Major scientific achievements as of 2017

Scientific achievement I (PhD related)

My PhD work focused on the exploration of potential negative cardio- and cerebrovascular consequences in response to energy drink consumption, which were investigated in young and healthy subjects. We used a randomized controlled crossover study design, in combination with state of the art equipment for assessment of blood pressure, heart rate, stroke volume, and cerebral blood flow velocity, to investigate hemodynamic responses to energy drink consumption:

- Blood pressure, stroke volume, and cerebral blood flow velocity were assessed on a beat-to-beat basis. From those parameters, cardiac output, total peripheral and cerebrovascular resistance were calculated. Additionally, we assessed indices for cardiac contractility and cardiac vagal tone parameters.

- Microvascular endothelial function was evaluated by using a combination of iontophoresis and laser Doppler flowmetry.

- We observed that:
  1. Ingestion of an energy drink resulted in an overall negative hemodynamic profile, which comprised of an elevated blood pressure and double product in combination with a lowered cerebral blood flow velocity.


  2. Putting additional mental stress imposed a cumulative cardiovascular load and reduced cerebral blood flow even under a mental challenge.

     ⇐ Grasser EK!, Dulloo AG, Montani JP. Cardio- and cerebrovascular effects in response to Red Bull consumption combined with mental stress. American Journal of Cardiology 2015 (IF: 3.4)

  3. Our findings provided the basis for a deeper investigation about the impact of the diverse ingredients contained in an energy drink (Figure 1 and 2), which led to a publication in the prestigious Advances in Nutrition journal. Moreover, this review has received great honor by the editor-in-chief, Prof. Katherine Tucker, for selecting it for a press release.


  4. In addition, we have provided evidence that the observed decrease in cerebral blood flow velocity differed significantly between sexes. A novel observation, which warrants future intervention studies to determine the mechanisms of such sex differences.


! Corresponding author
FIGURE 1:

Ingestion of sugar-sweetened energy drinks

Blood pressure ↑

Heart rate ↑

Cerebral blood flow velocity ↓

Cardiac workload ↑

FIGURE 2:

Potential vasoactive components in a RB energy drink

Sucrose (glucose + fructose)

CO (SV x HR) ↑

TPR ↓

EndoF ↑

Blood pressure

Vitamin B3, B5, B6, and B12

Caffeine

TPR ↑
**Scientific achievement II (after my PhD)**

Overconsumption of sugar-sweetened soft drinks is considered being a major public health concern with implications for the pathogenesis of obesity, type 2 diabetes and cardiovascular diseases. There is compelling evidence that consumption of sugar-sweetened beverages, as well as sugar, which is containing the fructose moiety, is associated with increased blood pressure levels. However, to date, the exact mechanisms for the impact of sugar-sweetened beverages on people’s blood pressure are still not clear.

In this context:

1. We demonstrated that the blood pressure-elevating effects of fructose were attenuated in the presence of glucose through a reduction in total peripheral resistance. Thus, in healthy and young adults, it seems likely that the regulation of blood pressure depends on a functional glucose metabolism where peripheral and central actions of insulin provide a major impact on blood pressure.

   - Grasser EK!, Dulloo A, Montani JP. Cardiovascular responses to the ingestion of sugary drinks using a randomised cross-over study design: Does glucose attenuate the blood pressure-elevating effect of fructose? British Journal of Nutrition 2014 (IF: 3.8)

2. We observed that galactose presented the interesting characteristics of a low-glycemic sugar with mild cardiovascular effects, which were in opposition to glucose and fructose.

   - Charrière N, Loonam C, Montani JP, Dulloo AG, Grasser EK!. Cardiovascular responses to sugary drinks in humans: galactose presents milder cardiac effects than glucose or fructose. European Journal of Nutrition 2017 (IF: 4.4)

3. Substantial inter-subject variability in blood pressure changes was observed in a healthy, non-obese subpopulation in response to an oral glucose load. In 63% of subjects, peak systolic blood pressure increased by more than 4 mmHg. Peak systolic BP changes, but not overall blood pressure changes, correlated with insulin sensitivity, with little influence of body composition.

   - Monnard CR, Fellay B, Scerri I, Grasser EK!. Substantial Inter-Subject Variability in Blood Pressure Responses to Glucose in a Healthy, Non-obese Population. Frontiers in Physiology 2017 (IF: 4.1)

4. A recent review, which focused on potential mechanisms for sugar induced blood pressure responses, revealed *(accepted for publication)*:
   
   - Potential mechanisms underlying differential effects of sugars on postprandial blood pressure regulation (Figure 3 and 4).
   - Provided evidence for additional molecular contributors, i.e. fibroblast-growth-factor-21, towards sugar-induced cardiovascular and metabolic responses (Figure 4).
   - Additionally, pre-existing glucose intolerance potentially exacerbates the cardiovascular responses to sugary drinks, thus potentially aggravating the cardiovascular risk in already susceptible individuals (Figure 4).

   - Monnard CR, Grasser EK!. Cardiovascular responses to sugar-sweetened beverages in humans: a narrative review with potential hemodynamic mechanisms. Advances in Nutrition 2018 (IF: 5.2)

!Corresponding author
Figure 3:

**Normal glucose tolerance**
- Glucose *acute ingestion*
- Plasma insulin ↑
- SNA ↑
- TPR ↓

**Impaired glucose tolerance**
- Glucose *acute ingestion*
- Plasma insulin ↑↑
- SNA ↑↑
- TPR ↓

= BP ↑

FIGURE 4:

**Impaired glucose tolerance**
- Sucrose *(glucose + fructose)* *acute ingestion*
  - Plasma insulin ↑↑
  - SNA ↑↑
  - TPR ↓

- Fructose *acute ingestion*
  - Plasma FGF 21 ↑↑
  - SNA ↑↑
  - TPR ↑

↑ BP ↑
**Scientific achievement III (after my PhD)**

Ingestion of water entails a variety of cardiovascular and physiological responses, which can be best explained by its impact on the autonomic nervous system. However, the precise effect remains elusive. In order to reveal potential cardiovascular mechanisms in response to drinking water, we provided evidence that:

1. Ingestion of cold- and room- but not body-tempered water reduced the workload to the heart through a reduction in heart rate and double product. These responses are potentially triggered by changes in cardiac vagal tone (Figure 5).

   ⇢ Girona M, **Grasser EK**, Dulloo AG, Montani JP. Cardiovascular and metabolic responses to tap water ingestion in young humans: does the water temperature matter? Acta Physiologica 2014 (IF: 4.9)

2. Drinking water decreased cardiac workload in a time-dependent fashion with little impact of sex (Figure 6).

   ⇢ Monnard CR, **Grasser EK**. Water ingestion decreases cardiac workload time-dependent in healthy adults with no effect of gender. Scientific Reports 2017 (IF: 4.3)

   ⇢ **Grasser EK**, Girona M, Dulloo AG, Montani JP. It is likely that the drinking of cold and room temperature water decreases cardiac workload. Acta Physiologica 2015 (IF: 4.9)

3. Drinking a large volume (500 mL) of water before a meal attenuated postprandial blood pressure responses in older adults (Figure 7).

   ⇢ Grobéty B, **Grasser EK**, Yepuri G, Dulloo AG, Montani JP. Postprandial hypotension in older adults: Can it be prevented by drinking water before the meal? Clinical Nutrition 2015 (IF: 4.6)

'Corresponding author

**FIGURE 5:**

[Images of graphs and data plots]
FIGURE 6:

![Graph showing changes in heart rate (HR) over time for men, women, and combined sexes.]

FIGURE 7:

![Graph showing changes in systolic blood pressure (SBP) over time for different volumes of fluid consumption and age groups.]

[Caption: A]
Scientific achievement IV (before and after my PhD studentship)

One, if not the most important, scientific achievement is the fact that I have been able to successfully publish as a first author in 4 completely, and independent from each other, different laboratories.* This fact provides evidence that I am able to work goal-orientated with a clear focus and strong abilities to cope with different personalities. Moreover, because I am still on good terms with my former work places, my mutual and consensual personality helped me a lot to achieve my above mentioned scientific merits.

*Grasser E, Steinecker B, Ahammer H, Schreibmayer W. Subunit stoichiometry of heterologously expressed G-protein activated inwardly rectifying potassium channels analysed by fluorescence intensity ratio measurement. Pflugers Archive 2008 (IF: 3.2)

*Grasser EK, Goswami N, Hinghofer-Szalkay H. Presyncopal cardiac contractility and autonomic activity in young healthy males. Physiological Research 2009 (IF: 1.5)


*Grasser EK*, Miles-Chan JL, Montani JP. Hemodynamic Responses to Energy Drink Consumption. JAMA. 2016 (IF: 44.4)

*Grasser EK, Ernst B, Thurnheer M, Schultes B. QT interval shortening in response to bariatric surgery induced weight loss depends on the correction formula. Obes Surg 2017 (IF: 3.9)

*Corresponding author.

Future scientific outlook

1. Studies in preparations as principal investigator

Blood pressure responses to sugar ingestion: preliminary results point toward an impact of ethnicity. Planned start: January 2018.

Sugary drinks and its impact on the cardiovascular and metabolic system: Does fibroblast growth factor 21 affect blood pressure regulation?

Cardiovascular responses to sugary drinks: An intra-subject variability study
2. Habilitation at the University of Fribourg: Submission planned for January 2018.

3. SNF grant submission planned for 2018 or 2019 with potential collaborations within Switzerland and Austria.

**External funding**

**Successful:**

SWISS HEART from 01.01.17 – 31.12.17: Co-applicant together with the principal investigator Dr. Jennifer Lynn Miles-Chan. Granted amount: 45,000 CHF.

**Rejected SNF grant submissions:**

1. Swiss National Science Foundation 2017
   - Committee’s decision from March 29, 2017, which included four reviewer comments: Still lacking scientific independence due to the research topic’s proximity to former research

2. Swiss National Science Foundation 2015
   - Committee’s decision from June 10, 2015: No last authorship, therefore lack of scientific independence.