

How to take variability of physiological brain perfusion into account?

## Manual and SOP documents

Documentation version 1.0

By Patricia Clement – Ghent University







## Content

INTRODUCTION	4
<ol> <li>PHYSIOLOGICAL VARIABILITY IN BRAIN PERFUSION</li> <li>PERFUSION MODIFIERS</li> <li>STANDARD OPERATING PROCEDURE (SOP)         <ul> <li>A. Main goals of the SOP</li> <li>B. SOP structure: from perfusion-modifier to SOP component</li> </ul> </li> </ol>	4 4 6 6 6
C. Recommendations	9
REFERRING TO THE SOP	12
<ol> <li>General references</li> <li>SOP component-specific references</li> </ol>	12 12
HOW TO USE THE SOP	14
1. QUESTIONNAIRES (Q)  I. General information  a. Personal details  b. Family and social life*  c. Education level  d. Professional life  e. Hobbies  f. Sports  g. Handedness*  h. Personality*  i. Caffeine consumption*  j. Nicotine consumption*  k. Alcohol consumption*  l. Recreational drug consumption  m. Diet  n. Health  o. Medication use  II. Day of scan  a. Mood	18 18 18 19 19 20 21 21 22 22 23 23 24 25 25 26 26
<ul> <li>b. Extreme sports</li> <li>c. Last caffeine consumption</li> <li>d. Last nicotine consumption</li> <li>e. Last alcohol consumption</li> <li>f. Last recreational drugs consumption</li> <li>g. Hunger and thirst</li> <li>h. Health</li> <li>i. Sleep</li> <li>j. Medication use</li> </ul>	26 27 27 27 28 29 29 29
2. MEASUREMENTS	31 <i>31</i>
<ul><li>I. During the scan session</li><li>a. Perfusion scan information</li><li>b. Wakefullness</li><li>c. Mood</li></ul>	31 31 32 32

EUROPEAN COOPERATION IN SCIENCE AND TECHNOLOGY

	d. Physiological measurements	33
11	I. After the scan session	34
	a. Body temperature and blood pressure	34
	b. Blood and urine sample	34
3.	Neuropsychology	36
	a. Symptom Checklist-90-Revised (SCL90)	36
	b. Stroop Test	36
	c. RBANS (Repeatable Battery for the Assessment of Neuropsychological Status)	37
	d. National Adult Reading Test	37
4.	Instructions	38
1.	Session instructions	38
	a. Time of day	38
	b. Scanner surroundings	38
11	I. Patient instructions before scan session	39
	a. Restrictions	39
11	II. Patient instructions during scan session	40
	a. Eyes	40
	b. Movement	40
	c. Resting state	40
	d. Wakefullness	40
ACKN	OWLEDGMENTS AND CONTACT INFO	41
1.	ACKNOWLEDGEMENTS	41
2.	CONFLICTS OF INTEREST	41
3.	CONTACT INFORMATION	41
REFER	RENCES	42
SUPPL	LEMENTARY FILES: SOP DOCUMENTS	43
SUPPL	EMENTARY FILES: SCORING	105



## Introduction

### 1. Physiological variability in brain perfusion

Brain perfusion is affected by numerous factors related to physiology, lifestyle, diet and medication use, leading to a large between- and within-subject perfusion variability (16.2% and 4.8%, respectively). This variability confounds the interpretation of brain perfusion measurements, for example in early pathological stages. Alternatively, physiological variations at the individual level, can be mistaken as abnormalities when not properly taken into account. Such unwanted variations of perfusion should be small compared to disease-related alterations if ASL-based perfusion measurements are to be used in individual patients.

#### 2. Perfusion modifiers

A perfusion **modifier** is defined as any **normal physiological variation** that gives rise to a change in cerebral perfusion. Those non-medication related perfusion modifiers can be classified into four groups, which have been used in the review for structuring the results sections (Table 1):

- 1/ Physiology, lifestyle and health
- 2/ Blood components
- 3/ Mental state, personality and cognition
- 4/ Caffeine and recreational drugs

Additionally, *medication* can be considered as a fifth group.

The specific effects of those non-medication related modifiers on absolute and relative cerebral perfusion have been described in the main review for which this manual is supplemented. In order to be able to take those effects into account, and hence decrease the variability causing interpretation difficulties, a standard operating procedure was proposed which is described in further detail in this manual.



Table 1 – Summary of non-medication related perfusion modifiers, classified into four groups.

Physiology, lifestyle and health	Blood components	Mental state, personality and cognition	Caffeine and recreational drugs
Age	Blood gases: O <sub>2</sub>	Stress	Caffeine
Occupation	Blood gases: CO <sub>2</sub>	Anxiety	Energy drinks
Social environment	Hematocrit	Yoga & meditation	Nicotine
Gender	Blood viscosity	Mood	Alcohol
Menstrual cycle	Hemoglobin	Cognitive capacity	Recreational opioids
Pregnancy	Fibrinogen	Creativity	Amphetamines
Menopause	Blood glucose	Personality	Cocaine
Diurnal rhythm	Homocysteine	Sleep	Cannabis
ВМІ	Cholesterol	Drowsiness/ sleepiness	Solvents & inhalants
Physical exercise / training	Ketone bodies	Open/closed eyes	MDMA & LSD
Altitude	ADMA	Mental activity	Psilocybin
Diving	Free fatty acids	Arousal	
Blood pressure			
Heart rate			
Body temperature			
Mobile phone			
Nutritional diet			
Hunger/satiety			
Fat intake			
Sugar intake			
Thirst			



### 3. Standard Operating Procedure (SOP)

#### A. Main goals of the SOP

A **standard operating procedure** is proposed in order to try to take this between- and within-subject perfusion variability into account. Although this procedure is mostly applicable in the context of perfusion measurements using arterial spin labeling (ASL), it can be used as a normalisation tool for other perfusion techniques as well.

The first main goal in the development of this SOP includes the acquisition of personalized profiles, in combination with perfusion data, from a large number of healthy subjects. This information would provide an opportunity to develop and evaluate the so-called theory of 'deep MRI physiotyping'. The theory claims that it would be possible to match a given volunteer to a specific physiotypic profile by using perfusion data and personalized information.

Secondly, this SOP was developed in order to provide perfusion researchers a means to correct for the effects of all perfusion-modifiers and reduce variability in perfusion data during in the context of their own study. In clinical settings, such a procedure is also recommendable, at least to account for the effects of the most important perfusion-modifiers. Some recommendations on which modifiers should be taken into account in a specific setting are provided in chapter *C. Recommendations*.

# B. SOP structure: from perfusion-modifier to SOP component

Each **perfusion-modifier** (Table 1) can be divided in multiple **modifier-specific aspects**; for example, caffeine can be divided in the aspects: 1/ acute use (what was used today); 2/ chronic use (daily use); and 3/ past use (daily use in the past).

In contrary, the structure of SOP is based on a more workable and intuitive approach, dividing the SOP in four **SOP categories** (code):

- 1/ Questionnaires (Q)
- 2/ Measurements (M)
- 3/ Neuropsychology tests (N)
- 4/ Instructions (I)

Table 2 summarizes the perfusion modifiers for each SOP category.



Table 2 – Summary of the perfusion-modifiers divided over the four subdivisions.

Questio	nnaire (Q)	Measurements (M)		Neuro- psychology (N)	Instructions (I)
Age	Thirst	Diurnal rhythm	Free fatty acids	IQ	Diurnal Rhythm
Occupation	Stress	Blood pressure	Stress	Cognitive capacity	Physical exercise/training
Social environment	Anxiety	Heart rate	Anxiety		Mobile phone
Gender	Mood	Body temperature	Mood		Hunger/Satiety
Menstrual cycle	IQ	Blood gasses: O <sub>2</sub>	Sleep		Fat intake
Pregnancy	Cognitive capacity	Blood gasses: CO <sub>2</sub>	Drowsiness/ Sleepiness		Sugar intake
Menopause	Creativity	Hematocrit	Arousal		Thirst
ВМІ	Personality	Blood viscosity	Caffeine concentration		Sleep
Physical exercise/ training	Drowsiness/ sleepiness	Hemoglobin	Nicotine concentration		Drowsiness/ Sleepiness
Altitude	Arousal	Fibrinogen	Alcohol concentration		Open/closed eyes
Diving	Caffeine	Blood glucose			Mental activity
Nutritional diet	Energy drinks	Homocysteine			Caffeine
Hunger/satiety	Nicotine	Cholesterol			Nicotine
Fat intake	Alcohol	Ketone bodies			Alcohol
Sugar intake	Recreational drugs	ADMA			Recreational drugs
Additional potential perfusion modifiers (not studied in literature/not included in review)					d in review)
Educational level	Pathology	Respiratory rate		Pathology	Medication
Handedeness	Medication				

Each SOP category comprises several **SOP components** (indicated with a code, e.g. Q.I.CAF). A perfusion-modifier and its aspects can thus be covered by several SOP components.

For clarity, the case of caffeine was visualized in Figure 1. The **perfusion-modifier** *caffeine* can be divided into three **modifier-specific aspects**: 1/ acute use; 2/chronic use; and 3/ past use. The acute use of caffeine, for example, is covered in the **SOP** components Q.II.CAF (category Questionnaires), M.II.BLO (category Measurements), and I.I.RES (category Specific instructions).



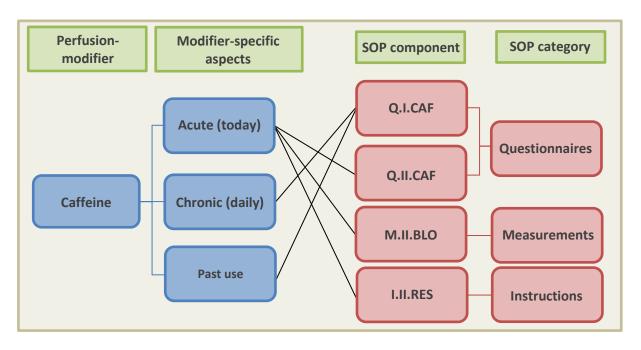


Figure 1 – SOP structure for the perfusion-modifier *caffeine*.



#### C. Recommendations

The SOP includes measures for (almost) all perfusion-modifiers, even those only minimally contributing to the variability, for purposes regarding the 'deep MRI physiotyping' theory. Often, the effects of some modifiers are still unknown or literature fails to provide consistent conclusions.

Due to this high amount of perfusion-modifiers and modifier-specific aspects, a classification was proposed based on the effect size on perfusion, and the prevalence and consistency in the literature (Table 3). The classification of the modifier-specific aspects is summarized in Table 4.

Table 3 – Legend of the color-coded classification based on the effects size on perfusion, and prevalence and consistency in the literature.

Colour	Effect size	Prevalence	Consistency		
	High	High	Consistent		
	Medium	High	Consistent		
	High to medium	High	Inconsistent		
	No quantitative information	High	Consistent and inconsistent		
	High to medium	Low	/		
	No quantitative information	Low	/		
0	Low	High and Low	Consistent and Inconsistent		
	Potential perfusion modifier/modifier specific aspect, not yet studied in literature				



Table 4 – Color-coded categories of modifier-specific aspects in relation to effect size, and current prevalence and consistency.

Effect size → Prevalence/ Consistency ♥	1 (> 24%, > 15 ml/100g/min)	2 (between 14% and 24% or between 6 and 15 ml/100g/min)	3 (<14%, < 6 ml/100g/min)	4 (Unknown)
A (High prevalence, consistent across studies)	Age (adult), age (child), physical exercise (during), hypercapnia, hypocapnia, NREM	Caffeine (acute), amphetamines (acute), cannabis (acute)		Mobile phone (during use – task), extraversion, introversion, amphetamines (abstinence)
B (High prevalence, inconsistent across studies)	Gender, physical exercise (after), physical training, active lifestyle, hypertension, hyperoxia, hematocrit, anxiety (all), long-term cognitive training, REM, alcohol (acute/abstinence long-term), cocaine (acute), cannabis (chronic)	Hypoxia, nicotine/smoking (acute/chronic/abstinence 24h), alcohol (chronic)	Hypoglycaemia, sad mood, happy mood	Satiety (after hunger), thirst, satiation (after thirst), IQ, memory performance, recreational opioids (acute/abstinence), cocaine (chronic), cannabis (abstinence), solvents and inhalants (chronic)
C (Low prevalence, low number of studies)	High altitude (short stay – months), circulating homocysteine, hyperketonemia (acute), open eyes, light, mental activity, alcohol (abstinence 24h), solvents and inhalants (acute), physical training (10 day training cessation)	Occupation, hyperthermia, hemoglobin, fibrinogen, waking up, awakened, former smoker, cocaine (former user 6mo)	Social environment, menstrual cycle, BMI, high altitude (medium stay – days), high altitude (long stay – weeks/months/years/native), fat intake, hyperketonemia (after 3 days), ADMA, stress, arousal, caffeine (chronic), MDMA (abstinence)	Pregnancy, menopause, diurnal rhythm, fat free mass, overweight, back after high altitude, (former) divers, hypotension, heart rate, mobile phone (during use − resting), mobile phone (after use − task + resting), high nitrate diet, fasting (Ramadan), sugar intake, blood viscosity, cholesterol (total/LDL/HDL), free fatty acids, anxiety (low → moderate / moderate → high), yoga/meditation, disgust, worry, anger, processing speed/attention, executive function, fluid ability, MMSE, cognition, short cognitive training, creativity, personality traits, wake/sleep transition, drowsiness/sleepiness, caffeine (abstinence), energy drink, acute NRT gum, recreational opioids (chronic), amphetamines (chronic), cocaine (abstinence/former user >1year), LSD, psilocybin (acute)
Potential modifier;	Educational level, handedness,	back after diving, body temperature (no	ormal range), fever, hypothermia,	respiratory rate, hypoglycaemia, other mood states, MDMA
not studied	(chronic/abstinence), psilocybin (chronic/abstinence), solvents and inhalants (abstinence), mescaline, barbiturates (recreational)			



Depending on the goal of the SOP in a given study and the setting of that study, specific **modifier-specific aspects** can be included, based on this table.

- General perfusion (ASL) research – high interest in correcting for variability: the use of *all* modifier-specific aspects *but those in B3 and C3* is recommended. Optionally, B3 and C3 can be included, although the effects of those modifier-specific aspects appear to be rather small.



- General perfusion (ASL) research – moderate interest in correcting for variability: the use of the modifier-specific aspects in A1, A2, A4, B1, B2 and B4 is recommended.



 Clinical use and general perfusion (ASL) research – low interest in correcting for variability: the use of the modifier-specific aspects in A1 (and preferably A2) is recommended.



The use of this colour code is maintained during the rest this manual and in the supplementary files to aid researchers and clinicians using perfusion imaging in the selection of the recommended **SOP components** complying with their needs.



## Referring to the SOP

When using this SOP in own perfusion research and in clinical setting, and publishing results based on this SOP, the general references should always be used. Moreover, depending on the specific SOP components used, additional references should be included in the manuscript, to refer to the original publications of tests incorporated in this SOP.

### 1. General references

Clement P, Mutsaerts H-J, Václavů L, Ghariq E, Pizzini FB, Smits M *et al.* Variability of physiological brain perfusion in healthy subjects — A systematic review of modifiers. Considerations for multi-center ASL studies. *Journal of Cerebral Blood Flow & Metabolism* 2018; 38(9): 1418-1437.

### 2. SOP component-specific references

#### Q.I.SOC - UCLA Loneliness Scale Version 3.0:

Russell, D. (1996). UCLA Loneliness Scale (Version 3): Reliability, validity, and factor structure. Journal of Personality Assessment, 66, 20-40.

## Q.I.EDU – International Standard Classification of Education: education level and education field

United Nations Educational, Scientific and Cultural Organisation, UNESCO Institute for Statistics. *International Standard Classification of Education ISCED 2011*. UIS/2012/INS/10/REV. (2012), available from http://unesdoc.unesco.org/images-/0022/002280/228085e.pdf

United Nations Educational, Scientific and Cultural Organisation, UNESCO Institute for Statistics. *ISCED fields of education and training 2013 (ISCED-F 2013): manual to accompany the International Standard Classification of Education 2011.* UIS/2014/INS/4 REV. (2014), available from http://unesdoc.unesco.org/images/0022/002280/228085e.pdf

#### Q.I.HAN – Edinburgh Handedness Inventory

Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 1971;9(1):97-113.

John OP, Donahue EM, Kentle RL. The Big Five Inventory--Versions 4a and 54. University of California, Berkeley, Institute of Personality and Social Research 1991.



John OP, Naumann LP, Soto CJ. Paradigm shift to the integrative Big Five trait taxonomy: History, measurement, and conceptual issues. In OP John, R W Robins, & L A Pervin (Eds), Handbook of personality: Theory and research (pp 114-158) New York, NY: Guilford Press 2008.

Benet-Martinez V, John OP. Los Cinco Grandes across cultures and ethnic groups: Multitrait multimethod analyses of the Big Five in Spanish and English. Journal of Personality and Social Psychology 1998;75:729-750.

#### Q.I.NIC – Fagerström Test for Nicotine Dependence

Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerstrom Tolerance Questionnaire. British journal of addiction 1991;86(9):1119-1127.

#### Q.I.NIC – Positive and Negative Affect Schedule - Expanded

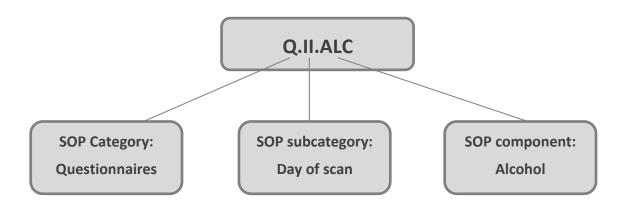
Watson D, Clark LA. The PANAS-X, Manual for the Positive and Negative Affect Schedule-Expanded form. Unpublished 1999;University of Iowa.



### How to use the SOP

The SOP for perfusion measurements consists of four SOP categories: questionnaires (Q), measurements (M), neuropsychology (N) and instructions (I). Each category consists of one to three subcategories (I/II/III) indicating the timing of the measure taken. All subcategories comprise several SOP components, which are indicated with a three-letter abbreviation, referring to the perfusion-modifier covered by the SOP component (e.g. ALC for alcohol).

Combining those three elements, each SOP component can be traced back by its **three- piece code**. For example:



This code indicates that this SOP component is a questionnaire about the perfusion-modifier alcohol which should be used during the day of the scan session. Specifically, this component queries the intake of alcohol during the scan session day (modifier-specific aspect: acute intake).

All SOP components, including codes, perfusion modifiers and modifier-specific components are summarized in Table 5. The highest classification colour is given for each **SOP component**. For ease of use, we recommend to include the <u>complete</u> SOP component in your own study-based set of the SOP (especially for the questionnaires), although sometimes even questions regarding other modifier-specific aspects are included which might not be needed for your own study purposes. All SOP documents can be found in the Supplementary files of this manual. For several SOP components, a scoring form is required for evaluating the information, which can be find in the Supplementary files of this manual as well. Those scoring files are indicated with the identical code as the SOP component, supplemented with an asterisk.



Table 4 – Summary of the components in the standard operating procedure. For each component, the SOP category, subcategory, code, perfusion-modifier and modifier-specific aspect is given. The need for a scoring form is indicated with an asterisk in the code column.

Category	Subcategory	SOP component	CODE	Perfusion-modifier	Modifier-specific aspect
Questionnaires	General info	Personal details	Q.I.PER	Age/Gender/BMI/IQ	Age/Gender/BMI/Overweight/IQ
Questionnaires	General info	Family and social life	Q.I.SOC(*)	Social environment	Social environment
Questionnaires	General info	Education level	Q.I.EDU	Education level	Education level
Questionnaires	General info	Professional life	Q.I.JOB	Occupation/Solvens and inhalant	Occupation/Solvents and inhalants (chonic)
Questionnaires	General info	Hobbies	Q.I.HOB	Creativity/Social environment/cognitive capacity	Creativity/Social environment/cognitive capacity
Questionnaires	General info	Sports	Q.I.SPO	Physical exercise/training/Altitude/Diving	Physical training/Active lifestyle/ Climbers/Divers/Former divers
Questionnaires	General info	Handedness	Q.I.HAN	Handedness	Handedness
Questionnaires	General info	Personality	Q.I.PER	Personality	Extraversion/Introversion/ Personality traits
Questionnaires	General info	Caffeine consumption	Q.I.CAF*	Caffeine/Energy drinks	Caffeine (chronic)/Caffeine (abstinence)/Energy drinks
Questionnaires	General info	Nicotine consumption	Q.I.NIC*	Nicotine	Nicotine (chronic)/Former smoker
Questionnaires	General info	Alcohol consumption	Q.I.ALC*	Alcohol	Alcohol (chronic)/Alcohol (abstinence long-term)
Questionnaires	General info	Recreational drug consumption	Q.I.DRU	Cannabis/Cocaine/Amphetamines/ Recreational opioids/MDMA&LSD/ Mescaline/Psilocybin/ Solvents and Inhalants/Barbiturates	Chronic / Abstinence / Former user
Questionnaires	General info	Diet	Q.I.DIE	Nutritional diet	High nitrate diet/Fasting (Ramadan)
Questionnaires	General info	Health	Q.I.HEA	Pathology /Stress/Anxiety	Pathology/Stress/Anxiety (all)/Anxiety (low → moderate/moderate → high)
Questionnaires	General info	Medication use	Q.I.MED	Medication	Medication (chronic)/Medication (past)
Questionnaires	Day of scan	Mood	Q.II.MOO*	Mood/Drowsiness/Sleepiness/Arousal	Happy mood/Sad mood/Fear/ Disgust/Worry/Anger/ Other mood states/Drowsiness/



					Sleepiness/Arousal
Questionnaires	Day of scan	Extreme sports	Q.II.SPO	Altitude/Diving	Back after high altitude/ Back after diving
Questionnaires	Day of scan	Last caffeine consumption	Q.II.CAF	Caffeine / Energy drinks	Caffeine (acute)/Caffeine (abstinence)/ Energy drinks
Questionnaires	Day of scan	Last nicotine consumption	Q.II.NIC	Nicotine	Nicotine (acute)/Nicotine (abstinence 24h)/Acute NRT gum
Questionnaires	Day of scan	Last alcohol consumption	Q.II.ALC	Alcohol	Alcohol (acute)/Alcohol (abstinence 24h)
Questionnaires	Day of scan	Last recreational drug consumption	Q.II.DRU	Amphetamines/Cannabis/Recreational opioids/Cocaine/Solvents and Inhalants/ MDMA & LSD/Psilocybin/ Barbiturates/Mescaline	Acute/Abstinence
Questionnaires	Day of scan	Hunger and thirst	Q.II.HUN	Hunger/Satiety/Fat intake/Sugar intake/ Thirst	Satiety (after hunger)/Fat intake/ Sugar intake/Thirst/Satiation (after thirst)
Questionnaires	Day of scan	Health	Q.II.HEA	Menstrual cycle/Pregnancy/Menopause	Menstrual cycle/Pregnancy/ Menopause/
Questionnaires	Day of scan	Sleep	Q.II.SLE	Drowsiness/Sleepiness	Drowsiness/Sleepiness
Questionnaires	Day of scan	Medication use	Q.II.MED	Medication	Medication (Acute)/(Abstinence short- term)
Measurements	During scan	Perfusion scan information	M.I.INF	Diurnal rhythm	Diurnal rhythm
Measurements	During scan	Wakefullness	M.I.WAK	Sleep/Drowsiness/Sleepiness	Wake-sleep transition/NREM/REM/ Waking up/Awakened/ Drowsiness/Sleepiness
Measurements	During scan	Mood	M.I.MOO	Mood/Arousal	Happy mood/Sad mood/Arousal
Measurements	During scan	Physiological measurements	M.I.PHY	Blood gases: O <sub>2</sub> /Blood gases: CO <sub>2</sub> / Heart rate/Respiratory rate/ Anxiety/Stress/Arousal	Hypercapnia/Hypocapnia/Hyperoxia/ Hypoxia/Heart rate/Respiratory rate/Stress/Arousal
Measurements	After scan	Body temperature/Blood pressure	M.II.BTP	Body temperature/Blood pressure	Hyperthermia/Fever/Normal range BT/ Hypothermia/Normal range BP/ Hypertension/Hypotension



Measurements	After scan	Blood sample	M.II.BLO	Hematocrit/Blood viscosity/Hemoglobin/ Fibrinogen/Blood glucose/Homocysteine/ Cholesterol/Ketone bodies/ADMA/ Free fatty acids/Other	Hct/Blood viscosity/Hb/ Fibrinogen/Hypocaemia/ Hyperglycaemia/ Circulating homocysteine/Total cholesterol/LDL/HDL/ Acute hyperketonemia/ADMA/ Free fatty acids/Acute concentration alcohol,nicotine,caffeine
Neuropsychology	/	SCL90	N.SCL	Pathology	Psychological problems / Psychopathology
Neuropsychology	/	Stroop test	N.STR	Cognitive capacity	Executive functioning (interference)
Neuropsychology	/	RBANS	N.RBA	Cognitive capacity	Memory (Immediate)/ Visuospatial/ Constructional/ Fluid Ability/Attention/ Memory (Delayed)
Neuropsychology	/	National adult reading test	N.NAR	IQ	IQ (premorbid)
Instructions	Session	Time of day	I.I.TOM	Diurnal Rhythm	Diurnal Rhythm
Instructions	Session	Scanner surroundings	I.I.SUR	Open/closed eyes/Mental activity	Lights/Mental activity
Instructions	Patient before	Restrictions	I.II.RES	Alcohol use/Caffeine use/Nicotine use/ Amphetamines/Cannabis/Recreational opioids/Cocaine/Solvents and Inhalants/ MDMA & LSD/Psilocybin/Barbiturates/ Mescaline/Medication/Mobile phone/ Hunger/Satiety/Fat intake/ Sugar intake/Thirst/Physical exercise	Acute/Abstinence Medication (acute/abstinence)/ Mobile phone (after use – resting)/ Satiety (after hunger)/Fat intake/ Thirst/Satiation after thirst/ Sugar intake/Physical exercise (after)
Instructions	Patient during	Eyes	I.III.EYE	Open/closed eyes	Open eyes
Instructions	Patient during	Movement	I.III.MOV	Physical exercise/training	Physical exercise (during)
Instructions	Patient during	Resting state	I.III.RST	Mental activity	Mental activity
Instructions	Patient during	Wakefullness	I.III.WAK	Sleep/Drowsiness/Sleepiness	NREM/REM/sleep-wake transition/ waking up/awakened/ drowsiness/sleepiness



### 1. Questionnaires (Q)

The category *Questionnaires* can be subdivided into two subcategories:

- I. General information: this subcategory includes questions regarding the general lifestyle and personal information of the patient and can be completed during the days before the scan session at home. This part of the questionnaire should evidently be completed only once during a longitudinal study, but should be reevaluated when the study duration exceeds several months. Perfusion modifiers such as caffeine use, diet, job, sports, handedness and personality are included in this subcategory.
- II. **Day of scan**: this subcategory queries specific patient information regarding the day of the scan session and should be completed **immediately before or after** <u>each</u> perfusion scan session.

#### I. General information

#### a. Personal details

Q.I.PER

Questions	Modifier	MS aspect	Colour
Date of birth	Age	Age	
Gender	Gender	Gender	
Height/weight	BMI	BMI	0
Height/weight	BMI	Overweight	
MRI examination	Stress	Stress	0
Country of birth / mother tongue <sup>1</sup>	IQ/cognitive capacity <sup>1</sup>	IQ/cognition <sup>1</sup>	

<sup>&</sup>lt;sup>1</sup> Querying the mother tongue is required when including the perfusion modifiers IQ and cognition as this information is often required when using neuropsychological tests.



### b. Family and social life\*

Q.I.SOC

Questions	Modifier	MS aspect	Colour
Family	Social	Social	0
situation/children	environment	environment	
UCLA loneliness	Social	Social	0
scale v.3*	environment*	environment*	

SOP-component specific reference – UCLA loneliness scale version 3:

Russell, D. (1996). UCLA Loneliness Scale (Version 3): Reliability, validity, and factor structure. Journal of Personality Assessment, 66, 20-40.

SOP-component scoring form – UCLA loneliness scale version 3\*:

Supplementary files: Scoring - Q.I.SOC\*

#### c. Education level

Q.I.EDU

Questions	Modifier	MS aspect	Colour
Education level	Education level	Education level	
Education field	Education level	Education level	

The SOP-component is based on the *International Standard Classification of Education 2011* (Educational level) and the *ISCED fields of education and training 2013* (*ISCED-F 2013*) *manual* (Education field) developed by the United Nations Educational, Scientific and Cultural Organization (UNESCO). It is advised to use this standard classification system in order to properly and consequently interpret the results from this SOP component, especially when implemented in multi-centre studies. Each question is supplemented by general information about each education level and field. These information boxes can be adapted by the researcher based on their own national educational system in order to aid the patients with completing the questionnaire.



#### **SOP-component specific reference – International Standard Classification of Education:**

United Nations Educational, Scientific and Cultural Organisation, UNESCO Institute for Statistics. *International Standard Classification of Education ISCED 2011*. UIS/2012/INS/10/REV. (2012), available from http://www.uis.unesco.org/Education/Documents/isced-2011-en.pdf.

United Nations Educational, Scientific and Cultural Organisation, UNESCO Institute for Statistics. *ISCED fields of education and training 2013 (ISCED-F 2013): manual to accompany the International Standard Classification of Education 2011.* UIS/2014/INS/4 REV. (2014), available from http://unesdoc.unesco.org/images/0022/002280/228085e.pdf.

### d. Professional life

Q.I.JOB

Questions	Modifier	MS aspect	Colour
Profession	Occupation	Occupation (current/past)	
Volatile substances (professional contact)	Solvents and Inhalants	Solvents and Inhalant (chronic)	

#### e. Hobbies

Q.I.HOB

Questions	Modifier	MS aspect	Colour
Hobbies (social)	Social environment	Social environment	0
Hobbies (creative)	Creativity	Creativity	
Hobbies (mental)	Cognitive capacity	Cognitive capacity	



### f. Sports

Questions	Modifier	MS aspect	Colour
General sports routine (current and past)	Physical exercise/training	Active lifestyle	
Competition/top class sports	Physical exercise/training	Physical training	
Mountain sports	Altitude	Climbers	
Diving	Diving	Divers/ Former divers	

### g. Handedness\*

Q.I.SPO

Questions	Modifier	MS aspect	Colour
Edinburgh Handedness Inventory	Handedness	Handedness	

#### **SOP-component specific reference – Edinburgh Handedness Inventory:**

Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 1971;9(1):97-113.

#### SOP-component scoring form – Edinburgh Handedness Inventory\*:

Supplementary files: Scoring - Q.I.HAN\*



#### h. Personality\*

Questions	Modifier	MS aspect	Colour
The Big Five Inventory	Personality	Extraversion/Introversion	
The Big Five Inventory	Personality	Personality traits	

#### **SOP-component specific reference – Big Five Inventory:**

John OP, Donahue EM, Kentle RL. The Big Five Inventory--Versions 4a and 54. University of California, Berkeley, Institute of Personality and Social Research 1991.

John OP, Naumann LP, Soto CJ. Paradigm shift to the integrative Big Five trait taxonomy: History, measurement, and conceptual issues. In OP John, R W Robins, & L A Pervin (Eds), Handbook of personality: Theory and research (pp 114-158) New York, NY: Guilford Press 2008.

Benet-Martinez V, John OP. Los Cinco Grandes across cultures and ethnic groups: Multitrait multimethod analyses of the Big Five in Spanish and English. Journal of Personality and Social Psychology 1998;75:729-750.

#### **SOP-component scoring form – Big Five Inventory\*:**

Supplementary files: Scoring - Q.I.PER\*

### i. Caffeine consumption\*

Q.I.CAF

Questions	Modifier	MS aspect	Colour
Current caffeine consumption	Caffeine	Caffeine (chronic)	0
Changes in caffeine consumption	Caffeine	Caffeine (Abstinence)	
Consumption energy drinks	Energy drinks	Energy drinks	

#### **SOP-component scoring form – Caffeine consumption\*:**

Supplementary files: Scoring - Q.I.CAF\*



### *j. Nicotine consumption\**

Questions	Modifier	MS aspect	Colour
Series A/B	Nicotine	Nicotine (chronic)	
Series C	Nicotine	Former smoker	
Series D	Nicotine	Nicotine (chronic)	
Series D	Nicotine	Former smoker	

#### **SOP-component specific reference – Fagerström Test for Nicotine Dependence:**

Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerstrom Tolerance Questionnaire. British journal of addiction 1991;86(9):1119-1127.

#### **SOP-component scoring form – Nicotine consumption\*:**

Supplementary files: Scoring – Q.I.NIC\*

### k. Alcohol consumption\*

Q.I.ALC

Questions	Modifier	MS aspect	Colour
Series A/B	Alcohol	Alcohol (chronic)	
Series C	Alcohol	Alcohol (abstinence long- term)	

#### **SOP-component scoring form – Alcohol consumption\*:**

Supplementary files: Scoring – Q.I.ALC\*



### l. Recreational drug consumption

Questions	Modifier	MS aspect	Colour
Drug A	Cannabis	Cannabis (chronic)/ Cannabis (abstinence)	
Drug B	Cocaine	Cocaine (chronic)	
Drug B	Cocaine	Cocaine (former user 6 mo)/ Cocaine (abstinence/former user > 1yr)	
Drug C	Amphetamines	Amphetamines (chronic)	
Drug C	Amphetamines	Amphetamines (abstinence)	
Drug D	Recreational opioids	Recreational opioids (chronic)	
Drug D	Recreational opioids	Recreational opioids (abstinence)	
Drug E	MDMA & LSD	MDMA (chronic)	
Drug E	MDMA & LSD	MDMA (abstinence)	0
Drug F	Mescaline	Mescaline	
Drug G	MDMA & LSD	LSD	
Drug H	Psilocybin	Psilocybin (chronic)/ Psilocybin (abstinence)	
Drug I	Solvents and Inhalants	Solvents and Inhalants (chronic)	
Drug I	Solvents and Inhalants	Solvents and Inhalants (abstinence)	
Drug J	Barbiturates	Barbiturates	



### m.Diet

Questions	Modifier	MS aspect	Colour
Diet	Nutritional diet	High nitrate diet/ Fasting (Ramadan)	

n. Health Q.I.HEA

Questions	Modifier	MS aspect	Colour
Pathology	Pathology	/	
Claustrophobia	Stress	Stress	0
Claustrophobia	Anxiety	Anxiety (all)	
Claustrophobia	Anxiety	Anxiety (low → moderate/ moderate → high)	

### o. Medication use

Q.I.MED

Questions	Modifier	MS aspect	Colour
Medication	Medication	Medacatin (chronic)/ Medication (past)	

<sup>!!</sup> As this SOP component can be rather confusing, especially for older patients, it is advised for the researcher to ask the patient to bring their regular medication to the scan session.



### II. Day of scan

a. Mood

Q.II.MO

Questions	Modifier	MS aspect	Colour
PANAS-X	Mood	Happy mood/Sad mood	0
PANAS-X	Mood	Disgust/Worry/Anger	
PANAS-X	Drowsiness/Sleepiness	Drowsiness/Sleepiness	
PANAS-X	Mood	Other mood states	
How happy VAS	Mood	Happy mood	0
How sad VAS	Mood	Sad mood	0
How aroused VAS	Arousal	Arousal	0

#### **SOP-component specific reference – Positive and Negative Affect Schedule - Expanded:**

Watson D, Clark LA. The PANAS-X, Manual for the Positive and Negative Affect Schedule-Expanded form. Unpublished 1999;University of Iowa.

#### **SOP-component scoring form – Mood\*:**

Supplementary files: Scoring - Q.II.MOO\*

Q.II.CAF

### b. Extreme sports

Questions	Modifier	MS aspect	Colour
Climbing/Skiing	Altitude	Back after high altitude	
Diving	Diving	Back after diving	



### c. Last caffeine consumption

Questions	Modifier	MS aspect	Colour
Today	Caffeine	Caffeine (acute)	
Yesterday	Caffeine	Caffeine (abstinence)	
Yesterday/today	Energy drinks	Energy drinks	

### d. Last nicotine consumption

Q.II.NIC

Questions	Modifier	MS aspect	Colour
Today	Nicotine	Nicotine (acute)	
Yesterday	Nicotine	Nicotine (abstinence 24h)	
Yesterday/today	Nicotine	Acute NRT gum	

### e. Last alcohol consumption

Q.II.ALC

Questions	Modifier	MS aspect	Colour
Today	Alcohol	Alcohol (acute)	
Yesterday	Alcohol	Alcohol (abstinence 24h)	



### f. Last recreational drugs consumption

Questions	Modifier	MS aspect	Colour
Previous month	Amphetamines	Amphetamines (acute)	
Previous month	Amphetamines	Amphetamines (abstinence)	
Previous month	Cannabis	Cannabis (acute)	
Previous month	Cannabis	Cannabis (abstinence)	
Previous month	Recreational opioids	Recreational opioids (acute)/(abstinence)	
Previous month	Cocaine	Cocaine (acute)	
Previous month	Cocaine	Cocaine (abstinence)	
Previous month	MDMA & LSD	LSD	
Previous month	Solvents and Inhalants	Solvents and Inhalants (acute)	
Previous month	Solvents and Inhalants	Solvents and Inhalants (abstinence)	
Previous month	Psilocybin	Psilocybin (acute)	
Previous month	Psilocybin	Psilocybin (abstinence)	
Previous month	MDMA & LSD	MDMA (acute)	
Previous month	MDMA & LSD	MDMA (abstinence)	0
Previous month	Barbiturates	Barbiturates	
Previous month	Mescaline	Mescaline	



### g. Hunger and thirst

Questions	Modifier	MS aspect	Colour
Last meal	Sugar intake	Sugar intake	
Last meal	Fat intake	Fat intake	0
Heaviness meal	Hunger/Satiety	Satiety (after hunger)	
Snack	Sugar intake	Sugar intake	
Snack	Fat intake	Fat intake	0
Satisfaction meal	Hunger/Satiety	Satiety (after hunger)	
Thirst	Thirst	Thirst/Satiation (after thirst)	

h. Health

Q.II.HEA

Questions	Modifier	MS aspect	Colour
Menstrual cycle	Menstrual cycle	Menstrual cycle	0
Menstrual cycle	Pregnancy	Pregnancy	
Menstrual cycle	Menopause	Menopause	

i. Sleep

Q.II.HEA

Questions	Modifier	MS aspect	Colour
$AII^{1}$	Drowsiness/Sleepiness	Drowsiness/Sleepiness	

<sup>&</sup>lt;sup>1</sup>The answer provided by these questions indicates as well the susceptibility of the patient to fall asleep, which can influence cerebral perfusion significantly.



### j. Medication use

Questions	Modifier	MS aspect	Colour
Medication	Medication	Medication (acute)/Medication (abstinence short-term)	

<sup>!!</sup> As this SOP component can be rather confusing, especially for older patients, it is advised for the researcher to ask the patient to bring the medication used during the days before the appointment to the scan session.



#### 2. Measurements

The category *Measurements* can be subdivided into two subcategories:

- I. **During the scan session**: several parameters concerning the scan session (sequence and timing) and the patient (wakefulness, mood and physiological parameters) should be recorded during the scan session, immediately after the perfusion scan. The information concerning those parameters are combined in only one file; the researcher can decide which SOP parameter should be taken into account for the study.
- II. After the scan session: before or after the scan session, blood pressure and body temperature should be measured and a blood sample should be taken. The information concerning those parameters are combined in only one file; the researcher can decide which SOP parameter should be taken into account for the study.

### I. During the scan session

### a. Perfusion scan information

M.I.INF

Measurement	Modifier	MS aspect	Colour
ASL sequence	Technical variability		
Time of scan	Diurnal rhythm	Diurnal rhythm	



### b. Wakefullness

Measurement	Modifier	MS aspect	Colour
Wakefulness level	Sleep	NREM	
Wakefulness level	Sleep	REM	
Wakefulness level	Sleep	Wake-sleep transition/waking up/awakened	
Wakefulness level	Drowsiness/sleepiness	Drowsiness/Sleepiness	
Wakefulness level	Stress	Stress	0

A wakefulness score should be asked immediately before and after the perfusion scan for several reasons. First of all, this score can indicate the level of tiredness and stress of the patient, as well as the evolution hereof throughout the perfusion scan. Secondly, asking this question might wake the patients who might be dozing off during long scan sessions.

c. Mood M.I.MOO

Measurement	Modifier	MS aspect	Colour
How happy VAS	Mood	Happy mood	0
How sad VAS	Mood	Sad mood	0
How aroused VAS	Arousal	Arousal	0

Querying the mood-state immediately after the perfusion scan can be accomplished by utilising a visual analogue scale on a screen in the MRI-scanner, which is often used for functional MRI. MRI-compatible, fiber-optic response devices, such as a track ball, can be used to allow the patient to answer those questions.

Alternatively, in settings where such materials are not available, the researcher can verbally ask the score for each question immediately after the perfusion scan or present the patient with these visual analogue scales immediately after the scan session by reusing the VAS of SOP component Q.II.MOO.



### d. Physiological measurements

Measurement	Modifier	MS aspect	Colour
End-tidal CO2	Blood gases: CO <sub>2</sub>	Hypercapnia / Hypocapnia	
Oxygen saturation	Blood gases: O <sub>2</sub>	Hyperoxia / (Hypoxia)	
Heart rate	Heart rate	Heart rate	
Respiratory rate	Respiratory rate	Respiratory rate	
Skin conductance	Stress	Stress	0
Skin conductance	Arousal	Arousal	0

Measuring physiological parameters can obviously only be achieved by utilizing MRI-compatible monitoring (and recording) equipment. Multiple monitoring equipment packages are available on the market. In first instance, these parameters can be monitored to guarantee the normality of the values during the perfusion scan to exclude modifying effects on cerebral perfusion. When required, recording the physiological data during the perfusion scan may enable the use of this data as a regressor in more advanced perfusion data analyses.



### II. After the scan session

### a. Body temperature and blood pressure

M.II.BTP

Measurement	Modifier	MS aspect	Colour
Body temperature	Body temperature	Hyperthermia	
Body temperature	Body temperature	Fever	
Body temperature	Body temperature	Normal range	
Body temperature	Body temperature	Hypothermia	
Blood pressure	Blood pressure	Normal range	0
Blood pressure	Blood pressure	Hypertension	
Blood pressure	Blood pressure	Hypotension	

## b. Blood and urine sample

M.II.BTP

Measurement	Modifier	MS aspect	Colour
Hematocrit	Hematocrit	Hematocrit	
Blood viscosity	Blood viscosity	Blood viscosity	
Hemoglobin	Hemoglobin	Hemoglobin	
Fibrinogen	Fibrinogen	Fibrinogen	
Blood glucose	Blood glucose	Hypoglycaemia	0
Blood glucose	Blood glucose	Hypoglycaemia	
Circulating homocysteine	Homocysteine	Circulating homocysteine	
Cholesterol	Cholesterol	Total/LDL/HDL	
Ketone bodies (U)	Ketone bodies	Acute hyperketonemia	



ADMA	ADMA	ADMA	0
Free fatty acids	Free fatty acids	Free fatty acids	
Other	Alcohol/Nicotine/Caffeine	Acute concentration	

Obviously the research can select which blood and urine sample parameters might be interesting for the study. The majority of the parameters (except for haematocrit) will not modify brain perfusion between normal ranges, which means that collecting a blood sample in a healthy population might be unnecessary. In elderly or patients, including some of those parameters might be useful.

The SOP component M.II.BLO consists of a table which is adaptable by the researcher depending on the tests conducted. For each measure, the unit and reference values are included, however those values are based on the values used in the laboratory of the first author of this SOP. It is advised that the researcher using this SOP adapts the reference values to those used in their own lab.

Moreover, additional parameters can be measured in the blood and urine sample, such as the concentration of alcohol, nicotine, cotinine and caffeine, indicating the acute consumption of those products. However, the correlation between those concentration and cerebral perfusion are still rather inconsistent.<sup>2-6</sup> Asking the subject about their last consumption (Q.II.CAF; Q.II.NIC; Q.II.ALC) might be more effective and cost-efficient.

In any case, it is advised to take haematocrit into account as the effects of this parameter can modify cerebral perfusion significantly (effect size category 1: >24%), even within normal ranges. This can be achieved either by collecting a blood sample, or by acquiring a blood T1 scan during the scan session which is likely to vary with haematocrit.<sup>7</sup>



### 3. Neuropsychology

The effects of neuropsychological aspects on cerebral perfusion is still limited and inconsistent. Additionally, the lack of standardized neuropsychological testing and the difficulty to test all domains of cognition complicates the inclusion of this aspect in the SOP. A consensus is needed on the choice of neuropsychological tests in order to define a specific physiotype. For instance, in the United States of America (USA), the National Institute of Health (NIH) toolbox sets an example of how neuropsychology can be standardized. Unfortunately, this framework is only validated in the USA for native English and Spanish speakers, despite ongoing efforts to translate this into other languages and cultures, including those of the European countries.

In order to test the most important major neuropsychological domains, it is recommended to choose a battery of neuropsychological tests assessing general cognition, memory, language, attention, verbal fluency, processing speed, executive function and visuospatial skills. In this SOP manual, several tests are suggested which cover the majority of those aspects. All tests included in this SOP are commercially available; country-specific scoring and norm values should be explored by the researcher.

Here we also recommend to rule out major psychiatric disorders.

#### a. Symptom Checklist-90-Revised (SCL90)

N.SCL

Neuropsychological test	Modifier	MS aspect	Colour
SCL-90	Pathology	Psychological problems / Psychopathology	

### b. Stroop Test



Neuropsychological test	Modifier	MS aspect	Colour
Stroop test	Cognitive capacity	Executive functioning (interference)	



# c. RBANS (Repeatable Battery for the Assessment of Neuropsychological Status) N.RBA

Neuropsychological test	Modifier	MS aspect	Colour
List Learning / Story Memory	Cognitive capacity	Memory (Immediate)	
Figure Copy / Line Orientation	Cognitive capacity	Visuospatial / Constructional	
Picture Naming / Semantic Fluency	Cognitive capacity	Fluid Ability	
Digit Span / Coding	Cognitive capacity	Attention	
List Recall / List Recognition / Story Memory / Figure Recall	Cognitive capacity	Memory (Delayed)	

#### d. National Adult Reading Test

N.NAR

Neuropsychological test	Modifier	MS aspect	Colour
National Adult Reading Test	IQ	IQ (Premorbid)	



#### 4. Instructions

The category *Instructions* can be subdivided into three subcategories:

- I. **Session instructions**: this subcategory includes practical instructions about the scan session which the researcher should take into account when scanning cerebral perfusion.
- **II. Patient instructions before scan session:** some 'do's and don'ts' should be instructed by the researcher to the patient a couple of days before the scan session.
- **III. Patient instructions during scan session:** at the start of the perfusion measurement, the researcher is advised to instruct the patient in an uniform manner, taking several perfusion modifiers into account.

Each SOP component file of this category includes **general advice** and a **checklist** to record if the instruction has been given. The column 'addition information' can be used to record irregularities or session- and patient-specific information. As an example: the researcher advised the subject not to perform heavy sports immediately before the scanning session. At arrival, the researcher notices that the patient is sweaty and panting due to the bike ride to the scanning facility. This information can be written down in the column 'additional information'.

#### I. Session instructions

#### a. Time of day

I.I.TOM

Instruction	Modifier	MS aspect	Colour
Time of day	Diurnal rhythm	Diurnal rhythm	

#### b. Scanner surroundings

I.I.SUR

Instruction	Modifier	MS aspect	Colour
Light out	Open/closed eyes	Lights	
Video/music	Mental activity	Mental acitivity	



#### II. Patient instructions before scan session

#### a. Restrictions

I.II.RES

Instruction	Modifier	MS aspect	Colour
Alcohol	Alcohol	Alcohol (acute/abstinence 24h)	
Recreational drugs	Amphetamines/Cannabis/ Recreational opioids/ Cocaine/MDMA&LSD/ Solvents & Inhalants/ Psilocybin/ Barbiturates/Mescaline	Acute / Abstinence	
Medication	Medication	Medication (acute/abstinence)	
Mobile phone	Mobile phone	Mobile phone (after use – resting)	
Foods and drinks	Hunger/Satiety/Thirst	Satiety (after hunger)/ Thirst/Satiation after thirst	
Foods and drinks	Fat intake/Sugar intake	Fat intake/Sugar intake	0
Physical activity	Physical exercise/training	Physical exercise (after)	



#### III. Patient instructions during scan session

a. Eyes

I.III.EYE

Instruction	Modifier	MS aspect	Colour
Eyes	Open/closed eyes	Open eyes	

b. Movement

I.III.MOV

Instruction	Modifier	MS aspect	Colour
Movement	Physical exercise/training	Physical exercise (during)	

#### c. Resting state

I.III.RST

Instruction	Modifier	MS aspect	Colour
Resting state	Mental activity	Mental activity	
Resting state	Yoga/Meditation	Meditation	

#### d. Wakefullness

I.III.WAK

Instruction	Modifier	MS aspect	Colour
Sleep	Sleep	NREM	
Sleep	Sleep	REM	
Sleep	Sleep	Wake-sleep transition/waking up/awakened	
Sleep	Drowsiness/Sleepiness	Drowsiness/Sleepiness	



### Acknowledgments and contact info

#### 1. Acknowledgements

The development of this standard operating procedure for perfusion measurements has been supported and funded by the European Cooperation in Science and Technology—Arterial spin labelling Initiative in Dementia (COST—AID Action BM1103).



#### 2. Conflicts of interest

The authors of this SOP and manual have no conflicts of interest to declare.

#### 3. Contact information

For more information on the use of the standard operating procedure, please contact the developing researcher:

#### **Patricia Clement**

Ghent University – Dep. Of Radiology and Nuclear Medicine

De Pintelaan 185, K12

9000 Ghent

**BELGIUM** 

patricia.clement@ugent.be







### References

- 1. Henriksen OM, Larsson HBW, Hansen AE, Gruner JM, Law I, Rostrup E. Estimation of intersubject variability of cerebral blood flow measurements using MRI and positron emission tomography. *J. Magn. Reson. Imaging* 2012; 35(6): 1290-1299.
- 2. Cameron OG, Modell JG, Hariharan M. Caffeine and human cerebral blood-flow a positron emission tomography study. *Life Sci.* 1990; 47(13): 1141-1146.
- 3. Domino EF, Minoshima S, Guthrie S, Ohl L, Ni LS, Koeppe RA *et al.* Nicotine effects on regional cerebral blood flow in awake, resting tobacco smokers. *Synapse* 2000; 38(3): 313-321.
- 4. Schwartz JA, Speed NM, Gross MD, Lucey MR, Bazakis AM, Hariharan M *et al.* Acute effects of alcohol administration on regional cerebral blood flow: the role of acetate. *Alcoholism, clinical and experimental research* 1993; 17(6): 1119-23.
- 5. Shinohara T, Nagata K, Yokoyama E, Sato M, Matsuoka S, Kanno I *et al.* Acute effects of cigarette smoking on global cerebral blood flow in overnight abstinent tobacco smokers. *Nicotine Tob. Res.* 2006; 8(1): 113-121.
- 6. Zubieta JK, Lombardi U, Minoshima S, Guthrie S, Ni LS, Ohl LE *et al.* Regional cerebral blood flow effects of nicotine in overnight abstinent smokers. *Biol. Psychiatry* 2001; 49(11): 906-913.
- 7. Lu H, Clingman C, Golay X, van Zijl PC. Determining the longitudinal relaxation time (T1) of blood at 3.0 Tesla. *Magnetic resonance in medicine* 2004; 52(3): 679-82.
- 8. Denboer JW, Nicholls C, Corte C, Chestnut K. National Institutes of Health Toolbox Cognition Battery. *Arch. Clin. Neuropsychol.* 2014; 29(7): 692-694.



### Supplementary files: SOP documents



# "Study title"

#### Goal

You are taking part in a study where "short description of study objective (3 lines)".

In this part of the questionnaire, personal details will be queried (e.g. gender, weight, education, etc.) as well as your daily habits (e.g. alcohol, smoking, coffee, etc.). If you have any questions or something is not clear, please do not hesitate to ask the researcher about it on the day of your examination. This part of the questionnaire contains "number" questions.

#### **Privacy**

We assure you that the information obtained in this questionnaire is encoded (using a subject ID), just like the radiological images obtained during this study. This means that the information you provide cannot be used to identify you.

Subject ID: #######

Date of MRI scan: .../.../......



Subject ID	

### Q.I.PER - Personal details

Date of birth:	/	/			
Gender:	□ Male	□ Fei	male		
Height:			cm		
Weight:			kg		
Have you ever had an	MRI examin	ation?	□Yes	□ No	
In which country were	you born?				
In which country was	your mother	born?			
In which country was	your father b	orn?			
Is English your mother	tongue?		□Yes	□No	
If the answer to the pr	evious quest	ion is "ı	<u>10":</u>		
When did you start sp	eaking Engli	sh (year	)?		
In what situations do y	ou speak Er	nglish?			
□ Work		□ Far	mily/Private		□ Both



Subject ID	

Subject 1D					(	)
Q.I.SO	C - Fami	ly and social lif	e		•	
What is your	current famil	y situation?				
□ Single		☐ Cohabiting	□M	arried		
□ Divorced		☐ Widow/Widower				
How many c	hildren do you	have?				
Some staten descriptive o		For each statement, please	indicate	how ofte	en the stater	nent is
			Never	Rarely	Sometimes	Often
How often of the people a		nat you are "in tune" with				
How often d	o you feel tha	t you lack companionship?				
How often of turn to?	do you feel th	at there is no one you can				
How often d	o you feel alo	ne?				
How often d	o you feel pai	t of a group of friends?				
	do you feel th the people	that you have a lot in around you?				
How often of to anyone?	do you feel th	at you are no longer close				
	lo you feel th ed by those a	at your interests and ideas ound you?				
How often d	o you feel out	going and friendly?				
How often d	o you feel clo	se to people?				
How often d	o you feel left	out?				



	Never	Rarely	Sometimes	Often	
How often do you feel that your relationships with others are not meaningful?					
How often do you feel that no one really knows you well?					
How often do you feel isolated from others?					
How often do you fee1 you can find companionship when you want it?					
How often do you feel that there are people who really understand you?					
How often do you feel shy?					
How often do you feel that people are around you but not with you?					
How often do you feel that there are people you can talk to?					
How often do you feel that there are people you can turn to?					



Subject ID	



#### Q.I.EDU - Education level

What is your highest level of education? Check the box below for more information about the different levels of education. If your degree is not listed here, please specify under "Other".

Early childhood education – early childhood educational development
Early childhood education – Pre-primary education
Primary education
Lower secondary education
Higher secondary education
Post-secondary non-tertiary education
Short-cycle tertiary education
Bachelor or equivalent
Master or equivalent
Doctoral or equivalent
Other:

- **Early childhood education early childhood educational development**: Education designed to support early development in preparation for participation in school and society. Programmes designed for children below the age of 3.
- **Early childhood education pre-primary education:** Education designed to support early development in preparation for participation in school and society. Programmes designed for children from age 3 to the start of primary education
- **Primary education**: Programmes typically designed to provide students with fundamental skills in reading, writing and mathematics and to establish a solid foundation for learning.
- Lower secondary education: First stage of secondary education building on primary education, typically with a more subjectoriented curriculum
- **Upper secondary education:** Second/final stage of secondary education preparing for tertiary education and/or providing skills relevant to employment. Usually with an increased range of subject options and streams.
- **Post-secondary non-tertiary education:** Programmes providing learning experiences that build on secondary education and prepare for labour market entry and/or tertiary education. The content is broader than secondary but not as complex as tertiary education.
- Short-cycle tertiary education: Short first tertiary programmes that are typically practically-based, occupationally-specific and prepare for labour market entry. These programmes may also provide a pathway to other tertiary programmes.
- Bachelor or equivalent: Programmes designed to provide intermediate academic and/or professional knowledge, skills and competencies leading to a first tertiary degree or equivalent qualification.
- Master or equivalent: Programmes designed to provide advanced academic and/or professional knowledge, skills and competencies leading to a second tertiary degree or equivalent qualification.
- **Doctorate or equivalent:** Programmes designed primarily to lead to an advanced research qualification, usually concluding with the submission and defence of a substantive dissertation of publishable quality based on original research.



What field is your education primarily classified in? For this question, check the box below for more information.

☐ Generic programmes and qualifications
□ Education
☐ Arts and humanities
☐ Social sciences, journalism and information
☐ Business, administration and law
□ Natural sciences, mathematics and statistics
□ Information and Communication Technologies
☐ Engineering, manufacturing and construction
☐ Agriculture, forestry, fisheries and veterinary
☐ Health and welfare
□ Services

- Generic programmes and qualifications:
  - Basic programmes and qualifications
  - Literacy and numeracy
  - Personal skills and development
- Education:
- Arts and humanities:
  - Arts
  - Humanities
  - Languages
- Social sciences, journalism and information
  - o Social and behavioural sciences
  - Journalism and information
- Business, administration and law
- Natural sciences, mathematics and statistics
  - Biological and related sciences
  - Environment
  - Physical sciences
  - Mathematics and statistics

- Information and Communication Technologies
- Engineering, manufacturing and construction
  - Engineering and engineering trades
  - Manufacturing and processing
  - Architecture and construction
- Agriculture, forestry, fisheries and veterinary
- Health and welfare
- Services
  - Personal services
  - Hygiene and occupational health services
  - Security services
  - Transport services



Subject ID	
-	

		CURD PEAR COUPEAGLION IN SCIENCE AND
Subject ID		
Q.I.JOB - Profe	essional life	
Are you currently engaged	l in a profession? This per	tains to your principal occupation.
□ Yes		→ Proceed to series B
□ No, I'm retired		→ Proceed to series A
□ No, I'm a studer	nt	→ Proceed to series A
☐ No, I'm unemplo	oyed	→ Proceed to series A
□ No, I'm a house	wife/house husband	→ Proceed to series A
□ No, I'm disabled		→ Proceed to series A
Series A		
Were you previously engage	ged in a profession? Stud	ent jobs will not be considered.
□ Yes		→ Proceed to the next question
□ No		→ Proceed to the next questionnaire
You were engaged in this p	orofession until when? Ple	ease provide the month and year.
Until		→ Proceed to series B



#### Series B:

your life.		
Is/was your prof	ession consistent with your	highest level of education?
	Yes	□ No
•	art in this profession? Pleaso	e provide the month and year.
The profession y	ou engage/engaged in, falls	under which category?
	Senior executives, branch r	managers, managers
	Specialists in scientific prof	essions
	Intermediate staff and tech	nnicians in scientific professions
	Administrative clerks	
	Services and sales staff	
	Farmers and skilled worker	rs in agriculture and fisheries
	Skilled worker	
	Factory workers, installation	ons, machines and assembly operators
	Unqualified workers and cl	erks
	Military forces	
	-	ou have worked under multiple statuses in this ou have worked the longest.
	Worker	
	Employee	
	Public servant	
	Self-employed / Independe	ent profession

For these series, please focus on the profession you exerted throughout the longest part of



	k/worked on, choose		-		-				ple syst	ems in this
		Day work	<							
		Night wo	rk							
		Shift wor	·k							
		Weekend	d work							
profession of the profession o	on, choose	e the sys Full-time Part-time 30% Other:	e (50%)	der whic	h you ha	ave worl	ked the	longest.	ple syst	ems in this
0	1	2	3	4	5	6	7	8	9	10
	extent are	e/were y	ou phys	sically or	manual	lly challe	_	this pro		
0	1	2	3	4	5	6	7	8	9	10
	extent are			•	_		ofession	1?		
0	1	2	3	4	5	6	7	8	9	10



etc. for professional reasons?	ct with volatile substances such as paint, gasoline, glue
□ Yes	→ Proceed to the next question
□ No	ightarrow Proceed to the next questionnaire
In what year did you first come into r	regular contact with these substances?
In what year did this stop?	



Subject ID	
,	



What are your regular hobbies? You can tick more than one option.

	Sports
	Creative hobbies (e.g. art, woodwork, jewellery, clothing, etc.)
	Dramatic hobbies (e.g. music, drama, magic, etc.)
	Collecting (e.g. stamps, coins, etc.)
	Manual hobbies (e.g. gardening, do-it-yourself, models, building, etc.)
	Social hobbies (e.g. youth group, sports club, seniors club, etc.)
	Thinking hobbies (e.g. cards, crosswords, chess, etc.)
	Reading
	Cooking and baking
	I don't have any hobbies

How much time do you spend on a particular hobby in a typical week? How long have you practiced this hobby? Answer this question for each hobby you listed in the first question.

Hobby	Time (hours/wk)	Number of years	Hobby	Time (hours/wk)	Number of years
Sports			Social		
Creative			Thinking		
Dramatic			Reading		
Collecting			Cooking and baking		
Manual					



Subject ID	
0 0.10 0 0 0 1	

Q.I.SPO – Sports		
On average, how often do you exercise each week?	?	times a week
On average, for how long do you exercise in each s	ession?	minutes
Do you also compete in sports competitions?	□ Yes	□No
Do you participate in top-class sports?	□ Yes	□No
How long have you trained using this exercise rout	ine? mo	onthyear
Are you a frequent climber/do you frequently rese	nt at high altitudes?	□ Yes □ No
Are you a frequent diver?		□ Yes □ No
Has your routine changed <i>significantly</i> compared t	to the past?	
Note: "much more" and "much less" means a <b>sign</b> example, completely stopping although it used to be a fluctuations in frequency or duration, thus, it does not as one extra sports session in the week.	a regular habit. This do	es not include weekly
Please complete: "I currently exerc the past"	cise than in	
☐ Much less	$\rightarrow$ Proceed to the nex	t question
□ Less	ightarrow Proceed to the nex	t questionnaire
☐ The same	$\rightarrow$ Proceed to the nex	t questionnaire
□ More	$\rightarrow$ Proceed to the next	t questionnaire
□ Much more	$\rightarrow$ Proceed to the nex	t question
In the previous question, you indicated that your e or "much less" compared to the past.	xercise routine has ch	nanged "much more"
On average, how often did you exercise each week	?	times a week
On average, for how long did you exercise each tim	ne?	minutes
Did you also compete in sports competitions?	□ Yes	□No
Did you participate in top-class sports?	□ Yes	□No
How long had you trained using your previous spor	ts routine?n	nonthyear



Subject ID	

#### Q.I.HAN - Handedness



Indicate your handedness by selecting the correct answer for the following activities. Only choose the "Always left" or "Always right" option if your preference is so strong that you would never use the other hand, unless absolutely forced to. For some activities, you need to use both hands. In these cases, we ask you to indicate your handedness for the object or activity in parentheses. Try to answer all of the questions and only leave one unselected if you've no experience with the task.

	Always right	Mostly right	No preference	Mostly left	Always left
Writing					
Drawing					
Throwing					
Scissors					
Toothbrush					
Knife (without fork)					
Spoon					
Broom (upper hand)					
Striking a match (match)					
Opening a box (lid)					
Which foot do you prefer to kick with?					
If you use only one eye, which one?					



#### **Q.I.PER - Personality**



Here are a number of characteristics that may or may not apply to you. For example, do you agree that you are someone who *likes to spend time with others*? Please indicate the extent to which you agree or disagree with that statement.

"I see myself as someone who..."

	Disagree strongly	Disagree a little	Neither agree, neither disagree	Agree a little	Agree strongly
Is talkative					
Tends to find fault with others					
Does a thorough job					
Is depressed, blue					
Is original, comes up with new ideas					
Is reserved					
Is helpful and unselfish with others					
Can be somewhat careless					
Is relaxed, handles stress well					
Is curious about many different things					
Is full of energy					
Starts quarrels with others					
Is a reliable worker					



	Disagree strongly	Disagree a little	Neither agree, neither disagree	Agree a little	Agree strongly
Can be tense					
Is ingenious, a deep thinker					
Generates a lot of enthusiasm					
Has a forgiving nature					
Tends to be disorganized					
Worries a lot					
Has an active imagination					
Tends to be quiet					
Is generally trusting					
Tends to be lazy					
Is emotionally stable, not easily upset					
Is inventive					
Has an assertive personality					
Can be cold and aloof					
Perseveres until the task is finished					
Can be moody					
Values artistic, aesthetic experiences					
Is sometimes shy, inhibited					



	Disagree strongly	Disagree a little	Neither agree, neither disagree	Agree a little	Agree strongly
Is considerate and kind to almost everyone					
Does things efficiently					
Remains calm in tense situations					
Prefers work that is routine					
Is outgoing, sociable					
Is sometimes rude to others					
Makes plans and follows through with them					
Gets nervous easily					
Likes to reflect, play with ideas					
Has few artistic interests					
Likes to cooperate with others					
Is easily distracted					
Is sophisticated in art, music, or literature					





### Q.I.CAF – Caffeine consumption

#### **CURRENT CAFFEINE CONSUMPTION**

On average, how much of these caffeinated products do you consume in a single day?

*Note: these drinks do not count:* 

- Caffeine-free coffee
- Caffeine-free tea
- Caffeine-free soft drink
- Herbal tea/ infusion: e.g. rose hip, chamomile, mint, nettle, rooibos, fruits, etc.

	>	
		coffee: ground coffee, latte, mocha latte, cappuccino
	<u></u>	espresso or instant coffee
	Ò	tea: green tea, black tea, white tea, Ice Tea
	<u>\``</u>	Coca cola, Pepsi cola (including light and zero variants)
		energy drink: e.g. Red Bull, Nalu, Golden Power, Monster, Burn.
11	!! In the	case of 500 ml cans (such as Burn and Monster),
		please double the amount.
		chocolate <i>(approx. 50 g, milk and black chocolate)</i> and



#### **CHANGES IN CAFFEINE CONSUMPTION**

Has this habit changed *significantly* in the last three months?

Note: "much more" and "much less" means a **significant** change in the habit of consuming caffeinated products, for example, completely stopping although it used to be a regular habit. Daily fluctuations (e.g. one more or one less cup of coffee or a piece of chocolate) are not included here.

Please complete: "I currently of caffeinated products than	
☐ Much less	→ Proceed to the next question
Less	→ Proceed to the next questionnaire
☐ The same	→ Proceed to the next questionnaire
□ More	ightarrow Proceed to the next questionnaire
☐ Much more	ightarrow Proceed to the next question
 more" compared to the past. How I	caffeine consumption has changed "much ong ago did this significant change in your
 weeks days	



On average, how many of these caffeinated products did you consume in one day **before this significant change**?

Note: these drinks do not count:

- Caffeine-free coffee
- Caffeine-free tea
- Caffeine-free soft drink
- Herbal tea/infusion: e.g. rose hip, chamomile, mint, nettle, rooibos, fruits, etc.

	coffee: ground coffee, latte, mocha latte, cappuccino
	espresso or instant coffee
	tea: green tea, black tea, white tea, Ice Tea
<u>\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\</u>	Coca cola, Pepsi cola (including light and zero variants)
	energy drink: e.g. Red Bull, Nalu, Golden Power, Monster, Burn.
!!! In the	e case of 500 ml cans (such as Burn and Monster),
	please double the amount.
	chocolate (approx. 50 g, milk and black chocolate) and
(	chocolate milk



Subject ID	
Subject 1D	

#### **Q.I.NIC – Nicotine consumption**



Do you smoke or use nicotine products; or have you ever smoked or used these nicotine products?

Note: nicotine products include nicotine patches, gum, inhaler, nose spray, mouth spray, lozenges and prescription buproprion hydrochloride.

☐ No, I have never smoked or used nicotine products	
$\rightarrow$	Proceed to the next questionnaire
☐ Yes, I smoke or use nicotine products	→ Proceed to series A
☐ Yes, I have smoked or used nicotine product	→ Proceed to series C

#### Series A

In the previous question, you indicated that you currently smoke or use nicotine products.

This part asks about your *current* smoking habit.

Currently, how often do you smoke or use nicotine products?

☐ Monthly or less	→ Proceed to series B
□ 2-4x /month	ightarrow Proceed to the next question
□ 2-3x /week	ightarrow Proceed to the next question
☐ More than 4x /week	ightarrow Proceed to the next question
□ Daily	→ Proceed to the next question



How much nicotine products do you usually smoke or use in one day? For each product you use, enter the amount per day and, if applicable, tick the dosage amount.

cigarettes					
e-cigarette cart	e-cigarette cartridges, dose:				
○ 0 mg (0%)	○ 24 mg (2.4%)				
○ 6 mg (0.6%)	○ 36 mg (3.6%)				
○ 12 mg (1.2%)	○ 48 mg (4.8%)				
○ 18 mg (1.8%)					
cigars					
full pipes					
nicotine patch,	dose:				
○ 5-7 mg	○ 25-35 mg				
○ 10-14 mg	○ 42 mg				
○ 15-21 mg					
nicotine gum, c	lose:				
○ 2 mg					
○ 4 mg					
nicotine inhale	r cartridges				
 sprays of nicoti	ne nose spray				
sprays of nicoti	ne mouth spray				
nicotine lozeng	es, dose:				
○ 1 mg	○ 2 mg				
○ 1.5 mg	O 4 mg				

→ Proceed to the next question



How soon	after waking do yo	ou smoke or us	e your first nicotine pr	oduct?
	Within 5 minutes			
	5 – 30 minutes			
	More than 30 min	utes		
•	•		co smoke or not use r ch or a library where si	nicotine products in places moking is prohibited.
	Yes	□ No		
Which nic	otine product wou	ld be most diffi	cult for you to give up	?
	The first at the sta	rt of the day, ir	the morning	
	Another one durin	g the day		
Do you sn	noke or use nicotin	e products mor	re frequently in the mo	orning?
	Yes	□ No		
Do you sn	noke or use nicotin	e products eve	n when you spend mos	st of the day sick in bed?
	Yes	□ No		
				→ Proceed to series B
Carios D				
Series B				
How long	have you had this l	nabit of smokin	ng or using nicotine pro	oducts?
	years		months	→ Proceed to series D
Series C				
-	vious question, yo but you have done		-	t smoke or use nicotine
How long	has it been since y	ou stopped sm	oking or used nicotine	products?
	years		months	→ Proceed to series D



#### **Series D**

In the first question, you indicated that you currently smoke or use nicotine products or have previously smoked or used nicotine products. This part asks about your habit of smoking and using these substances *throughout your entire life*.

In total, how ma	any years have you smoked or used	nicotine products? years			
At what age did	you start smoking or using nicotine	e products? years			
On average thro	oughout your life, how often do you	smoke or use nicotine products?			
	☐ Monthly or less	→ Proceed to the next questionnaire			
	2-4x /month	ightarrow Proceed to the next question			
	2-3x /week	ightarrow Proceed to the next question			
	☐ More than 4x/week	→ Proceed to the next question			
	Daily	ightarrow Proceed to the next question			
	•	do you usually smoke or use in one day? r day and, if applicable, tick the dosage			
	cigarettes				
<u> </u>	e-cigarette cartridges, dose	::			
	○ 0 mg (0%)	O 24 mg (2.4%)			
	○ 6 mg (0.6%)	○ 36 mg (3.6%)			
	○ 12 mg (1.2%)	○ 48 mg (4.8%)			
	○ 18 mg (1.8%)				
	cigars				
	full pipes				



nicotine patch, dose:		
○ 5-7 mg	○ 25-35 mg	
○ 10-14 mg	○ 42 mg	
○ 15-21 mg		
nicotine gum, dose	:	
○ 2 mg		
○ 4 mg		
nicotine inhaler car	tridges	
sprays of nicotine r	ose spray	
sprays of nicotine r	nouth spray	
nicotine lozenges,	dose:	
○ 1 mg	○ 2 mg	
○ 1.5 mg	○ 4 mg	



Subject ID	
Judject 1D	

### Q.I.ALC - Alcohol consumption

#### **Series A**

ln	this	section,	your	current	alcohol	consumption	is	queried.
----	------	----------	------	---------	---------	-------------	----	----------

Currently,	, how often	do you drinl	k alcoholic drinks?
------------	-------------	--------------	---------------------

□ Never	→ Proceed to series B
☐ Monthly or less	→ Proceed to series B
□ 2-4/month	ightarrow Proceed to the next question
□ 2-3/week	→ Proceed to the next question
☐ More than 4/week	→ Proceed to the next question

On days when you drink alcohol **currently**, what is the average number of glasses of alcohol that you drink **on that day**?

glasses:

□ Daily

- Beer (normal beers)
- Wine
- Port/sherry
- Liqueur
- Aperitifs (Passoa, Kir, etc.)
- Cognac
- Spirits/shots
- Jenever

cocktails:

- Mojito
- Margarita
- Gin and tonic
- Cosmopolitan
- Vodka Redbull
- ...

glasses of local beer:

- St. Bernardus
- Duvel
- Leffe
- West Vleteren





→ Proceed to the next question







→ Proceed to the next question



How often have you (as a woman) drunk six or more units or (as a man) eight or more units on a single occasion in the past year?

	Note:	1 unit =		<b>E</b>				
		1.5 units =	YY	38				
		2.5 units = 1	Local beers					
	□ Nev	or						
		than mont	hly					
	□ Monthly							
	□ Weekly							
	□ Dail	y or almost	daily					
						$\rightarrow$	Proceed to	series B
Series B								
How long have you had this alcohol habit? months year						year		
						-	> Proceed	to series C
Series C								
In this section	ı, your a	alcohol con	sumption t	through	out your l	life is q	ueried.	
In total, how many years have you consumed alcohol, either in large or small quantities?								
								years
At what age d	id vou s	tart drinkin	ng alcoholic	: drinks?				vears
At what age did you start drinking alcoholic drinks? years								
On average throughout your life, how often do you drink alcoholic drinks?  ☐ Never → Proceed to the next questionnaire								
	□ Nev						•	
	□ Mor	nthly or less	5		→ Procee	ed <i>to th</i>	e next ques	tionnaire
	□ 2-4/	month/			→ Procee	ed to the	e next ques	tion
	□ 2-3/	/week			→ Procee	ed to the	e next ques	tion
	□ Mor	re than 4/	week		$\rightarrow$ Procee	ed to the	e next ques	tion
	□ Dail	У			→ Procee	ed to the	e next ques	tion



On average, on days when you drank alcohol **throughout your whole life**, how many glasses of alcohol did you drink **in one day**?

glasses:		
- - - - - -	Beer (normal beers) Wine Port/sherry Liqueur Aperitifs (Passoa, Kir, etc.) Cognac Spirits/shots Jenever	T E
cocktails:	Mojito	Y T
- - -	Margarita Gin and tonic Cosmopolitan Vodka Redbull	
-		
glasses	of local beer:	m and a second
- - -	St. Bernardus Duvel Leffe	ш

West Vleteren



Subject ID	



#### Q.I.DRU - Recreational drug consumption

Do you sometimes use one of these drugs or have you ever used these in the past? Medicinal use of one of these products does **not** apply here. You can tick more than one option.

$\ \square$ I do not use any of these drugs.	→ Proceed to the next questionnaire				
□ Cannabis/Marijuana/Weed	ightarrow Complete A on the table				
□ Cocaine	ightarrow Complete B on the table				
☐ Amphetamines (excluding ecstasy)	ightarrow Complete C on the table				
☐ Opiates /Opioids (heroin, methadone, morphine, codeine,					
fentanyl, etc.)	ightarrow Complete D on the table				
□ Ecstasy	ightarrow Complete E on the table				
□ Mescaline	ightarrow Complete F on the table				
□ LSD	ightarrow Complete G on in the table				
☐ Psilocybin/Mushrooms	ightarrow Complete H on the table				
☐ Inhalants, e.g. poppers, gasoline, glue, nitrous oxide,					
nitrites, etc.	ightarrow Complete I on the table				
□ Barbiturates	ightarrow Complete J on the table				
☐ Other drugs:					
	→ Complete K on in the table				

(1) At what age did you start using this drug?



In the previous question, you indicated that you use one or more of the drugs or have used these in the past. We would like to ask some additional questions about this usage. To do this efficiently, please complete the table on the following page for the drugs (A-K) you identified in the first question. The exact questions (1-5) and possible answers are the same for each drug. A parenthesised answer code is provided that you can use to complete the table:

(=) / 10 1111	ar also are 1 an area a grand and area.	100.		
(2) Currei	ntly, how often do you use this drug?			
	□ Never <i>(0)</i>			
	☐ Every 2 months or less (1)			
	☐ Monthly <b>(2)</b>			
	☐ 2-4 times per month <i>(3)</i>			
	□ 2-3 times per week <i>(4)</i>			
	☐ 4 or more times per week <b>(5)</b>			
(3) Has th	nere been a <i>significant</i> change in your	use of this drug compared to past usage?		
Note: "much n		ant change, for example, completely stopping		
	Please complete: "I currently consume this drug than in the past"			
	☐ Much less ()	→ Proceed to the next question (4 + 5)		
	□ Less (-)	→ Proceed to the next drug		
	☐ Just as much (=)	→ Proceed to the next drug		
	□ More <i>(+)</i>	→ Proceed to the next drug		
	☐ Much more (++)	→ Proceed to the next question (4 +5)		
(4) At wh	at age did your use of cannabis increa	se to your current usage? year		
(5) How o	often did you use cannabis in the past	?		
	<ul><li>□ Never (0)</li><li>□ Every 2 months or less (1)</li></ul>			
	☐ Monthly (2)			
	□ 2-4 times per month (3)			
	□ 2-3 times per week (4)			
	☐ 4 or more times per week (5)			



	Recreational drug	Age started (1)	Frequency (2)	Significant change (3)	Age at change (4)	Previous frequency (5)
	Answer code	Year	0 →5	→++	Year	0 →5
А	Cannabis/Marijuana/weed					
В	Cocaine					
С	Amphetamines (excl. ecstasy)					
D	Opiates/Opioids					
Ε	Ecstasy					
F	Mescaline					
G	LSD					
Н	Psilocybin/Mushrooms					
1	Inhalants					
J	Barbiturates					
К	Other:					



Subject ID	



J.I.DIE – Diet	
e you on any of the following diets? If you on a special diet that is not listed, ple ecify it.	ase
☐ I'm not on a diet	
□ Vegetarian/Vegan	
□ Weight control diet	
○ Low calorie diet (e.g. Weight Watchers)	
○ Low carb diet (e.g. Atkins diet)	
○ Low-fat diet	
○ Crash diet (e.g. 17 day diet, soup diet, etc.)	
□ Medical diet	
○ Gluten-free diet	
○ Low-salt diet	
○ Ketogenic diet	
○ Diabetic diet	
Cholesterol lowering diet	
○ Lactose-free diet	
□ I am on a different diet:	

How many months have you been on the diet or may you not consume the listed foods or consume these to a limited extent?

months



Subject ID	

### Q.I.HEA - Health



What diseases have you been diagnosed with? Please also specify the diseases.

Note: for this section, you can always ask the researcher for help. ☐ Brain and nervous system disorders: ☐ Cardiovascular diseases: ☐ Disorders of the blood: ☐ Disorders of the stomach and intestines: ☐ Respiratory disorders: ☐ Hormonal disorders: ☐ Gynaecological disorders: ☐ Diseases of the bladder and urinary tract: ☐ Bacterial or viral infection: ..... □ Disorders of the immune system or allergy: \_\_\_\_\_ ☐ Skin diseases or disorders of the senses: □ Skeletal disorders: □ Oncological diseases: □ Pain, fever, inflammation: ☐ Other:



Are you inclined towards claustrophobia or have you ever experienced a claustrophobic panic attack?
□ Yes
□ No
If you have any other relevant information not addressed in the above list, please indicate it
here.



Subject ID	





Correctly completing the following tables is the task of the researcher in collaboration with the patient. This part consists of two sections:

- Medication/treatments that the patient is currently taking/undergoing on a **regular** basis
- Medication/treatments that the patient took/underwent on a regular basis in the
   past, but which the patient has now stopped

Complete each column per medication: brand name, product name, dose/strength, dosage form/administration, frequency/quantity, total daily dose, start (and end) date, and indication.

To complete this section as correctly as possible, it is recommended that you bring your frequently used medication with you on the day of the examination.



### SERIES A - Current medication/treatments taken/undergone on a regular basis

#	Brand name	Product name	Dose / strength	Dosage form / Administration method	Frequency	Total/day Dose	Start date	Indication
e.g.	Cozaar	Losartan potassium	50 mg	Oral	1x/day	50 mg	20/04/2015	High blood pressure
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								
11								
12								
13								
14								
15								
16								
17								



### SERIES B - Past medication/treatments taken/undergone on a regular basis

#	Brand name	Product name	Dose / strength	Dosage form / Administration method	Frequency	Total/day Dose	Start date	End date	Indication
e.g.	Cytoxan	Cyclophosphamide	9 mg/kg	IV	Daily, 5 days	45 mg/kg	1/11/2014	5/11/2014	Lung cancer
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									
11									
12									
13									
14									
15									
16									
17									



# "Study title"

#### Goal

You are taking part in a study where "short description of study objective (3 lines)".

In this part of the questionnaire, you will be asked about your mood and consumptions during the previous and current day. If you have any questions or something is not clear, you can ask the researcher about it on the day of your examination. This part of the questionnaire contains "number" questions.

### **Privacy**

We assure you that the information obtained in this questionnaire is encoded (using a subject ID), just like the radiological images obtained during this study. This means that the information you provide cannot be used to identify you.

Subject ID: #######

Date of MRI scan: .../.../......



Subject ID	



### Q.II.MOO - Mood

This scale consists of a number of words and phrases that describe different feelings and emotions. Read each item and indicate to what extent you feel this way RIGHT NOW.

	Very slightly or not at all	A little	Moderately	Quite a bit	Extremely
Cheerful					
Disgust					
Attentive					
Bashful					
Sluggish					
Daring					
Surprised					
Strong					
Scornful					
Relaxed					
Irritable					
Delighted					
Inspired					
Fearless					
Disgusted with self					
Sad					



	Very slightly or not at all	A little	Moderately	Quite a bit	Extremely
Calm					
Afraid					
Tired					
Amazed					
Shaky					
Нарру					
Timid					
Alone					
Alert					
Upset					
Angry					
Bold					
Blue					
Shy					
Active					
Guilty					
Joyful					
Nervous					
Lonely					
Sleepy					



	Very slightly or not at all	A little	Moderately	Quite a bit	Extremely
Excited					
Hostile					
Proud					
Jittery					
Lively					
Ashamed					
At ease					
Scared					
Drowsy					
Angry at self					
Enthusiastic					
Downhearted					
Sheepish					
Distressed					
Blameworthy					
Determined					
Frightened					
Astonished					
Interested					



	Very slightly or not at all	A little	Moderately	Quite a bit	Extremely
Loathing					
Confident					
Energetic					
Concentrating					
Dissatisfied with self					
How happy do you  Neutral  How sad do you fee		icating how	you feel on the	As ha	appy as I can imagine ad as I can magine
How aroused/emot	tionally stimulated d	o you feel rig	ght now?		ery much



Subject ID	
Jubject 1D	



## Q.II.SPO – Extreme sports

SERIES A – HIGH ALTITUDE SPORTS	
Did you recently reside at high altitude (e.g.	climbing, winter sports,)?
□ Yes	→ Proceed to the next question
□ No	→ Proceed to series B
How long did you stay at high altitude?	
How long ago did you return?	
SERIES B – DIVING	
Did you recently went diving?	
□ Yes	→ Proceed to the next question
□ No	ightarrow Proceed to the next questionnaire
How long ago did you went diving?	



Subject ID	
,	



### Q.II.CAF – Last caffeine consumption

Yesterday and today, at what times you did you consume caffeine products? Please complete the table as specifically as possible with the time, amount (e.g. 2 cups, 1 can (250 ml), etc.) and the product.

Note: Caffeine products include:

- Coffee: ground coffee, latte, mocha latte, cappuccino, espresso, instant coffee)
- Prea (green tea, black tea, white tea, Ice Tea)
- W Coca cola, Pepsi cola (including light and zero variants)
- Energy drink (Red Bull, Nalu, Golden Power, Monster, Burn)
- Chocolate (milk and dark chocolate)
- Chocolate milk

#### This does **not** include:

- Caffeine-free coffee
- Caffeine-free tea
- Caffeine-free soft drink
- Herbal tea/infusion: e.g. Rose hip, chamomile, mint, nettle, rooibos, fruits, etc.

#### For example

Time (hr:min)	Quantity	Product
07:30	2 cups	Ground coffee
09:45	1 cup	Green
12:15	1 glass	Coca Cola Zero



### **Yesterday**

Time (hr:min)	Quantity	Product

### **Today**

Time (hr:min)	Quantity	Product



Subject ID	



### Q.II.NIC - Last nicotine consumption

Yesterday and today, at what times you did you consume nicotine products? Please complete the table with the amount (e.g. 2, 1 inhalation, etc.), the product and the specifics (dose, brand name, etc.).

*Note: Nicotine products include:* 

- Cigarettes, e-cigarettes
- Cigars, pipe
- Nicotine patch
- Nicotine gum
- Nicotine inhaler, nasal spray, mouth spray
- Nicotine lozenges

Note: Products with a nicotine dose of 0 mg must also be recorded.

#### For example

Time (hr:min)	Quantity	Product	Specifications
08:00	1	Cigarette	Marlboro Gold Original
10:00	1 inhalation	E-cigarette	V2 red tobacco Mint Tea 1.8%
10:25	1	Nicotine gum	Nicorette 2 mg
	•••		



### **Yesterday**

Time (hr:min)	Quantity	Product	Specifications

### **Today**

Time (hr:min)	Quantity	Product	Specifications



Subject ID	



## Q.II.ALC – Last alcohol consumption

Yesterday and today, at what times you did you consume alcoholic products? Please complete the table with the time, amount and product.

### For example

Time (hr:min)	Quantity	Product	
20:00	1	Beer	
20:30	2	Jenever shots	
21:15	1	Gin and tonic	
22:00	1	Ename Blond	



### **Yesterday**

Quantity	Product
	Quantity

### **Today**

Time (hr:min)	Quantity	Product



Subject ID	

### Q.II.DRU - Last recreational drug consumption

At what times in the past month have you taken drugs? Please complete the table below specifying the date, the estimated time, the amount and the product.

### For example

Date	Time (hr:min)	Quantity	Product
30/04/2015	20:30	1 joint	Cannabis
05/05/2015	01:30	1 pint	Ecstasy
21/05/2015	16:00		Mushrooms

### The previous month

Date	Time (hr:min)	Quantity	Product



Subject ID

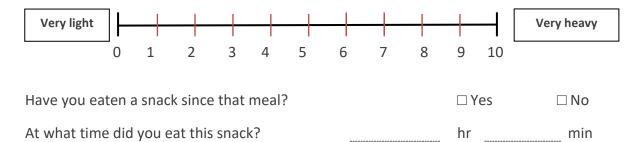
### Q.II.HUN - Hunger and thirst

Today, at what time did you eat your last main meal? \_\_\_\_\_ hr \_\_\_\_ min

How heavy was your last meal?

Note:

0 = very light. 5 = a normal meal. 10 = very heavy.



How satisfied were you with this last meal?

Note:

0 = I'm still very hungry. 5 = I'm satisfied. 10 = I ate too much.



How thirsty are you right now?

Note:

0 = I'm not thirsty and my mouth is not dry.

10 = I've never been so thirsty and my mouth has never been as dry as it is now





Subject ID	
Subject ib	
,	



Q.II.HEA – Health
Madam, where are you currently in your menstrual cycle? The first week starts on the first day of menstruation or the first day of your pill-free week.
□ 1 <sup>st</sup> week
□ 2 <sup>nd</sup> week
□ 3 <sup>rd</sup> week
□ 4 <sup>th</sup> week
☐ I don't menstruate because:



Subject ID	



### Q.II.SLE - Sleep

Answer the following questions by indicating how you feel on the bar.

About how many hours sleep did you get last night?

How sleepy do you feel right now?

I do not feel sleepy at all



Subject ID	

### Q.II.MED - Medication



Correctly completing the following tables is the task of the researcher in collaboration with the patient. In this part, medication that the patient has used in the past few days on a sporadic basis, such as painkillers or anti-inflammatories is queried.

Complete each column per medication: brand name, product name, dose/strength, dosage form/administration, frequency/quantity, total/day dose, start date, time and indication.

To complete this section as correctly as possible, it is recommended that you bring the medication used during the days before your appointment with you on the day of the examination.



### Medication taken in the past few days (sporadically)

#	Brand name	Product name	Dose / strength	Dosage form / Administration method	Frequency	Total/day Dose	Start date	Time (hr:min)	Indication
e.g.	Dafalgan	Paracetamol	500 mg	Oral	Two	1 g	30/04/2015	14:30	Headache
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									
11									
12									
13									
14									
15									
16									
17									



# "Study title"

#### Goal

This questionnaire is part of a study in which "short description of study objective (3 lines)".

This part of the questionnaire is meant for the researcher to record all measurements during the perfusion scan session.

### **Privacy**

We assure that the information obtained in this questionnaire is encoded (using a subject ID), just like the radiological images obtained during this study. This means that the information you provide cannot be used to identify you.

Subject ID: #######

Date of MRI scan: .../.../......



Subject ID	

### M.I.INF - Perfusion scan information

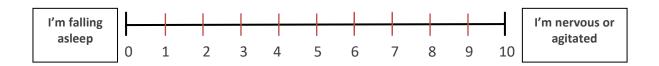
Perfusion sequence:		
Time start perfusion scan:	h	min
Duration perfusion scan:	min	S

### M.I.WAK - Wakefulness



'On a scale from 0 to 10, how awake are you right now?

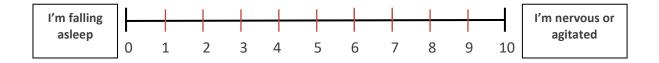
0 means "I'm falling asleep, 10 means "I'm nervous or agitated", 5 means "I'm awake but not nervous"



Wakefulness *after* the pefusion scan: ask the patient:

'On a scale from 0 to 10, how awake are you right now?

0 means "I'm falling asleep, 10 means "I'm nervous or agitated", 5 means "I'm awake but not nervous"

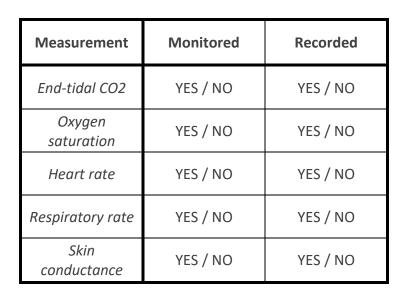




### M.I.MOO - Mood

Score <i>'positive'</i> :	
Score 'positive':	
Score <i>'arousal'</i> :	

### **M.I.PHY – Physiological measurements**





Subject ID	

## M.I.BTP – Body temperature and blood pressure

Body temperature:		°C/°F
Blood pressure:	/	mmHg

### M.I.BLO - Blood and urine sample

Measure	Value	Unit	Reference
	BLOOD	SAMPLE	·
Hematocrit		%	♀35.8-43.7/♂39.0-49.7
Whole blood viscosity		cP (mPa.s)	
Hemoglobin		g/dl	♀11.8-14.8/♂12.9-17.3
Fibrinogen		Mg/dl	200-400
Blood glucose		Mg/dl	74-106
Circulating homocysteine		μmol/l	<12
Total cholesterol		Mg/dl	<190
LDL		Mg/dl	<110
HDL		Mg/dl	ੂ39-96 / ∂32-72
ADMA		μmol/l	0.4-0.8
Free fatty acid profile			
URINE SAMPLE			
Ketone bodies		Mg/dl	- / Trace / Small / Moderate / Large



Subject ID	

### I.I.TOM - Time of day



It is advised to scan the patients within one study during the same time of day if possible. This might especially be recommendable in longitudinal studies to avoid intra-subject variability caused by the diurnal rhythm.

Instruction	Taken into	o account?	Additional information (hr:min)
Time of day	□ YES	□ NO	

### **I.I.SUR – Scanner surroundings**



It is advised to turn off (or at least dim) the light both in the scanner room as in the magnet bore. Videos and music for patient comfort should be switched off. All possible distractions during the perfusion scan should be eliminated.

Instruction	Taken into	account?	Additional information
Lights scanner room	□ YES	□ NO	
Lights magnet bore	□ YES	□ NO	
Video	□ YES	□ NO	
Music	□ YES	□ NO	
Other distractions	□ YES	□ NO	



Subject ID	
------------	--

### I.II.RES - Restrictions



In general, restricting daily life habits might induce extra variability due to withdrawal effects. For example, asking a patient to quit **medication**, is not only unethical, but withdrawal might influence cerebral perfusion. This counts for other lifestyle related factors, such as **caffeine**, **alcohol and nicotine** as well. However, it is advisable to recommend the patient to continue their daily life and habits, but to avoid circumstances inducing deviations from this pattern such as a student party the day before the scan session. Acute effects of those habits, are queried in multiple SOP components of Q.II.

For **recreational drugs**, the researcher can obviously point out that the use of such drugs in the days before the perfusion scan are not recommendable (except for studies including addiction patients).

Restrictions regarding **mobile phone** use is probably not necessary, however asking the subject not to take calls during the last 30 minutes before the start of the scan session might be advisable. As hunger and thirst can modify cerebral perfusion, it is advised to allow the subject to **eat and drink** before the scan session. Again, eating during the last 30 minutes before the start of the scan session might be recommendable.

Finally, it might be advisable to ask the patient not to perform **heavy physical activities** during the day of the scan session.

Instruction	Taken into	account?	Additional information
Alcohol	□ YES	□ NO	
Recreational drugs	□ YES	□ NO	
Caffeine	□ YES	□ NO	
Nicotine	□ YES	□ NO	
Medication	□ YES	□ NO	
Mobile phone	□ YES	□ NO	
Foods and drinks	□ YES	□ NO	
Physical activity	□ YES	□ NO	

Standard Operating Procedure for Perfusion Measurements and Arterial Spin Labeling (ASL)			
Subject ID			
• .	his kind of communication	t reduce the variability caused by several often reassures the patient which might	
Instruct the patient:			
	next scan, I would like to as s, don't fall asleep and try no specific. Just		
I.III.EYE – Ey	es		
Instruction	Taken into account?	Additional information	
Closing eyes	□ YES □ NO		
I.III.MOV – Movement			
Instruction	Taken into account?	Additional information	
Don't move	□ YES □ NO		
I.III.RST – Resting state			
Instruction	Taken into account?	Additional information	
Don't think about anything specific. Just relax.	□ YES □ NO		
I.III.WAK – Wakefulness			

Instruction	Taken into account?		Additional information
Don't sleep	□ YES	□ NO	



## Supplementary files: Scoring



Subject ID	
------------	--

### Q.I.SOC\* - Scoring Sociaal Leven

#### **UCLA Loneliness Scale Version 3**

### **Scoring instructions:**

Indicate the score for each statement: Never = 1; Rarely = 2; Sometimes = 3; Often = 4. The reverse score is already used for questions 1, 5, 6, 9, 10, 15, 16, 19 and 20.

Calculate the loneliness score by summing all statements scores.

	Never	Rarely	Someti mes	Often
How often do you feel that you are "in tune" with the people around you?	4	3	2	1
How often do you feel that you lack companionship?	1	2	3	4
How often do you feel that there is no one you can turn to?	1	2	3	4
How often do you feel alone?	1	2	3	4
How often do you feel part of a group of friends?	4	3	2	1
How often do you feel that you have a lot in common with the people around you?	4	3	2	1
How often do you feel that you are no longer close to anyone?	1	2	3	4
How often do you feel that your interests and ideas are not shared by those around you?	1	2	3	4
How often do you feel outgoing and friendly?	4	3	2	1
How often do you feel close to people?	4	3	2	1
How often do you feel left out?	1	2	3	4
How often do you feel that your relationships with others are not meaningful?	1	2	3	4
How often do you feel that no one really knows you well?	1	2	3	4
How often do you feel isolated from others?	1	2	3	4
How often do you feel you can find companionship when you want it?	4	3	2	1
How often do you feel that there are people who really understand you?	4	3	2	1
How often do you feel shy?	1	2	3	4
How often do you feel that people are around you but not with you?	1	2	3	4
How often do you feel that there are people you can talk to?	4	3	2	1
How often do you feel that there are people you can turn to?	4	3	2	1

Sum [20-80]	
-------------	--



Subject ID

### Q.I.HAN\* - Handedness



### The Edinburgh Inventory

#### **Scoring instructions:**

Indicate the score for each activity: Always right = 2; Mostly right = 1; No preference = 0; Mostly left = 1; Always left = 2.

Calculate the scores for the 'right' activities and the 'left' activities separately. Using the formula, the total score can be calculated.

	Always right	Mostly right	No preference	Mostly left	Always left
Writing	2	1	0	1	2
Drawing	2	1	0	1	2
Throwing	2	1	0	1	2
Scissors	2	1	0	1	2
Toothbrush	2	1	0	1	2
Knife (without fork)	2	1	0	1	2
Spoon	2	1	0	1	2
Broom (upper hand)	2	1	0	1	2
Striking a match (match)	2	1	0	1	2
Opening a box (lid)	2	1	0	1	2
Which foot do you prefer to kick with?	2	1	0	1	2
If you use only one eye, which one?	2	1	0	1	2

Score Right	Left	

Total score = 
$$\frac{R-L}{R+L} \times 100 =$$

Pure left-handed = -1.0

Mixed left-handed = -0.5

Neutral = 0.0

Mixed right-handed = +0.5

Pure right-handed = +1.0



Subject ID	
------------	--

### Q.I.PER\* - Personality

### The Big Five Inventory

### **Scoring instructions:**

Indicate the score for each statement: Disagree strongly = 1; Disagree a little = 2; Neither agree, neither disagree = 3; Agree a little = 4; Agree strongly = 5. The reverse score is already used for questions 2, 6, 8, 9, 12, 18, 21, 23, 24, 27, 31, 34, 35, 37, 41 and 43.

Calculate the corresponding statement scores for each personality trait and fill in the table.

	Disagree strongly	Disagree a little	Neither agree, neither disagree	Agree a little	Agree strongly
Is talkative	1	2	3	4	5
Tends to find fault with others	5	4	3	2	1
Does a thorough job	1	2	3	4	5
Is depressed, blue	1	2	3	4	5
Is original, comes up with new ideas	1	2	3	4	5
Is reserved	5	4	3	2	1
Is helpful and unselfish with others	1	2	3	4	5
Can be somewhat careless	5	4	3	2	1
Is relaxed, handles stress well	5	4	3	2	1
Is curious about many different things	1	2	3	4	5
Is full of energy	1	2	3	4	5
Starts quarrels with others	5	4	3	2	1
Is a reliable worker	1	2	3	4	5
Can be tense	1	2	3	4	5
Is ingenious, a deep thinker	1	2	3	4	5
Generates a lot of enthusiasm	1	2	3	4	5
Has a forgiving nature	1	2	3	4	5
Tends to be disorganized	5	4	3	2	1
Worries a lot	1	2	3	4	5
Has an active imagination	1	2	3	4	5
Tends to be quiet	5	4	3	2	1
Is generally trusting	1	2	3	4	5
Tends to be lazy	5	4	3	2	1
Is emotionally stable, not easily upset	5	4	3	2	1



	Disagree strongly	Disagree a little	Neither agree, neither disagree	Agree a little	Agree strongly
Is inventive	1	2	3	4	5
Has an assertive personality	1	2	3	4	5
Can be cold and aloof	5	4	3	2	1
Perseveres until the task is finished	1	2	3	4	5
Can be moody	1	2	3	4	5
Values artistic, aesthetic experiences	1	2	3	4	5
Is sometimes shy, inhibited	5	4	3	2	1
Is considerate and kind to almost everyone	1	2	3	4	5
Does things efficiently	1	2	3	4	5
Remains calm in tense situations	5	4	3	2	1
Prefers work that is routine	5	4	3	2	1
Is outgoing, sociable	1	2	3	4	5
Is sometimes rude to others	5	4	3	2	1
Makes plans and follows through with them	1	2	3	4	5
Gets nervous easily	1	2	3	4	5
Likes to reflect, play with ideas	1	2	3	4	5
Has few artistic interests	5	4	3	2	1
Likes to cooperate with others	1	2	3	4	5
Is easily distracted	5	4	3	2	1
Is sophisticated in art, music, or literature	1	2	3	4	5

Personality trait	Sum of statement scores	Score
Extraversion [8-40]	1, 6, 11, 16, 21, 26, 31, 36	
Agreeableness [9-45]	2, 7, 12, 17, 22, 27, 32, 37, 42	
Conscientiousness [9-45]	3, 8, 13, 18, 23, 28, 33, 38, 43	
Neuroticism [8-40]	4, 9, 14, 19, 24, 29, 34, 39	
Openness [10-50]	5, 10, 15, 20, 25, 30, 35, 40, 41, 44	



Subject ID	
------------	--



### Q.I.CAF\* - Caffeine consumption

#### **CURRENT CAFFEINE CONSUMPTION**

### **Scoring instructions:**

Calculate the daily dose of caffeine per kg of body weight consumed, using this table and the quantities given by the patient.

Product	Quantity	Dose (mg)	Total product dose (mg) = quantity x dose
Coffee		102	
Espresso/instant coffee		40	
Tea		27	
Coca Cola/Pepsi Cola		21	
Energy drink		73	
Chocolate/chocolate milk		12	

Total daily dose (mg) =			
	Body	weight (kg) =	/
Daily dasa n	or ka of body woi	aht (ma/ka) =	-
Daily dose p	er kg of body wei	gnt (mg/kg) =	



#### **CHANGES IN CAFFEINE CONSUMPTION**

This section is important if the subject significantly changed their caffeine consumption habit in the past three months. This can lead to changes in perfusion (withdrawal effects or stronger acute effects). Normalisation (tolerance) is likely to be achieved after about two months.

### **Scoring instructions:**

Calculate the daily dose of caffeine per kg of body weight consumed before the change, using this table and the quantities given by the patient.

Product	Quantity	Dose (mg)	Total product dose (mg) = quantity x dose
Coffee		102	
Espresso/instant coffee		40	
Теа		27	
Coca Cola/Pepsi Cola		21	
Energy drink		73	
Chocolate/chocolate milk		12	

	Total dai	y dose (mg) =	
	Body	weight (kg) =	/
Della deserv			=
Daily dose p	per kg of body wei	gnt (mg/kg) =	



Subject ID	
------------	--

## Q.I.NIC\* - Nicotine consumption

#### **CURRENT NICOTINE CONSUMPTION – SERIES A**

#### **Scoring instructions:**

Calculate the total dose of nicotine consumed, using this table and the quantities and dose given by the patient. This should not be calculated for patient using nicotine on a monthly basis or less. Based on the frequency of use, the frequency parameter can be deducted. Use this parameter in combination with the total dose in order to calculate the total daily dose of nicotine consumption.

Product	Quantity	Dose (mg)	Total product dose (mg) = quantity x dose
Cigarettes		1	
E-cigarettes		0/6/12/18/24/36/48	
Cigars		5	
Pipe		5	
Plaster		7/14/21/35/42	
Gum		2/4	
Inhaler		15	
Nose spray		0.5	
Mouth spray		1	
Lozenges		1/1.5/2/4	

Total dose (mg) =	Frequency parameter
/	Monthly or less $\rightarrow x$
Frequency parameter =	2-4x / month → <b>10</b>
	2-3x /weeks <b>→ 2.8</b>
Total daily dose (mg) =	More than 4x /week → 1.2
	Daily → 1



#### **CURRENT NICOTINE CONSUMPTION – SERIES A**

### Fagerström Test for Nicotine Dependence

#### **Scoring instructions:**

Calculate the dependency score and level based on the scores of each questions. Calculate the answer for the last question based on the 'total dose' derived from the previous section.

How soon after waking do you smoke or use y	your first nicotine product?	Score
☐ Within 5 minutes		→ 3
☐ 5 – 30 minutes		<b>→ 2</b>
☐ More than 30 minutes		→ 1
Do you or would you find it difficult not to so For example, a church or a library where smo   Yes  No  Which nicotine product would be most difficult  The first one at the start of the da  Another one during the day	king is prohibited.  ult for you to give up?	places where it is prohibited  Yes $\Rightarrow$ 1  No $\Rightarrow$ 0
Do you smoke or use nicotine products more ☐ Yes ☐ No	frequently in the morning?	Yes → 1 No → 0
Do you smoke or use nicotine products even	when you spend most of the day sick	in bed?
□ Yes □ No		Yes → 1 No → 0
Daily nicotine dose:		L
☐ Equal to or less than 10 mg		→ 0
□ 11-20 mg		→ 1
□ 21-30 mg		→ 2
☐ 31 mg or more		→ 3
Low dependency = 1 - 2		
Low to moderate dependency = 3 - 4	Sum [1-10]	
Moderate dependency = 5 - 7		
High dependency = 8 - 10		



#### LIFELONG NICOTINE CONSUMPTION - SERIES D

#### **Scoring instructions:**

Calculate the total dose of nicotine consumed, using this table and the quantities and dose given by the patient. This should not be calculated for patient using nicotine on a monthly basis or less. Based on the frequency of use, the frequency parameter can be deducted. Use this parameter in combination with the total dose in order to calculate the total daily dose of lifelong nicotine consumption. Multiply this by the duration of total nicotine use (\*) to calculate the nicotine index.

In total, how many years have you smoked or used nicotine products? \_\_\_\_\_\_ years ◆

Product	Quantity	Dose (mg)	Total product dose (mg) = quantity x dose
Cigarettes		1	
E-cigarettes		0/6/12/18/24/36/48	
Cigars		5	
Pipe		5	
Plaster		7/14/21/35/42	
Gum		2/4	
Inhaler		15	
Nose spray		0.5	
Mouth spray		1	
Lozenges		1/1.5/2/4	

Frequency parameter	Total dans (ma)	
Monthly or less $\rightarrow x$	Total dose (mg) =	
2-4x / month → <b>10</b>		/
2-3x /weeks <b>→ 2.8</b>	Eroguanov narameter –	
More than 4x /week → 1.2	Frequency parameter =	
Daily $ ightarrow$ 1		=
Nicotine index =	Total daily dose (mg) =	
		X
Dura	ation of total nicotine use 💠 =	
(N.B. Pack year = nicotine index / 20)		



Subject ID	
------------	--

## Q.I.ALC\* - Alcohol consumption

#### **CURRENT ALCOHOL CONSUMPTION – SERIES A**

#### **Scoring instructions:**

Calculate the current daily dose per kg of body weight of alcohol consumption based on the number of units of alcohol, frequency of use and body weight given by the patient.

	Units
	1
YY	1.5
	2.5

Frequency parameter
Never → X
Monthly or less $\rightarrow X$
2-4x / month → <b>10</b>
2-3x /weeks <b>→ 2.8</b>
More than $4x$ /week $\rightarrow$ 1.2
Daily $ ightarrow$ 1

Number of units of alcohol =	
	/
Frequency of use =	
	=
Total number of units / day =	
	X
Dose of pure alcohol/unit (g) =	14
	=
Total daily dose of alcohol (g) =	
	/
Body weight (kg) =	
	=
Daily dose per kg	
of body weight (kg) =	



#### LIFELONG ALCOHOL CONSUMPTION – SERIES C

#### **Scoring instructions:**

Calculate the alcohol index based on the number of units of alcohol, frequency of use and total duration of alcohol consumption ( $\uparrow$ ) given by the patient.

In total, how many years have you consumed alcohol, either in large or small quantities?

		years •
	Units	Frequency parameter
	1	Never $\rightarrow X$ Monthly or less $\rightarrow X$ 2-4x / month $\rightarrow 10$
YY	1.5	2-3x /weeks $\rightarrow$ 2.8 More than 4x /week $\rightarrow$ 1.2
	2.5	Daily → 1
Number of units of alc	cohol =	
Frequency of use =		=
Total number of units	/ day =	x
Dose of pure alcohol/	unit (g) =	14
Total daily dose of alc	ohol (g) =	x
Total duration of alcol	nol consumption → =	
Alcohol index =		=



### Q.II.MOO\* - Mood

### Positive and Negative Affect Schedule - Expanded

### **Scoring instructions:**

Indicate the score for each statement: Very Slightly = 1; A little = 2; Moderately = 3; Quite a bit = 4; Extremely = 5. Complete the table for each mood state.

Mood factor	Sum of statement scores	Score
General positive emotion [10-50]	31 + 25 + 3 + 52 + 47 + 37 + 13 + 55 + 39 + 8	
General negative emotion [10-50]	18 + 44 + 34 + 40 + 11 + 38 + 32 + 42 + 26 + 50	
Fear [6-30]	18 + 44 + 53 + 34 + 40 + 21	
Hostility [6-30]	37 + 38 + 11 + 9 + 2 + 56	
Guilt [6-30]	32 + 42 + 51 + 46 + 15 + 60	
Sadness [5-25]	16 + 29 + 48 + 24 + 35	
Joviality [8-40]	22 + 33 + 12 + 1 + 37 + 47 + 41 + 58	
Self-assurance [6-30]	39 + 3 + 57 + 28 + 6 + 14	
Attentiveness [4-20]	25 + 3 + 59 + 52	
Shyness [4-20]	30 + 4 + 49 + 23	
Fatigue [4-20]	36 + 19 + 5 + 45	
Serenity [3-15]	17 + 10 + 43	
Surprise [3-15]	20 + 7 + 54	
Basic positive affect (joviality + self-assurance + attentiveness)/3 [6-30]	(22 + 33 + 12 + 1 + 37 + 47 + 41 + 58 + 39 + 3 + 57 + 28 + 6 + 14 + 25 + 3 + 59 + 52)/3	
Basic negative affect (sadness + guilt + hostility + fear)/4 [5,75-28,75]	(16 + 29 + 48 + 24 + 35 + 32 + 42 + 51 + 46 + 15 + 60 + 37 + 38 + 11 + 9 + 2 + 56 + 18 + 44 + 53 + 34 + 40 + 21)/4	



### Visual Analogue Scale Mood

#### **Scoring instructions:**

Measure the score for each VAS-scale using a ruler.

How happy do you feel right now?



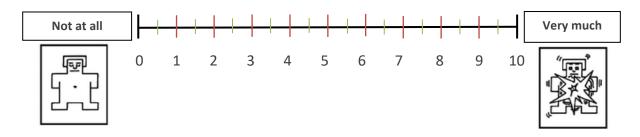
Score 'positive':

How sad do you feel right now?



Score *'negative'*:

How aroused/emotionally stimulated do you feel right now?



Score 'arousal':