Pituitary hormone secretion in familial longevity : The Switchbox Study

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CHAPTER 2

Switchbox Leiden: study design and data collection

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STUDY POPULATION AND RECRUITMENT STRATEGY

To study endocrine and metabolic regulation in relation with health in old age, participants were recruited from the Leiden Longevity Study (LLS)(1). The LLS was designed to study genotypes and phenotypes which could explain inter-individual differences in familial human longevity(2).

Between January 2012 and April 2013, 494 offspring from long-lived siblings and partners from the LLS were asked via an invitation letter to participate in the Switchbox study (Fig. 1). These participants were selected based on previous obtained information(1), and were middle-aged (55-77 yr) and had a body mass index (BMI) between 19 and 33 kg/m^2. Of the 494 participants, 218 participants were willing to participate in the Switchbox study. After a medical screening by phone for all participants who agreed to participate, and an additional home visit for the participants willing to participate in the more intensive study program (group A), 135 participants were found eligible to participate according to the exclusion criteria listed in Table 1.

Table 1 In- and exclusion criteria for Switchbox participants

Exclusion criteria Switchbox participants	
Laboratory results	Fasting Plasma glucose > 7 mmol/L Hemoglobin < 7.1 mmol/L TSH < 0.3 mU/L or > 4.8 mU/L fT4 < 10 pmol/L or > 24 pmol/L
Disease history	Any significant chronic disease; renal, hepatic or endocrine disease
Medication use	Hormone therapies Use of medication known to influence lipolysis
Lifestyle	Recent weight changes (> 3 kg weight gain/loss within last 3 months) Extreme diet therapy Alcohol consumption of more than 28 units/week Smoking addiction
Others	Severe claustrophobia Difficulties to insert IV cannula Blood donation (< 2 months) Participation in other research project (< 3 months or >2 within 1 year)

Data collection of the Switchbox Study

Between March 2012 and July 2013 all participants underwent the study protocol, after an overnight fast at the study center of the Leiden University Medical Center as described in Fig. 2. A short description of the different study parts is presented below.

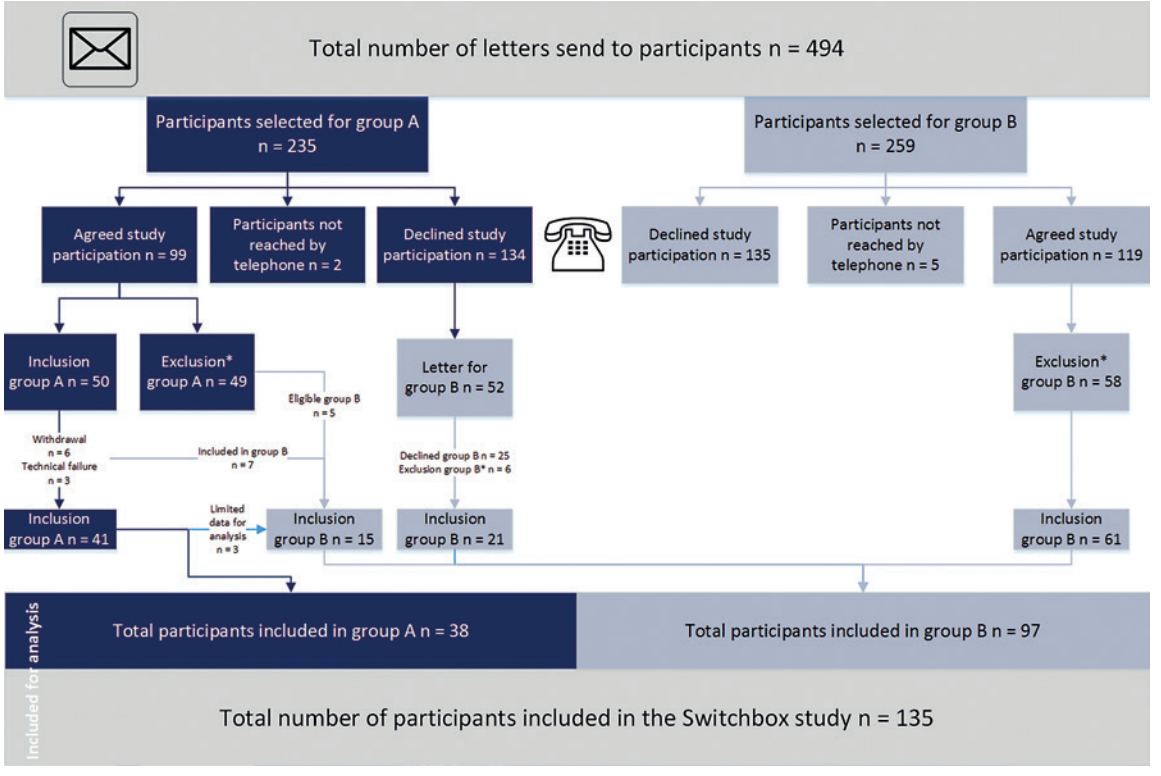

Figure 1 Recruitment flowchart of Switchbox participants.

Study details on Group A and B are depicted in Fig. 2. *Participants were not eligible for the study according to the in- and exclusion criteria listed in table 1

Trier social stress test: Study participants were randomized such that half of them received a stress condition according to the Trier social stress test (TSST)(3) and the other half a placebo non-stress condition. The TSST is a widely used laboratory protocol that reliably stimulates biomarkers of stress in all age ranges(4).

fMRI: Several tests were selected during functional imaging to assess emotional working memory, emotion regulation and behavior, in half of the participants under stress condition and the other half in resting/non-stressed condition.

Questionnaires: Different questionnaires, including the MINI(5) and geriatric depression scale(6), were used for screening of psychiatric diseases including depression. Moreover, validated questionnaires for the assessment of e.g. neuroticism, anxiety traits (STAI)(7), mood and personality(8) were completed. Also neurocognitive tests, including the controlled word association test (COWAT)(9) for verbal fluency and digit span to assess working memory`s number storage capacity, were performed. Two questionnaires were completed to assess the quality of sleep (Pittsburg Sleep Quality Index(10)) and the chronotype (Munich sleep questionnaire(11)).*Blood samples:* Fasted whole blood samples were taken between 12.00h and 13.00h, plasma and serum samples were used for measurements of hormones and additional serum aliquots were stored at -80°C for future studies.

Body composition measurements: Body composition, including fat mass and lean mass were measured using a Bioelectrical Impedance Analysis meter at a fixed frequency of 50kHz (Bodystat® 1500 Ltd, Isle of Man, British Isles)(12).

Indirect calorimetry: Participants had two times a 30 minutes indirect calorimetry session using a ventilated hood system (Care Fusion Canopy Jaeger Oxycon Pro, Houten, The Netherlands) after 14 hours of fasting and after a standardized meal (nutridrink, Nutricia, Zoetermeer, The Netherlands). Participants were kept under standardized conditions, lying awake and emotionally undisturbed. Inspired oxygen (VO2) and expired carbon dioxide were measured (VCO2) and amongst other resting metabolic rate were calculated using standard formulas(13).

Continuous physiological measurements: For continuous measurements over a 5 day period of electrocardiography, core body temperature, breathing rate and physical activity an Equivital monitor (Equivital EQ02 SEM, Hidalgo, UK) was used. In order to assess core body temperature, each participant swallowed one Core Body Temperature Capsule (Capsule REF 500-0100-02, Respironics Inc., Murrysville, PA, USA) at each of three consecutive days (Fig. 2). Additionally, participants were asked to wear activity watches on their wrist and ankle (GENEActive, Kimbolton, UK) for

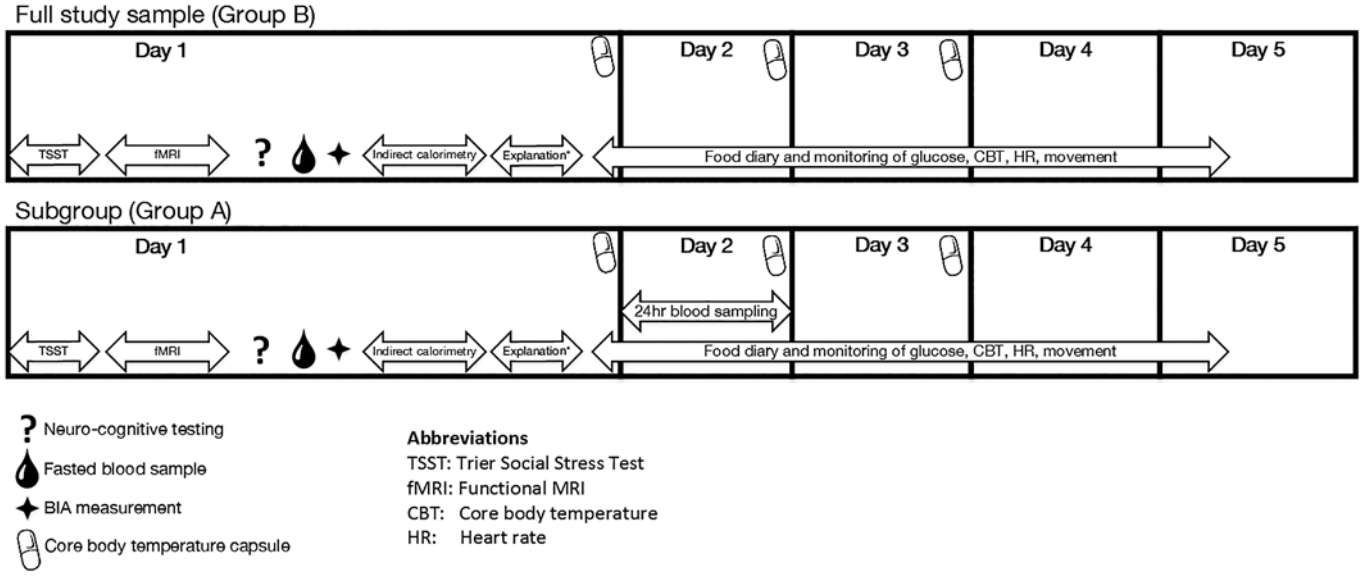

Figure 2 Recruitment flowchart of Switchbox participants.

Study details on Group A and B are depicted in Fig. 2. *Participants were not eligible for the study according to the in- and exclusion criteria listed in table 1

more detailed measurements of physical activity. For continuous measurements of glucose over the 5 day period, a continuous glucose monitor was applied (Medtronic MiniMed Inc., Northridge, CA, USA).

Diaries: During the study period, participants were asked to fill out details on food intake, charging times of the monitors, capillary blood glucose, physical activity and sleeping times.

24-hour blood sampling: Of the 135 participants, 38 participants had a complete series of 24-hour blood samples. Details on the procedure for 24 hour blood sampling can be found in the next chapter.

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