetate in fatty acids



Incorporation of ¹³C-SCFA in cholesterol



n = 12



Plasma SCFA depend on type of fibre







SCFA produced after wheat derived fibre fractions



n = 10

Do SCFA have functional effects on the brain?

• Hypothesis:

SCFA mediate the effect of the microbiota on the brain in humans

- Intervention study in humans with known amounts of SCFA administered to the colon as colon delivery capsules
- Outcome parameters: response to stress



Stress response and cortisol



- Help elucidate pathophysiology
- risk factors for the development of affective disorders
- predictors of treatment response





Study design









Maastricht acute stress task



Mental stress 2043 -17 -17 -17 -17





Serum SCFA increase after intervention



SCFA are efficiently absorbed



Fecal SCFA (mM)

SCFA reduce cortisol response





Changes in SCFA were associated with changes in cortisol response





- Δ mean SCFA + 2 SD - Δ mean SCFA + 1 SD - Δ mean SCFA - Δ mean SCFA - Δ mean SCFA - 1 SD - Δ mean SCFA - 2 SD

Conclusions

- Colon delivery capsules are efficient tools to evaluate the physiological role of colonic bacterial derived metabolites in humans
- Dietary interventions with fermentable carbohydrates can alter systemic SCFA concentrations
- Nutritional interventions that target the microbiota might be interesting in affective and mood disorders Furture research:
 - Elucidate the mechanisms
 - Evaluate the effect in patients with mood disorders

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