SAP and Study Protocol

V1.0 – 29.5.2018

Title of Study:

„Influence of Flavanol-rich chocolate on visual acuity, contrast sensitivity and retinal perfusion“

Initiator: University Eye Hospital Munich,
Prof. Dr. med. Siegfried Priglinger
1. Personnel

a) Principle investigator: Prof. Dr. med. Siegfried Priglinger
Head of Department
University Eye Hospital Munich
Mathildenstr. 8
80336 Munich

b) Sub-investigator: Jakob Siedlecki
University Eye Hospital Munich
Mathildenstr. 8
80336 Munich

2. Rationale

The positive health effects of cocoa beans have been discussed for some years now. Their most important ingredient, the Flavan-3-ol („Flavanol“ or „Catechin“), is discussed to have antioxidative properties and to induce vessel dilation by release of nitric oxide\textsuperscript{1,2,3}.

A shortly published report indicates that visual acuity and contrast sensitivity improve after ingestion of Flavanol-rich chocolate (316 mg) within two hours. However, this study was not blinded to the participants, who knew which chocolate they were eating and which effect there would be to expect\textsuperscript{4}.

The FLAVIKA study shall now prove whether this effect of dark chocolate is reproducible concerning subjective (visual acuity and contrast sensitivity) and objective (measuring of retinal perfusion) measures after dark and milk chocolate consumption.

3. Study aims

This prospective trial is to investigate whether the ingestion of flavanol-rich dark chocolate (2x 200 mg Flavanol, Lavlé Belgian Chocolates, The Good Chocolate Company, Brüssel, Belgien) can improve retinal perfusion and thus improve visual acuity and contrast sensitivity.
Primary end point: To assess the changes in retinal perfusion measured on OCT angiography two hours after ingestion of flavanol-rich dark chocolate.

Secondary end points: To assess the changes in ETDRS visual acuity measured at 4 meters two hours after ingestion of flavanol-rich dark chocolate.

To assess the changes in Pelli-Robson and Mars contrast visual acuity measured two hours after ingestion of flavanol-rich dark chocolate.

4. Design

Monocentric, prospective, randomized, double-blind, interventional cross-over trial.

**Randomization:** Flavanol-rich dark chocolate (2x 10 g Lavlé Belgian Chocolate, equaling 400 mg Flavanol, The Good Chocolate Company, Brussle, Belgium) or milk chocolate

5. Study population

The study will enroll healthy participants between the age of 18 and 65 years willing to undergo the study procedure.

6. Study procedures

The participants will be examined on two days one week apart, once randomized to flavanol-rich dark chocolate, once to milk chocolate. On both dates, the following examinations will be performed before and two hours after chocolate ingestion:
1. **ETDRS visual acuity**: Binocular visual distance acuity will be tested on a retroilluminated ETDRS chart at 4 meters with the participant’s habitual correction.

2. **Pelli-Robson contrast visual acuity**: Contrast sensitivity will be tested on a non-retroilluminated Pelli-Robson chart at 1 meter with the participant’s habitual correction.

3. **Mars contrast visual acuity**: Contrast sensitivity will be tested on a non-retroilluminated Mars chart at reading distance with the participant’s habitual correction.

4. **OCT-Angiography**: Using optical coherence tomography, confocal scanning laser ophthalmoscopy and the SSADA algorithm, en-face vessel density will be imaged and calculated into a percentage of vessel-covered area.

7. **Statistical analysis and sample size calculation**

Concerning the tested hypotheses, statistical significance will be defined as p<0.05. For intra-individual changes in macular perfusion, visual acuity and contrast sensitivity, a Wilcoxon signed rank test will be employed to test for significant differences between baseline and post-interventional parameters.

Sample size calculation is based on the assessment of changes in macular perfusion on OCT angiography serving as primary outcome measure. As recently reported, significant changes in vessel density are subject to diurnal variation, resulting in the suggestion to define significant changes (as opposed to diurnal variation) as >8 % value change in the superficial and >10 % change in the deep retinal plexus. Using the same OCT angiography system, macular perfusion in the superficial plexus in the parafovea, central 3 and 6 mm is 48 – 51 % in our setting, with a standard deviation of +/- 3.0 %. Applying the 8 and 10 % value changes reported in the aforementioned study on our mean macular perfusion value of approximately 50 %, a 4 % absolute change results for the superficial plexus, and a 5 % absolute change results for the deep plexus. Therefore, a significant change in macular vessel density in our study is defined as a mean increase of 4.0 %.

Calculating statistical power from these figures, a participant number of n=18 is sufficient to achieve a power of 0.8.


