neuroSHARE Measurement of Neurodegenerative Diseases Study Protocol

SHARE Wave 10 in the Czech Republic

1. Background and Aims

Neurodegenerative diseases such as Alzheimer's and Parkinson's disease are among the most disabling conditions associated with aging and represent a growing health, long-term health care as well as socio-economic challenge in European societies. Embedding biomarkers of health risk and disease in longitudinal biosocial surveys such as the Survey of Health, Ageing and Retirement in Europe (SHARE) is key to objectively measure health in cross-national surveys. These tests can provide important clues concerning disease risk factors, early diagnosis, and disease prevention along with key health, long-term care and socioeconomic aspects related to disease progression, including the potential long-term neurological consequences of COVID-19 infection.

The neuroSHARE project in the Czech Republic is designed as a country-specific sub-project of the Survey of Health, Ageing and Retirement in Europe (SHARE) and includes new tests and functional assessments of speech, olfactory (smell) and specific sleep dysfunctions, which will be fielded to the full sample of 4,000 panel and refresher respondents in wave 10 of SHARE survey in the Czech Republic. Respondents with abnormal test results are offered the opportunity to attend a subsequent personal medical appointment, which is not part of the study itself. Resulting anonymised data from the project will be made available to registered SHARE users together with other SHARE data. All tests are inexpensive, non-invasive, and can be performed and assessed repeatedly. The smell test and sleep questionnaire are validated tests used in other major surveys. The smell test is the omitted part of the HCAP (Harmonized Cognitive Assessment Protocol) study that was collected in the Czech Republic in wave 9.

Speech, olfactory (smell) and sleep dysfunctions belong among the earliest and most important signs of neurodegenerative diseases and depression. In Parkinson's and Alzheimer's disease, decreased sense of smell precedes the occurrence of motor and cognitive symptoms by years or even decades. Prosodic changes of speech are evident already in the prodromal stages of both diseases. The strongest risk factor for later development of Parkinson's disease and Dementia with Lewy Bodies is the Rapid-Eye-Movement Sleep Behavior Disorder (RBD), a specific sleep dysfunction manifested as dream enactment behaviour. Importantly, the combination of the self-reported RBD Questionnaire, the smell and speech test is presumably the most robust biomarker predictor of prodromal neurodegeneration scalable to larger populations. Finally, these tests are also important determinants of the long-term neuropsychiatric burden associated with depression and olfactory dysfunctions related to the Covid-19 pandemic.

The primary research aims of the neuroSHARE Study are:

1. investigation of potential neuropsychiatric burden (i.e., the risk of Parkinson disease, Dementia with Lewy Bodies, Alzheimer disease, depression etc.) of COVID-19 associated with olfactory dysfunction;
2. investigation of associations between olfactory function, motor and cognitive speech parameters, cognition, quality of life, and other health-related parameters;
3. quantification of the risk of developing various neuropsychiatric disorders for elderly subjects with olfactory and speech dysfunction; and,
4. evaluation of the feasibility of population screening of prodromal neurodegeneration.

The secondary research aims are:

1. examination of cross-cultural differences in identification of particular smells included in the test;
2. refinement of reference range for the smell test for the age group 50+; and

3. examination of aging-related speech changes for the age group 50+.

2. Objectives and content of the neuroSHARE Study

Including the collection of newly developed survey measures of neurological functions in SHARE for robust early markers of neurodegenerative diseases and depression into a social survey such as SHARE is of important scientific value as it opens up multiple research possibilities:

- Identification of causal relationships: markers of neurodegenerative diseases will help to understand the complex relationships between social status and health and their physiological pathways.
- Pre-clinical information: markers of the most prevalent neurodegenerative diseases allow to identify pre-disease pathways, since the physiological processes are often below the individual‘s threshold of perception. Such validated markers can be used to identify candidates for future trials with neuroprotective compounds.
- Improvement in the measurement of neurodegenerative diseases is an important value added to the subjective interpretation of respondent health. Neuromarkers enable researchers to validate respondents’ self-reports and therefore to study the amount and determinants of under-, over-, and misreporting in large-scale population surveys.

A fundamental advantage of including the collection of markers of neurodegenerative diseases into a large-scale survey such as SHARE is the simultaneous availability of objective measurements and socio-demographic data in a representative population.

Three simple, non-invasive tests will be performed[1]:

1. Smell (olfactory) test for the evaluation of an individual’s smell threshold as well as the ability to recognise well-known scents. The final score is computed by summing each correctly identified scent with scores ranging from 0-11. Additional questions are asked after the smell test to identify if participants suffered from an upper airway infection at the time of the interview, are active smokers, or have allergies that might affect their sense of smell.

2. REM Sleep Behavior Disorder Screening Questionnaire (RBD-SQ) is an internationally validated, self-administered paper questionnaire to evaluate the quality of REM sleep of each respondent. It consists of 13 yes/no questions. The final score is computed as a sum of all “yes” answers and ranges from 0-13.

3. Speech test as a short vocal examination that records five speaking tasks (sustained vowels, syllable repetitions, reading passage, repeating a fairy tale, and a short monologue) for capturing all motor and cognitive aspects of speech production.

The combination of coded data from these three simple, non-invasive tests will provide researchers with very robust early markers of prodromal neurodegeneration scalable to larger populations. These tests are important health, health care and economic factors for the ageing European society.

3. neuroSHARE Study Design

The neuroSHARE project in the Czech Republic is designed as a country-specific sub-project of Wave 10 of SHARE. SHARE is a multidisciplinary and cross-national panel database of micro data on health, socio-economic status and social and family networks. For details see www.share-eric.eu.

[1] The following tests will all be administered during the first test round of the neuroSHARE Study as part of the SHARE Wave 10 Field Rehearsal. After the evaluation of this round of testing, the total number of tests and questions will be reduced so that the overall duration of the sub-project (including the collection of additional consent) will not exceed 25-30 minutes (in accordance with the duration indicated below).

Responsible parties for the neuroSHARE sub-study in the Czech Republic:

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(hereafter SHARE-ERIC)

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Scientific Partners: *First Faculty of Medicine, Department of Neurology*
Charles University and General University Hospital
Katerinska 30, 128 00 Prague 2, the Czech Republic
Scientific coordinator: Petr Dusek
(hereafter FFM)

Czech Technical University in Prague
Department of Circuit Theory, Faculty of Electrical Engineering
Technicka 2, 166 27 Prague 6, the Czech Republic
Scientific coordinator: Jan Rusz
(hereafter CTU)

Sample size and target population
The sample size for the neuroSHARE Study will include all refresher (baseline) and panel respondents in the Czech Republic who complete the main interview. The participation in the neuroSHARE Study is voluntary. Should a respondent refuse to participate in the neuroSHARE Study, no tests will be performed.

Target population
4,000 of all refresher and panel respondents in the Czech Republic who complete the main CAPI interview in Wave 10.

Expected consent rate and total sample size of completed neuroSHARE Study
Based on HRS and ELSA olfactory tests and previous "drop-off" experience in SHARE-CZ, the expected consent rate is 90% of the target population. The expected number of respondents who will complete the neuroSHARE Study is 3,600.

Time Schedule
The neuroSHARE Study will be tested in the Field Rehearsal.
The neuroSHARE Study main data collection will occur during the regular wave 10 schedule.

<u>Fieldwork Procedures Methodology</u>

Data Collection
The neuroSHARE Study will be collected immediately after the completion of the main CAPI interview. The total duration is expected to be around 25-30 minutes. This includes the collection of additional consent of the respondents to participate in the study as well as the tests of the neuroSHARE project itself.

Sampling Procedures
As the neuroSHARE Study follows immediately after the completion of the main SHARE CAPI (computer assisted personal interviewing) interview, there are no additional sampling procedures. After the main CAPI interview is completed, the CaseCTRL will automatically start an application to

obtain consent for the participation in the neuroSHARE Study from all baseline and panel respondents (see below: Consent of the Respondent).

Advance/Invitation Letter
A short description of the neuroSHARE project will be inserted in the invitation/advance letter for SHARE Wave 10 in the Czech Republic. SHARE-CZ is responsible for the formulation of the advance letter, the delivery of a generic English version to SHARE-ERIC and the translation to Czech. The Survey Agency will be responsible for printing and mailing the letter to respondents.

The following additional paragraph will be added in the SHARE invitation/advance letter:

> After the completion of the SHARE interview, we would like to invite you to take part in an additional short questionnaire and tests related to the early detection of common neurodegenerative illnesses like Alzheimer's and Parkinson's disease. Participation in this additional part is voluntary and completely independent from your decision to participate in the SHARE interview.
> Three simple and non-invasive but powerful tests of smell, sleep and speech were developed by researchers at the First Faculty of Medicine and the Czech Technical University. If you decide to also participate in these additional tests, we would like to offer you additional 300 CZK payment for your participation.

Contact Procedures
The neuroSHARE Study relies on the general contact procedures (including related documentation of contact attempts) of SHARE. There are no additional contact procedures related to the neuroSHARE Study.

Incentives: Payments for Respondents
In the advance letter and in CAPI item ne001, respondents are informed about an additional payment for completing the neuroSHARE Study in the amount of 300 CZK. Because all respondents who complete the CAPI main SHARE interview will have already provided their information needed to receive the payment of 500 CZK for the completion of the main interview, there are no additional tasks related to neuroSHARE Study with respect to the additional payment; the amounts simply have to be added in case of a participation. Therefore, respondent who will also complete the neuroSHARE Study will receive one payment in the amount of 800 CZK sent from the Survey Agency to the respondent's bank account or by a postal voucher.

Payments for Interviewers
Interviewers will receive an additional payment of 300 CZK from the Survey Agency for each completed neuroSHARE interview (including all tests and questionnaires). The additional payment will be paid as a part of the interviewer's remuneration. There are no additional tasks related to the interviewer's neuroSHARE additional payment.

Consent of the Respondent
At the end of the main SHARE CAPI interview, the CaseCTRL will automatically run two successive neuroSHARE consent questions, ne001 and ne002. These questions will contain information about the neuroSHARE Study and the consent to participate (ne001) and the consent to be recontacted (ne002) regarding an offer of a subsequent personal medical appointment. At the beginning of ne001 the interviewer will hand over a neuroSHARE information leaflet, which contains all important information about the sub-study and addresses frequently asked questions. With regard to data processing and protection the consent questions and the information leaflet will refer to the general SHARE data protection statement, which has been handed over to the respondents at the beginning of the main SHARE interview. The interviewer will be trained how to ask these questions and answer all questions that the respondents may have. The consent will be documented in the CAPI, meaning that the interviewer enters the answers of the respondent in the CAPI, where they will be stored.

The following question ne001 will be asked of all baseline and panel respondents:

ne001: Consent to participate in neuroSHARE sub-study

As in every wave of the SHARE Study in the Czech Republic, we add a short questionnaire on important topics. In this wave, we would like to ask you to take part in small additional study with tests that enable research on neurodegenerative diseases such as Alzheimer's and Parkinson's disease that are among the most disabling conditions associated with ageing.

By participating, you will make a valuable contribution to research based on SHARE data and help us to enhance the data collected through SHARE. In this study, you will be asked to complete a short questionnaire about your sleep, voice and smell. Furthermore, we would also like to test your ability to smell with sticks containing various scents and record your voice in repeating vowels, syllables, reading a short text, and telling a fairy tale and a monologue. The total time for these tests is approximately 25-30 minutes. The tests are simple to perform and non-invasive.

As for the main SHARE interview, in which you just participated, this small additional study is conducted under the responsibility of *SHARE-ERIC* in cooperation with the *Economics Institute of the Czech Academy of Sciences*. Additionally, we cooperate with researchers of the *First Faculty of Medicine of the Charles University and the General University Hospital* and the *Czech Technical University* in this additional study.

As a reward for participating in this study we would like to offer you an additional payment of 300 CZK.

Let me stress that participating in this interview is voluntary and that the information is kept confidential. For all details how we ensure confidentiality of your data as well as details about your rights, please refer to the Data Protection Statement that you received at the start of today's SHARE interview. I will be pleased to answer any question that you may have and provide you with more information about the study.

Do you agree to participate in this additional study?

IWER: Hand out the neuroSHARE Study Information Leaflet to Respondent. Allow the Respondent sufficient time for reading. Answer all questions of the Respondent.

1. Yes, Respondent has consented to participate
5. No, Respondent has refused to participate. No neuroSHARE interview possible.

If ne001==1: Continue to ne002
If ne001==5: End of CaseCTRL consent application.

In case the respondent answers "No", the interview will be stopped and the respondent will not be subject to the neuroSHARE Study. The CaseCTRL application will stop automatically.

In case the respondent answers "Yes", the CaseCTRL application will start the following ne002 consent question:

ne002: Consent to be recontacted for a subsequent personal medical appointment

Thank you very much for your participation in this study.

Early detection of common neurodegenerative illnesses, such as Parkinson's and Alzheimer's disease, is essential for a timely treatment that can halt or slow the progression of these diseases. Therefore, it is important to diagnose them at their early stage before the full onset of symptoms.

It is known that some relatively mild symptoms are associated with a higher risk of the disease. These include deterioration of the sense of smell, changes in articulation, or signs of a sleep disorder characterised by dream enactment, i.e., movements, speech or other manifestations during one's sleep that reflect dreams' content.

Please note that none of the tested symptoms such as an impaired sense of smell, a change in speech, or sleep disturbances does by itself imply your suffering from a neurodegenerative disease. Each of these symptoms is non-specific and may have a variety of other causes.

However, in the case that your results were outside the normal range, we feel it is our obligation to offer you a preventive personal medical appointment at the *Department of Neurology at the General University Hospital of the First Faculty of Medicine at the Charles University*, where physicians can conduct a proper preventive clinical neurological examination and a cognitive testing focused on diagnosing these diseases.

We are offering you the possibility of these expert examinations because preventive care is an important part of successful and effective treatment of these diseases.

If you would like to be contacted by the medical personnel of the Department of Neurology in the case that the evaluation of the test results shows that your results were outside the normal range, **we need your consent to provide your name and phone number to the professional medical personnel at the *Department of Neurology at the General University Hospital of the First Faculty of Medicine at the Charles University*.**

Do you agree to this data transfer in order to be contacted by them for an offer of a personal medical appointment?

1. Yes
5. No

IWER:
Thank you very much for your willingness to participate in the additional short study. Let us begin with the questionnaire.

Please fill the cover page of the neuroSHARE Study Questionnaire.
Please proceed with the instructions in the questionnaire.

The interviewer now proceeds with the neuroSHARE Study Questionnaire and tests.

The CaseCTRL automatically starts the Speech Test App on interviewer's notebook that will be later used in the speech test. See the Appendix for a detailed description of the speech test and steps of data transfer procedures.

4. THE NEUROSHARE STUDY QUESTIONNAIRE

All instructions, testing procedures, questions needed for all steps are contained in the neuroSHARE Study Questionnaire. The neuroSHARE Study Questionnaire also serves as the recording booklet for the smell test. ***See Appendix for the Questionnaire.***

The tasks related to the questionnaire have to be carried out by the interviewer in the following order:

Cover page: Identification of the respondent (administered by the interviewer)
On the cover page of the neuroSHARE Study Questionnaire, the interviewer fills the following information: the respondent's pidcom ID, year of birth, first name, gender, the interviewer ID and the date of the interview. After the cover page is filled, the neuroSHARE Study starts with the smell test.

Smell test with sniffin' sticks (administered by the interviewer, 10 minutes)

The smell test was designed by the National Social Life and Aging Project (NSHAP) and was used in ELSA and HRS. The smell test "completes" the HCAP interview from wave 9 in the Czech Republic and harmonises SHARE with ELSA and HRS. For attaining harmonisation with HRS and ELSA surveys, the neuroSHARE Study uses the same procedures, equipment, and questionnaire as the ELSA 50+ Memory and Thinking (HCAP) Smell Test from January 2018.

Smell test is a test of the respondent's olfactory (smell) ability, using a set of special smell pens designed for the purpose. The equipment used in the smell test is scientifically validated commercially available product which tests an individual's smell threshold as well as the ability to recognise well-known scents. The final score is computed by summing each correctly identified scent with scores ranging from 0-11.

In the first part of the smell test, the respondent is asked to smell a blue (practice) pen first. In the next step, respondents are asked to smell a series of red pens, presented to them in six groups of three pens. From each group of three, they are asked to identify which pen has the same scent as was on the original blue pen (other pens have no scent). The strength of the scent on the pen (concentration of n-butanol) varies between the groups of three. The second part of the smell test involves five black pens, each with a different scent. The respondent is given the first pen to smell and is shown a showcard listing four possible scents; their task is to identify which of the scents the pen smells like. This is repeated for all five black pens, with different showcards for each pen. The correct scents needed to be identified in this part of the test are rose, garlic, orange, fish and peppermint.

After the smell test, a few additional questions are asked to identify if the respective participant suffered from an upper airway infection at the time of the interview, is an active smoker, or has allergies that might affect the respondent's sense of smell.

Smell test self-completed questionnaire (2 minutes)

The final part of the smell test consists of four questions in the neuroSHARE Study Questionnaire, which will be filled in by the respondent.

Sleep "test" self-completed questionnaire (2 minutes)

REM Sleep Behavior Disorder Screening Questionnaire (RBD-SQ) is an internationally validated, self-administered questionnaire of 13 yes/no questions. The questions will be filled in by the respondent. The Czech translation of the questions was performed and validated by researchers of the scientific partner of the neuroSHARE Study, the FFM of Charles University. The RBD-SQ license requirement has been obtained from the Movement Disorder society with which the FFM researchers collaborate on other scientific projects.

Speech test self-completed questionnaire (2 minutes)

The first part of the speech test consists of three sets of questions in the neuroSHARE Study Questionnaire. The questions that relate to speech ability of the respondent, including possible medical treatment, and how the respondent assumes that it is perceived by others and will be filled in by the respondent.

Speech test recording (administered by the interviewer, 10 minutes)

While the respondent is answering the self-completed questionnaire, the interviewer connects the microphone to the interviewer's notebook. As mentioned above, the Speech Test App is running and waiting for the start of the speech test. The CaseCTRL automatically copies all SHARE-internal important details for the respective respondent from the CaseCTRL into the Speech Test App: the audio file name consists of the pidcom ID and the date and time of the test. In addition, an additional text file is automatically created and stored together with the audio file. This text file includes the

pidcom ID, gender, year of birth, first name of the respondent, date and time of the test, interviewer ID and the notebook ID. This procedure ensures that the speech test recordings can later on be connected with the neuroSHARE questionnaire data and the main SHARE questionnaire data of the same respondent.

The Speech Test App initial screen also asks the interviewer to input the same pidcom ID that is written on the cover page of the neuroSHARE Study Questionnaire (to match possible errors in the questionnaire).

Next, the interviewer follows the neuroSHARE Study Questionnaire for detailed instructions. It is carried out with a head-mounted condenser microphone and is based on five speaking tasks including sustained vowels, syllable repetitions, reading a text passage, repeating a fairy tale and a short monologue. The test is a validated approach to catch all aspects of motor production. As the other tests, the speech test does not ask the respondent about any personal or factual information. It is recognised, however, that the recording of a humans' voice itself may be considered to be personal data, and therefore need to be protected in an appropriate manner (see below and Appendix: neuroSHARE Speech Test Recording and Transfer Protocol).

The speech test was developed and validated by researchers of the scientific partner of the neuroSHARE Study, the Czech Technical University and does not require any license. The microphone is a commercially available product Sennheiser HSP 2 that does not require any license.

After the interview has been conducted the tasks described in the following section have to be carried out.

5. PROCESSING, HANDLING AND PROTECTION OF THE NEUROSHARE DATA FILES

neuroSHARE Speech Test Recording and Data Transfer

The speech test is administered and recorded by the Speech Test App. After the end of the speech test, the Speech Test App automatically closes down and then encrypts (using the RSA encryption), zips, saves the neuroSHARE Study Speech File into a pre-specified folder, and then also automatically closes.

The encrypted neuroSHARE Study Speech Files are transferred directly to the Czech Technical University (CTU) secure server using HTTPS transfer protocol. The transfer is initiated manually by the interviewer at the same time he or she synchronises of the main SHARE CAPI interview (frequency specified by the Survey Agency, at least twice a week). The transfer is administered by running the Speech Test App and selecting the transfer function. For a backup purposes, the neuroSHARE Study Speech Files are moved to a different folder on the interviewer's notebook with other backup files from the main SHARE CAPI interview.

All the steps are listed in detail in the Appendix: neuroSHARE Speech Test Recording and Transfer Protocol.

Processing and coding of neuroSHARE Study Audio Files

The CTU secure server is located in a closed server room, which can only be accessed with a specific security token held only by authorised staff who are partners in the neuroSHARE project. Each neuroSHARE Study Speech File will be analysed and coded into 9 parameters (numerical variables) derived from the audio file associated with each respondent's identifiers to produce a neuroSHARE Study Speech Data file in csv format. Data coding and software procedures will be monitored by the SHARE-CZ team. The neuroSHARE Study Speech Data file will not contain any contact information and will be encrypted (using the RSA encryption). This RSA-encrypted file will then be transferred to SHARE-CZ secure server using the HTTPS transfer protocol.

The coded parameters are acoustic motor speech and cognitive language measures that can be associated with changes in aging but also development of neurodegeneration. For motor speech assessment, quality of voice is assessed using the harmonics-to-noise ratio (HNR) via a sustained phonation paradigm, sequential motion rates are assessed using the diadochokinetic rate (DDKR) and consonant articulation is assessed using the voice onset time (VOT) via the fast syllable repetition paradigm. Loudness variations are assessed through the standard deviation of intensity contour (IntSD), pitch variations by the standard deviation of pitch contour (F0SD), and articulation rate through the net speech rate (NSR) via reading passage, while pauses characteristics are assessed using the duration of pause intervals (DPI) via monologue. The reading passage is of special importance for the acoustic analyses as it better reflects the necessary standardisation. The prolonged pauses are obtained from the monologue which better reflects both speech-motor execution and cognitive-linguistic processing.

The language assessment is based on monologue. Here, content density is calculated as the ratio of open-class words to closed-class words. N-grams parameter counts the occurrence of two, three, and four grams repetitions in the utterance. The Moving-Average Type–Token Ratio (MATTR) quantifies lexical richness based on the vocabulary using a method that is independent of the text length; MATTR window size is set to 70 words in accordance with our available sample length and previous recommendations for determining the subject's vocabulary.

Table of Speech Features

No.	Name	Description	Type	Values
1	sf_hnr	harmonics-to-noise ratio (HNR)	numerical	-10-30
2	sf_ddkr	diadochokinetic rate (DDKR)	numerical	0-100
3	sf_vot	voice onset time (VOT)	numerical	0-1000
4	sf_intsd	standard deviation of intensity contour (IntSD)	numerical	0-100
5	sf_nsr	net speech rate (NSR)	numerical	0-10
6	sf_dpi	duration of pause intervals (DPI)	numerical	0-1000
7	sf_cd	content density (CD)	numerical	0-100
8	sf_ngrams	N-grams (NGRAMS)	numerical	0-1
9	sf_mattr	Moving-Average Type–Token Ratio (MATTR)	numerical	0-1

Speech Test software

The analysis is conducted in MATLAB (MathWorks, Natick, MA) at the CTU in Prague. Freely-available algorithms described in previous studies (see pp. 16-22) as well as a freely-available toolbox called "dysarthria analyzer" are used to perform all analyses. The Faculty of Electrical Engineering at CTU in Prague has longstanding experience and equipment for the analysis, processing, and interpretation of speech signals in neurological diseases, as well as own licenses for software required for speech analyses.

Coding of neuroSHARE Study Questionnaire

The paper and pencil based neuroSHARE Study Questionnaires are delivered by the interviewer in person or postal mail to the Survey Agency during fieldwork. At the end of the fieldwork, the CaseCTRL/export data file will consist of pidcom ID, gender, year of birth, first name, date of

interview, interviewer ID, and answers to ne001 and ne002 questions. To this file the Survey Agency will match and code answers from the neuroSHARE Study Questionnaire for each respondent into a new neuroSHARE Study Questionnaire Data file in csv format, which will be stored in an encrypted form (using the RSA encryption). Data coding will be monitored by the SHARE-CZ team. The data file will not contain any contact information. The smell test recording booklet will be coded following the same methodology as in ELSA, HRS smell tests harmonised within the Gateway to Global Ageing. The RSA-encrypted neuroSHARE Study Questionnaire Data file will be transferred to SHARE-CZ secure server using the HTTPS transfer protocol as soon as it has been compiled by the Survey Agency after the end of the fieldwork.

Creating the final neuroSHARE Study Data File
The SHARE-CZ team will create the final neuroSHARE Study Data File by merging the neuroSHARE Study Questionnaire Data file with the neuroSHARE Study Speech Data file, using the common identifiers.

Delivery of the neuroSHARE Study Data file to SHARE-ERIC (SHARE Central)
SHARE-CZ team will upload the neuroSHARE Data File to the secure central SHARE server (SHARE Transfer server, which is run by SHARE Central and uses the HTTPS protocol) together with full documentation. The SHARE-CZ team will verify, clean, and deliver standard coded dta and csv files as well as STATA do files required for labelling data and full documentation. The SHARE Central team will merge the delivered data with the SHARE main Wave 10 data using the identifiers. This data will be made available to registered scientific researchers in accordance with the SHARE Conditions of Use in an anonymised form and without internal ID numbers. Only this released data may be used for research subsequently. The usage of any internal data for research purposes is prohibited.

6. Procedure for offering subsequent personal medical appointment in case of abnormal test results – NOT PART OF THE STUDY –

Selection of respondents for offer of the opportunity to attend a personal medical appointment
Selection of respondents with abnormal test results will be based solely on information contained in the neuroSHARE Study Data File. No other data from SHARE will be used.

The preliminary definition of abnormal results is: a) results outside 95% confidence interval for the speech test, b) test score of 5 or more for the RBDSQ sleep test, and c) identification of 3 or fewer scents in the smell test. These benchmarks will be fine-tuned so that approximately 5% of respondents will be invited for a personal medical appointment (approximately 150-180 respondents).

The selection will be conducted based on a statistical analysis run by SHARE-CZ team. Pidcom IDs of these selected respondents (with abnormal rest results) will be compiled by SHARE-CZ team and then be linked with the consent information contained in ne002. After this, a list of pidcom IDs of only those respondents with abnormal results who also answered “Yes” to question ne002 will be transferred to the Survey Agency using the HTTPS transfer protocol and subsequently be used by the Survey Agency to provide the contact information of these respondents (name and phone number) to the authorised staff at the FFM who are partners in the neuroSHARE project. The contact information will be encrypted (using the RSA encryption). This RSA-encrypted file will be transferred from the Survey Agency to a secure server at FFM using the HTTPS transfer protocol. The FFM secure server is located in a closed server room, which can only be accessed with a specific security token held only by authorised staff at the FFM who are partners in the neuroSHARE project.

Contacting Selected Respondents for the personal medical appointment
The authorised staff who are partners in the neuroSHARE project at the FFM will contact the selected respondents and offer the opportunity to attend a personal medical appointment. The selected respondents will not be contacted for any other purposes or other research projects. There will be a maximum of 8 attempts to contact and schedule an appointment for each selected respondent. In the case of a refusal to participate in the offered medical examination, a request to not be called again, a request for deletion of personal data, or a withdrawal of consent, the respondent will not be contacted

again. Respondents will be contacted within 1 year of the end of fieldwork. Each contact attempt and its result will be documented. The scheduling process will be monitored and supervised by the SHARE-CZ team.

The medical examination will be performed by an authorised neurologist at the FFM who is a partner in the neuroSHARE project. At the beginning of the personal medical appointment, the respondent will be asked for consent for the medical examination as a patient. The appointment, the medical examination and the outcomes of this personal appointment will not be a part of the SHARE study. FFM is fully responsible for these matters and may only contact the respondents in accordance with the procedures agreed in advance with SHARE-ERIC. SHARE-ERIC will not provide to the FFM any data collected in the SHARE survey or data collected during the neuroSHARE study (apart from the name and telephone number of the respondents as described above).

As a compensation for the costs and time related to the medical evaluation each respondent that takes part in the medical examination will receive an additional payment of 500 CZK. This payment will be administered by the authorised staff at the FFM who are partners in the neuroSHARE project. The payment will be in cash at the time of the examination.

The FFM is the most respectable faculty of medicine in the country and the General University Hospital in Prague is one of the largest and best-known hospitals in the Czech Republic. The Department of Neurology has large expertise in the diagnosis and treatment of Parkinson's disease and dementias. It is expected that respondents invited for personal medical appointment will appreciate this opportunity for a preventive examination.

Data separation of survey data from respondent contact data
Because the neuroSHARE Study follows immediately after the main SHARE CAPI interview without any additional contact procedures and information, each respondent's contact data are separated from the data collected as part of the neuroSHARE Study (in the same manner as this is the case in SHARE for all contact data). Only after the selection of respondents who also gave consent to be recontacted in question ne002, the Survey Agency will provide the contact information of these respondents (name and phone number) to the authorised staff at the FFM, who are partners in the neuroSHARE project. The contact information will be transferred in form of a RSA-encrypted file from the Survey Agency to a secure server at FFM using the HTTPS transfer protocol. This RSA-encrypted file will not contain any SHARE survey data or any other data collected as part of the neuroSHARE study.

7. MATERIALS, SAFETY AND INTERVIEWER TRAINING FOR THE NEUROSHARE STUDY

Material needed for the neuroSHARE Study
The neuroSHARE Study Questionnaire is developed and translated by SHARE-CZ and scientific partners. It will be printed by the Survey Agency and provided to interviewers at the beginning of the fieldwork. The Olfactory Sniffin' Sticks Set and related equipment (cotton gloves) will be purchased by the FFM and delivered to the Survey Agency. The Speech Test microphone, cables, and other equipment will be purchased by the CTU and delivered to the Survey Agency. The Speech Test App will be developed by the CTU, provided to the Survey Agency and installed on interviewer notebooks. The consent questions and the technical measures of copying required information from the CaseCTRL to the recording file will be developed and implemented by Centerdata. The teams at SHARE-CZ, CTU, and Centerdata will collaborate on the development of the software and IT solutions and implement them together with the Survey Agency.

Each interviewer will receive one set of smell test and one set of speech test equipment. The single set of all equipment items will last for the whole duration of the fieldwork. All equipment will be returned to the FFM (smell test equipment) and the CTU (recording equipment) after the end of fieldwork. The Survey Agency will be responsible for all other related material needs as envelopes, writing utensils, data storage equipment and other minor items.

Safety

There are no safety issues or risks associated with the neuroSHARE Study. All tests are non-invasive, do not involve the collection of biological materials, do not require physical activity, are performed while the respondent is seated, and occur in the same place as the main SHARE interview. All tests are either self-complete paper and pencil questionnaires or simple non-invasive smell and speech measurements performed by interviewers with special training (see below) led and supervised by experts of the Scientific Partners. All tests are validated, internationally accepted, and used procedures with no known risks or safety issues. The study is subject to review by the Ethics Committee of the General University Hospital.

Training of Interviewers

Interviewers are trained in depth to carry out the collection of the neuroSHARE Study and to perform the smell and speech tests. The interviewers will receive a specific training for neuroSHARE Study for several hours at the national training sessions (which are conducted prior to each SHARE data collection wave). Most of this time will be dedicated to supervised hands-on training sessions regarding the speech and smell tests.

SHARE-CZ and scientific partner researchers from FFM and CTU will personally educate and train the Survey Agency personnel (interviewers) and their instructors at the National Training Sessions. In particular, the scientific partners from CTU will instruct interviewers how to properly conduct the speech test, including how to connect and setup the microphone and how to use the Speech Test App.

Relevant Literature

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APPENDIX: NEUROSHARE STUDY QUESTIONNAIRE

See a separate document: neuroshare-questionnaire.pdf

APPENDIX: NEUROSHARE SHOWCARDS

SHOWCARD 1
1. Chamomile
2. Raspberry
3. Rose
4. Cherry

SHOWCARD 2
1. Smoke
2. Glue
3. Garlic
4. Grass

SHOWCARD 3
1. Orange
2. Blueberry
3. Strawberry
4. Onion

SHOWCARD 4
1. Bread
2. Fish
3. Cheese
4. Ham

SHOWCARD 5
1. Chive
2. Peppermint
3. Pine
4. Onion

SHOWCARD 6: SPEECH TEST READING TEXT

Když člověk poprvé vsadí do země sazeničku, chodí se na ni dívat třikrát denně: tak co, povyrostla už nebo ne? I tají dech, naklání se nad ní, přitlačí trochu půdu u jejích kořínků, načechrává jí lístky a vůbec ji obtěžuje různým konáním, které považuje za užitečnou péči. A když se sazenička přesto ujme a roste jako z vody, tu člověk žasne nad tímto divem přírody, má pocit čehosi jako zázraku a považuje to za jeden ze svých největších osobních úspěchů.

APPENDIX: NEUROSHARE SPEECH TEST RECORDING AND TRANSFER PROTOCOL

(Developed by Centerdata, FFM, CTU, SHARE-CZ and implemented by Survey Agency)

1. After the SHARE CAPI interview is completed, the CaseCTRL will automatically run two neuroSHARE consent questions: ne001 and ne002.The answers of the respondent will be entered and stored/documented in the CAPI.

2. For respondents who gave consent in ne001, the CaseCTRL will automatically start the Speech Test App. It will also copy important details from the CaseCTRL into the Speech Test App in the following manner: the audio file name consists of the pidcom ID and the date and time of the test, and an additional text file is created and stored together with the audio file, which will include the pidcom ID, gender, year of birth, first name of the respondent, date and time of the test, interviewer ID and the notebook ID.

3. The neuroSHARE Study starts with the smell test, followed by the sleep test and the speech test. All steps and procedures are described in the paper neuroSHARE Study Questionnaire. The cover page of the questionnaire will also contain the following information filled in by the interviewer: pidcom ID, gender, year of birth, first name, interviewer ID. Respondents' answers are recorded in the neuroSHARE Study Questionnaire by the interviewer. The Speech Test App cover screen also asks the interviewer to enter the same pidcom ID that is written on the cover page of the paper and pencil neuroSHARE Study Questionnaire (to match possible errors in the questionnaire).

4. At the end of the neuroSHARE Study, the speech test (consisting of five speaking tasks) is recorded by the Speech Test App. After the end of the speech test, the Speech Test App automatically closes and then encrypts (using the RSA encryption), zips and saves the neuroSHARE Study Speech File into a pre-specified folder.

5. While the neuroSHARE Study Questionnaire is delivered to the Survey Agency personally by the interviewer or by postal mail, the encrypted neuroSHARE Study Speech Files are transferred directly to the Czech Technical University (CTU) secure server using HTTPS transfer protocol. The transfer is initiated manually by the interviewer at the same time he or she synchronises of the main SHARE CAPI interview (frequency specified by the Survey Agency, at least twice a week). The transfer is administered by running the Speech Test App and selecting the transfer function. For a backup purposes, the neuroSHARE Study Speech Files are moved to a different folder on the interviewer's notebook with other backup files from the main SHARE CAPI interview.

6. The CTU secure server is located in a closed server room, which can only be accessed with a specific security token held only by authorised staff, who are partner in the neuroSHARE project. Each neuroSHARE Study Speech File will be analysed and coded into nine parameters and stored together with each respondent’s identifiers in a neuroSHARE Study Speech Data file. The neuroSHARE Study Speech Data file will not contain any contact information and will be encrypted (using the RSA encryption). This RSA-encrypted file will then be transferred to SHARE-CZ secure server using the HTTPS transfer protocol.

7. At the end of the fieldwork, the CaseCTRL/export data file will consist of pidcom ID, gender, year of birth, first name, date of interview, interviewer ID, and answers to ne001 and ne002 questions. With this file the Survey Agency will match and code answers from the neuroSHARE Study Questionnaire for each respondent into a new neuroSHARE Study Questionnaire Data file, which will be stored in an encrypted form (using the RSA encryption). The data file will not contain any contact information. The RSA-encrypted neuroSHARE Study Questionnaire Data file will be transferred to SHARE-CZ secure server using the HTTPS transfer protocol as soon as it has been compiled by the Survey Agency after the end of the fieldwork.

8. The SHARE-CZ team will create the final neuroSHARE Data File by merging the files of point 6. (neuroSHARE Study Speech Data file) and 7. (neuroSHARE Study Questionnaire Data file) using the common identifiers.

9a. Only the final neuroSHARE Data File will be used for selecting respondents to be recontacted in order to offer the opportunity to attend a personal medical appointment (expected: ca 5% of respondents). The selection will be conducted based on a statistical analysis run by SHARE-CZ team. Pidcom IDs of these selected respondents (with abnormal rest results) will be compiled by SHARE-CZ and then be linked with the consent information contained in ne002.

9b. After this, a list of pidcom IDs of only those respondents with abnormal results who also answered "Yes" to question ne002 will be transferred by SHARE-CZ to the Survey Agency using the HTTPS transfer protocol.

9c. This list will subsequently be used by the Survey Agency to provide the contact information of these respondents (name and phone number) in a RSA-encrypted file. This RSA-encrypted file will be transferred from the Survey Agency to a secure server at FFM using the HTTPS transfer protocol. This data transmission may only be initiated by the Survey Agency after explicit prior approval of SHARE-ERIC.

9d. The FFM secure server is located in a closed server room, which can only be accessed with a specific security token held only by authorised staff at the FFM who are partners in the neuroSHARE project. The authorised staff who are partners in the neuroSHARE project at the FFM will contact the selected respondents and offer the opportunity to attend a personal medical appointment. The appointment, the medical examination and the outcomes of this personal appointment will not be a part of the SHARE study. FFM is fully responsible for these matters and may only contact the respondents in accordance with the procedures agreed in advance with SHARE-ERIC.

10. SHARE-CZ team will upload the neuroSHARE Data File to the secure central SHARE server (SHARE Transfer server, which is run by SHARE Central and uses the HTTPS protocol) together with full documentation.

11. The SHARE Central team will merge the delivered data with the SHARE main Wave 10 data using the common identifiers. This data will be made available to registered scientific researchers in accordance with the SHARE Conditions of Use in an anonymised form and without internal ID numbers. Only this released data may be used for research subsequently. The usage of any internal data for research purposes is prohibited.