Besançon, March 31st 2021

Dear Committee,

Please find enclosed our submission for the 2021 Call for Research Proposals – Laboratories of the Fondation pour l'Audition, entitled

DASHES: *New data-driven techniques for the diagnosis, prognosis and rehabilitation of impairments of speech prosody perception in brain-stroke survivors*

The project is a collaboration between the psychoacoustics team of PI JJ Aucouturier (FEMTOST, Besancon) and the neurophysiology team of co-PI Lionel Naccache (Hôpital Pitié-Salpêtrière, Paris), and proposes to study impairments of speech prosodic perception in stroke survivors using a novel data-driven psychoacoustic technique, reverse correlation.

Our proposed research is highly relevant to hearing health and to the mission of the Fondation pour l'Audition. For stroke survivors, healthy hearing conditions their access to healthcare, communication with family, and positive physical and psychological outcomes. The project will both further our understanding of these conditions and provide new mobile clinical tools to improve their diagnosis and rehabilitation. Beyond stroke, the project will also provide a case-study for the application of reverse-correlation to general speech therapy practice, benefiting patients across the whole spectrum of hearing impairments.

We are deeply excited by this proposal, which optimally combines the skills of our two teams while also delivering a transformative outcome for hearing health in a condition affecting more than 100,000 persons every year in France alone. We hope you will agree, and thank you for your consideration.

Jean-Julien Aucouturier

Possible referees for the project include :

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2021 RESEARCH GRANT APPLICATION

TITLE of the PROJECT: DASHES: New data-driven techniques for the diagnosis, prognosis and rehabilitation of impairments of speech prosody perception in brain-stroke survivors

AMOUNT REQUESTED (€): 300k€ **Individual project** ☐ **Collaborative project** ☒

YEARS of SUPPORT: 1 ☐ 2 ☐ 3 ☒ **New submission** ☐ **Resubmission** ☒

Start date of the project: 01 Oct. 2021 **End date of the project:** 30 Sept. 2024

The undersigned have reviewed the present application, certify the statements herein are true, complete and accurate, have read the policies of FONDATION POUR L'AUDITION concerning research support and accept to comply with such policies if the present application is awarded.

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DATE & SIGNATURE: 31/03/2021

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DATE, SEAL of the INSTITUTION & SIGNATURE: 31/03/2021

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ABSTRACT

Hearing impairments concern up to 86% of brain-stroke survivors, a 38% excess compared to controls of the same age, yet stroke-related hearing is not as well studied as the more obvious symptoms of aphasia or motor loss. The objectives of project DASHES is to improve the diagnosis, prognosis and rehabilitation of hearing disorders in stroke survivors. Specifically, we aim to study impairments of speech prosodic perception using a novel data-driven psychoacoustic technique, reverse correlation.

To do so, the project will combine the psychoacoustical expertise of Jean-Julien Aucouturier (FEMTO-ST, Besançon) with the clinical expertise of Lionel Naccache (Hôpital Pitié-Salpêtrière, Paris). The project will, first, conduct a prospective diagnostic study on N=60 stroke patients and controls, in order to evaluate the relevance of reverse-correlation data as a marker of prosodic impairments. Second, the project will use this novel patient data for theoretical investigations such as lesion-symptom mapping, in order to better understand how prosodic processing differ between patients and controls. Finally, the project will develop a novel mobile audio-health platform to facilitate the adoption of the reverse-correlation procedure in clinical practice and to collect remote patient data to assist medical decision-making.

The rational of the reverse correlation technique is to uncover a listener's mental representation of certain prosodic patterns (e.g. the different intonation of "really?" vs "really!") by analysing a large set of responses to random stimuli. In our encouraging pilot data, we discovered that mental representations derived with reverse-correlation in stroke patients reveal processing abnormalities can be related to the aetiology of the lesion.

The expected results of the project are threefold: (1) we will provide a new tool able to diagnose stroke-related prosody impairments beyond existing gold standards, (2) we will provide a finer characterisation of symptomatological profiles in these patients and (3) we will provide a new prognosis metric, implemented in a mobile application, to quantify how well a patient reacts to speech therapy day after day.

These objectives are highly relevant to hearing health and to the mission of the FPA. For stroke survivors, healthy hearing conditions access to healthcare, communication with family, and positive physical and psychological outcomes. The project will both further our understanding of these conditions and provide new clinical tools to improve their diagnosis and rehabilitation. Beyond stroke, the project will also provide a case-study for the application of reverse-correlation to general speech therapy practice, benefiting patients across the whole spectrum of hearing impairments.

CO-INVESTIGATOR

The undersigned have reviewed the present application, certify the statements herein are true, complete and accurate, have read the conditions and policies of FONDATION POUR L'AUDITION concerning research support and accept to comply with such conditions and policies if the present application is awarded.		
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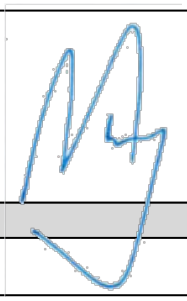
DATE & SIGNATURE:	*29-03-2021* 	
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DATE, SEAL of the INSTITUTION & SIGNATURE:	*29-03-2021* 	

Describe in a few words why support from FONDATION POUR L'AUDITION is critical for this project:

Support from FONDATION POUR L'AUDITION is critical for the project for three reasons. First, the proposal is a resubmission as a "*Laboratory*" proposal of a project previously accepted as part of the 2019 *PhD studentship* call (applicant: Mélissa Jeulin, co-supervised by JJ Aucouturier and Marie Villain), but which unfortunately couldn't proceed for administrative reasons (PhD applicant declined). This situation has left us without funding to proceed with the project, despite very encouraging pilot data.

Second, one of the project's co-applicant, Dr Marie Villain, is one of the country's only few speech-language pathologists with a PhD (Neuroscience, 2016). Because joint academic-clinical positions for speech therapists are still institutionally rare in France, Villain is currently holding a full-time clinical position in the APHP/Pitié-Salpêtrière Readaptation unit, which severely limits her time for the project, and research in general. Support from FONDATION POUR L'AUDITION will allow her to take a 2-year sabbatical (*disponibilité*) from her current position, and work as a postdoctoral fellow in Prof. Naccache's team, which will constitute an ideal context to develop her scientific and professional skills. Through the example of Marie, the project will offer a reflection on good practices on how to provide research training for speech therapists, and an institutional precedent to encourage scientific careers for speech therapists with the same profile.

Finally, the project coincides with PI JJ Aucouturier's relocation to the FEMTO-ST institute in Besançon, France. The institute has a strong record of development of health technologies, including innovations in robotics for ear surgery, but these developments have not been associated institutionally with the cause of hearing health. Support from FONDATION POUR L'AUDITION, which would constitute the first source of funding for Aucouturier's new team, would provide an impetus to develop a hearing health identity for the team and set the stage for similar projects across the FEMTO-ST institute.

Relevance for FPA's mission

Our objectives are highly relevant to hearing health. With 100,000 cases per year in France, stroke is the most common cause of neurological disability, and up to 86% of survivors are expected to develop hearing impairments.

The project fits closely with the FPA's mission to bring together research and clinical practice: (1) it will set up a novel collaboration between a researcher (Aucouturier) and a clinician (Naccache); (2) it will support two years of postdoctoral training for a speech therapist (Villain) aiming to pursue a joint academic-clinical career; and (3) it will allow the first-time application of a novel research technique, reverse-correlation, to the stroke clinical context.

The project also fits with the FPA's mission to provide broader access to screening with mobile applications such as Höra. Project DASHES will indeed develop its own mobile application for the rapid administration of reverse-correlation tests to patients.

Finally, beyond strokes, the project is a case-study for developing tools for a broader spectrum of patients, and which target not only low-level auditory skills but also our ability to comprehend emotional speech, to communicate expressively with peers and family and to enjoy music – all of which correspond to the fundamental mission of the FPA.

RESEARCH PLAN

A. SPECIFIC AIMS:

The broad, long-term objectives of project DASHES is to improve the diagnosis, prognosis and rehabilitation of hearing disorders in brain-stroke survivors. These objectives are highly relevant to hearing health. With 100,000 cases per year in France, stroke is the most common cause of neurological disability (Lecoffre et al., 2017), and **up to 86% of survivors are found to develop peripheral or central hearing impairments limiting their comprehension of speech and music, a 38% excess compared to controls of the same age (Koohi et al, 2017).** For stroke survivors even more than for the general population, healthy hearing conditions access to healthcare, communication with family, physical and psychological outcomes (Bullier et al, 2020).

Specifically, project DASHES aims to study impairments of speech prosodic perception in brain-stroke survivors using a novel data-driven psychoacoustic technique, reverse correlation (Ponsot et al, 2018; Goupil et al. 2021). The reverse correlation technique is able to uncover a listener's mental representation of certain prosodic patterns (e.g. "really?" vs "really!") by analysing a large set of responses to randomly-manipulated stimuli. Based on encouraging pilot data, the project will evaluate the relevance of reverse-correlation as a marker of prosodic impairments in speech therapy practice.

From a theoretical point of view, DASHES will improve our comprehension of the mechanistic bases of prosodic impairments in brain-stroke patients. Mental representations derived with reverse-correlation can reveal both morphological (ex. patients attending to the wrong part of a word) and computational abnormalities (ex. correct mental representations, but large amounts of sensory noise), both of which can be related to the aetiology or location of the lesion.

From a clinical point of view, DASHES will provide a new paradigm to diagnose prosody impairments beyond existing gold standards, provide a prognosis metric to quantify how well a patient reacts to speech therapy week after week, and develop a novel mobile audio-health platform to assist medical decision-making for these patients.

B. BACKGROUND AND SIGNIFICANCE:

a. Speech prosody and strokes

Consciously or not, we convey paraverbal information with our speech. The words and syntactic structures that we use reveal our attitudes, both towards the topic of conversation and towards the person we converse with. But besides words, the sole sound of our voice is also rich in information about our attitudes and emotional states (Gussenhoven, 2002): higher fundamental frequency/pitch when happy than sad, faster speech rate when excited, raising intonation/prosody when surprised or uncertain (Banse & Scherer, 1996; Goupil et al. 2021).

Following a stroke, our capacity to perceive linguistic or emotional prosody (i.e., the "melody" of speech) may be altered (Uekermann et al., 2008; Villain et al., 2016). **In a study of N=28 patients with right-hemisphere lesions, 15 (54%) were found impaired in prosodic comprehension, among whom 10 of them (35%) had otherwise relatively preserved discourse abilities (Côté et al. 2007).** Because of the "invisible" nature of this impairment, hearing deficits after stroke have not been as extensively studied as the more obvious symptoms of aphasia or motor loss. While many authors have proposed that prosodic functions are right-lateralized (Schirmer & Kotz, 2006), there is debate about the mechanisms that explain different types of impairments (selective impairments of prosodic perception may correspond to right STG lesions – Sheppard et al. 2020), different types of acoustical difficulties (pitch or rhythm, Shah, Baum & Dwivedi, 2006), or different time scales (local or global, Paulmann, 2015). It is therefore theoretically important to better characterize the mechanistic basis of prosodic impairments after stroke.

The current gold standard in clinical practice to evaluate aprosody in patients with right-hemisphere lesions is the Montreal battery for the Evaluation of Communication (MEC, Joanette, Ska & Côté, 2004). The 14 tasks of the MEC battery allows the systematic evaluation of four components of verbal communication (pragmatics, discourse, lexical-semantic and prosody), with good inter-rater reliability for all subtests, except – unfortunately – the one devoted to prosodic perception (Côté et al., 2007). In addition, the battery is plagued with a high-rate of false negative, and does not allow a fine characterization of the impairments (Aura, 2012). Other less common tools exist ("Battery of Emotional Expression and Comprehension" (Cancelliere & Kertesz, 1990); "Aprosodia Battery" (Ross, Thompson & Yenkosky, 1997) but they only concern emotional prosody (and not the equally important "linguistic" prosody of e.g., interrogative or declarative sentences), and have never been validated in French.

It is therefore clinically important to develop metrics that are more sensitive and more versatile to assess perceptive prosodic impairments in these patients.

Current treatments for aprosodia have mostly applied two different approaches: imitative, in which clinicians provide a model of the target sentence; and cognitive–linguistic, in which individuals are provided cues about the perceptual characteristics of each emotional tone (Rosenbek et al. 2004). However, several factors make the comparative evaluation of these interventions difficult and medical decision-making suboptimal regarding treatment options (Benedetti et al. 2021). First, as already noted, we lack standardized tests that are sensitive and flexible enough to assess perceptive prosodic impairments, including small progressive changes within a patient. Second, the fact that interventions often have a delayed effect on patients makes them difficult to assess immediately after the intervention, especially with highly-fatigable patients such as stroke survivors. Finally, functional improvements are best measured in the patient's home environment, but we lack tools to do so.

A second clinical gap filled by the project is to provide a mobile application for the fast assessment of prosodic impairments which can be used remotely, in the patient's home environment, to monitor recovery from symptoms and assist medical decision-making regarding speech therapy interventions.

b. Reverse-correlation, a promising strategy to evaluate prosody perception in patients with right-hemisphere lesions

In our recent work (Ponsot et al., *PNAS* 2018; Goupil et al. *Nature Communications* 2021), we demonstrated the use of a novel data-driven paradigm (reverse-correlation) to uncover healthy participant's mental representation of specific prosodic judgements.

To do so, we developed a voice-processing algorithm able to manipulate the temporal pitch dynamics of arbitrary recorded voices in a way that is both fully parametric and realistic (Burred et al. 2019). We then used this technique to generate thousands of new, natural-sounding variants of the same word utterance, for instance a recording of the word "really", each with a randomly manipulated pitch contour. We then asked human listeners to evaluate hundreds of pairs of such random pronunciations, deciding in each pair which sounds e.g. most interrogative. By superposing the random prosodic profiles of the utterances that were chosen in each pair, we were able to reconstruct the participants' mental representation of what constitutes an interrogative prosody for this word: a final rise of the pitch on the second syllable of the word, as shown in Figure 1.

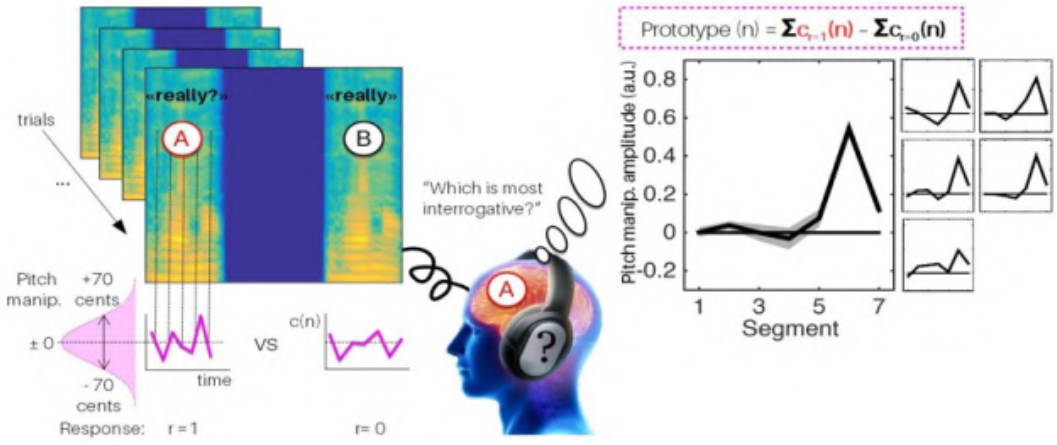


*Figure 1. Accessing mental representations of interrogative prosody by using reverse correlation. (**Left**) Utterances of the same word "vraiment" ("really") were digitally manipulated to have random pitch contours. Participants were presented pairs of manipulated words and judged which was most interrogative. (**Right**) Prosodic mental representations, or prototypes, were computed as the mean pitch contour of the voices perceived as interrogative ("really?"), minus those judged declarative ("really."). As predicted, the prototypes associated with interrogative judgments showed a clear pitch increase at the end of the second syllable, which was observable both in averaged and in individual prototypes.*

Mental representations derived with reverse-correlation present important advantages for clinical application.

1. they can be robustly determined at the level of the individual patient (see the near-identical replication of the overall pattern in five healthy participants in Figure 1), and thus allows correlation with individual metrics and etiology for the purpose of diagnosis.
2. they can be measured at regular intervals, allowing the prognostic study of symptom evolution.

3. they offer a qualitative insight into the patient's cognitive process, revealing if a patient e.g. pays attention to different parts of a word than healthy controls, and this information can be used to assist medical decision-making for these patients.
4. finally, they have excellent test-retest reliability and they can be extracted relatively efficiently from a small number of sound comparisons, a property we will use to build a mobile hearing-health platform to monitor the day-by-day recovery profiles of patients undergoing rehabilitation.

C. PRELIMINARY STUDIES

The study of Ponsot et al. (2018) provides normative data about the mental representations of interrogative prosody for a group of n=15 healthy adults. In addition, we have conducted a pilot study on a group of n=9 right hemisphere stroke patients, and n=11 matched controls.

This preliminary data revealed several key insights that motivate the present application (Figure 2):

1. there was a large, significant difference between the mental representation of interrogative prosody of controls and patients, which indicates that our measure is sensitive to the pathology (Figure 2A).
2. there were considerable individual variations among patients, some of which had mental representations that had similar morphological features (i.e. final rising intonation) as controls (Figure 2B-top), and others having strongly abnormal representations (e.g. expecting a rise on the first syllable, Figure 2B-bottom), which suggests that the measure is sensitive to individual patient characteristics
3. the distance between a given patient's representation and that of the control group scaled as a function of some clinical indicators, such as the severity of the lesion (indexed here as the number of months post-stroke at which a patient is included in the study, Figure 2C), which suggests that the measure is sensitive to characteristics that are clinically relevant, and
4. there were significant differences between a given patient's representations measured in successive weekly sessions, which suggests the measure would be able to track improvements or degradation of the patient's mental representations (ex. Figure 2D, patient 3 moving from a significantly degraded representation in week 1 to a normal representation in week 3).

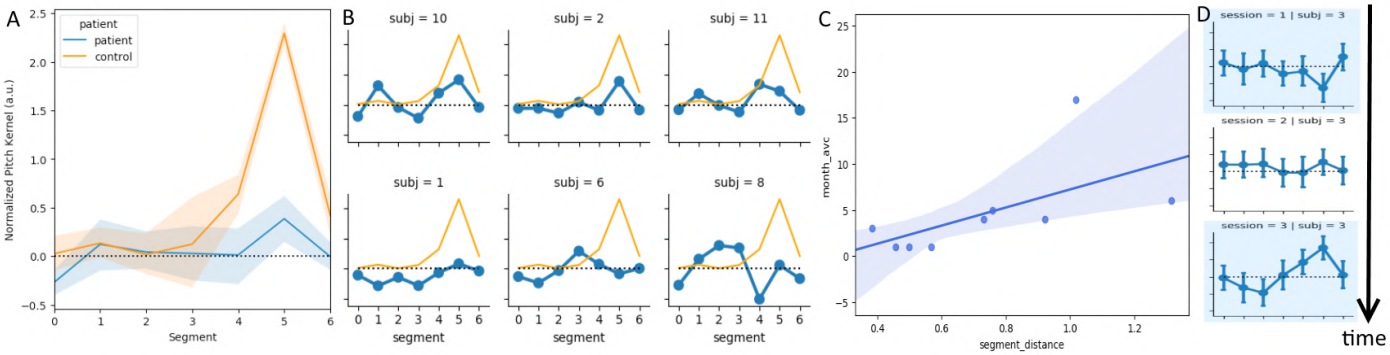


Figure 2: Preliminary data on the mental representations of interrogative prosody extracted by reverse-correlation in a group of n=11 controls (orange), and n=9 stroke patients (blue). ***A:*** *group averaged of the representations.* ***B:*** *individual patient data, compared to control group, for a subset of 6 patients. Top: close to normal representations; bottom: abnormal representations.* ***C:*** *the distance between a patient's representation and that of the control group scales as a function of lesion severity, indexed by number of month post-stroke at the time of inclusion.* ***D:*** *Weekly representations for patient 3, measured on three consecutive weeks.*

D. RESEARCH DESIGN AND METHODS

WP1. Validation study

The first objective of the project is to validate the reverse-correlation methodology as a tool to discriminate between right-hemisphere stroke patients with and without prosodic impairment.

Design: prospective diagnostic research study, in a national multicentric manner, non-randomized, with a control group.

Recruitment will be conducted at the Service de Médecine Physique et Réadaptation, Pitié-Salpêtrière Hospital (Paris), at the Saint-Louis – Lariboisière – Fernand Widal Hospital (Paris), as well as in several associated centers. Inclusion period will be 24-months, during which we aim to collect data from a minimum of 60 patients.

Inclusion criteria: supratentorial right-hemisphere ischaemic and haemorrhagic brain stroke (1st episode), confirmed with imagery, and dating less than 1y at the time of inclusion; right-handedness; age > 18yo; French native language; affiliated to *Securité Sociale*; signed informed consent

Exclusion criteria: declined consent, language comprehension deficits (score < 10/15 on the BDAE instruction following task), disorders of wakefulness/consciousness, dementia, severe dysarthria, psychiatric antecedents (>2 months in-patient), major visual or auditory impairment (> 40dB HL)

Procedure: Patients will be presented with 150 pairs of pronunciations of the word “vraiment” (which can be understood either as interrogative – “vraiment ?” - or declarative – “vraiment !”) manipulated with random pitch variations on 6 segments of 71ms. Patients will be asked to detect within each pair the variant that sounds most interrogative. Sounds will be delivered dichotically, with identical headphones (Beyerdynamics DT770), at a comfortable loudness level (~70dB SPL) for all patients and controls.

Analysis: Patient data will be analysed using the procedure of Ponsot et al. (2018), by subtracting the average pitch profile of sounds recognized as declarative (i.e. words that were not chosen in each pair) from the average pitch profile of sounds recognized as interrogative (i.e. words chosen in each pair). This profile constitutes the mental representation that each patient has for an interrogative pronunciation of the word “vraiment”. We will then compute the distance between each patient’s profile to the average profile of the control group (cf. Figure 2C), and use this criterion as diagnostic.

Novelty: The procedure and analysis to extract mental representation for prosody are world-unique, being recently developed for healthy participants by the project’s partners (Ponsot et al., 2018; Goupil et al. 2021) and have never before been applied to characterize hearing deficits in stroke patients.

Feasibility: The feasibility of WP1 is excellent. The procedure has already been validated on patients of the same population (see C. PRELIMINARY STUDIES, above). We estimate the recruitment in WP1 of ca. 20 patients meeting our inclusion criteria per year in each of the centers, amounting to 40 patients per center during the 24-month inclusion period. As a reference, our pilot study recruited 9 patients in only 3 months. We have obtained ancillary funding from DGOS (PHRIP ProsAVC 2020-2024) covering the administrative part of data collection.

Expected results: to characterize the distribution of the diagnostic criteria in the general population on the one hand, and in a group of patients on the other hand, and to show that the two distributions can lead to the definition of a threshold allowing to discriminate patients without prosody impairments from patients with aprosody. Our preliminary data suggests good discriminative power between groups on the basis of this criteria (Figure 3), which we will confirm by including more patients and establish a pathological threshold. We will use the MEC inguistic and emotional prosody comprehension and production subtasks as references, despite their known limitations.

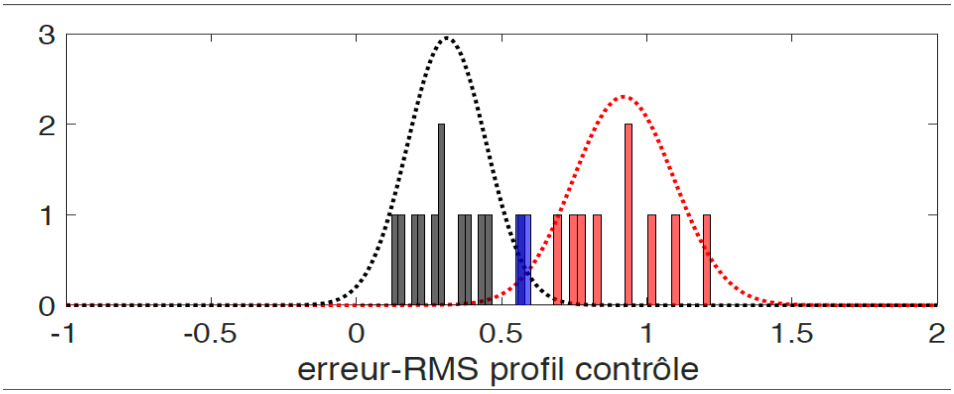


Figure 3: Distribution of a diagnostic criteria defined as the distance between an individual's mental representation to the mental representation of a control group, as extracted by reverse correlation. Represented here in a group of healthy controls (grey) and a group of right-hemisphere stroke patients (red), from our preliminary data.

Potential difficulties and solutions: Many factors can underlie impaired pitch processing in neurological disorders, even in the absence of measurable loss of audibility using typical audiometric tests (Russo et al. 2008). It is possible that mental representations in the patient group exhibit variations that are non specific to prosodic processing, but rather indicative of e.g. auditory attention, central or peripheric auditory processing, and that this diversity impairs the diagnosticity of our criteria for prosodic deficits. To

control for this possibility, we will also test patients for a greater diversity of auditory symptomes, including amusia (MBEA, Peretz, Champod & Hyde, 2003), anxiety and depression (Hospital Anxiety and Depression Scale, Zigmond & Snaith, 1983), auditory attention (LAMA, Ambert-Dahan et al, 2013), central auditory deficits (AIRTAC2, Del-Fabro & Desmons, 2014) and auditory threshold (audiograms), and use hierarchical cluster analysis to group participants according to similarities in their results on these tasks.

Importance for the broad long-term objectives: It is expected that the diagnostic criteria derived by reverse-correlation will be more sensitive and more versatile than the existing gold-standard (MEC) to assess prosodic impairments in patients.

Ethics: Ethical approval for the study was obtained from CPP IDF5, Decision of 22/07/2020.

WP2. Computational modeling

A secondary objective of the project will use data collected as part of WP1 for subsequent theoretical investigations aiming to derive computational models of prosodic processing in patients and controls.

1) Computational modeling of trial-to-trial responses

Contrary to healthy participant data, our pilot study has shown that patient reverse-correlation data can be noisy, because of frequent drifts of attention and perseverations (Gandola et al. 2013). In addition, to improve the acceptability of the method, it is important to optimize the duration of the test (currently set at 150 trials for patients vs 700 trials for healthy participants) because patients are more fatigable than controls. This objective uses data collected in WP1 to improve the robustness and speed of the procedure to compute mental representations.

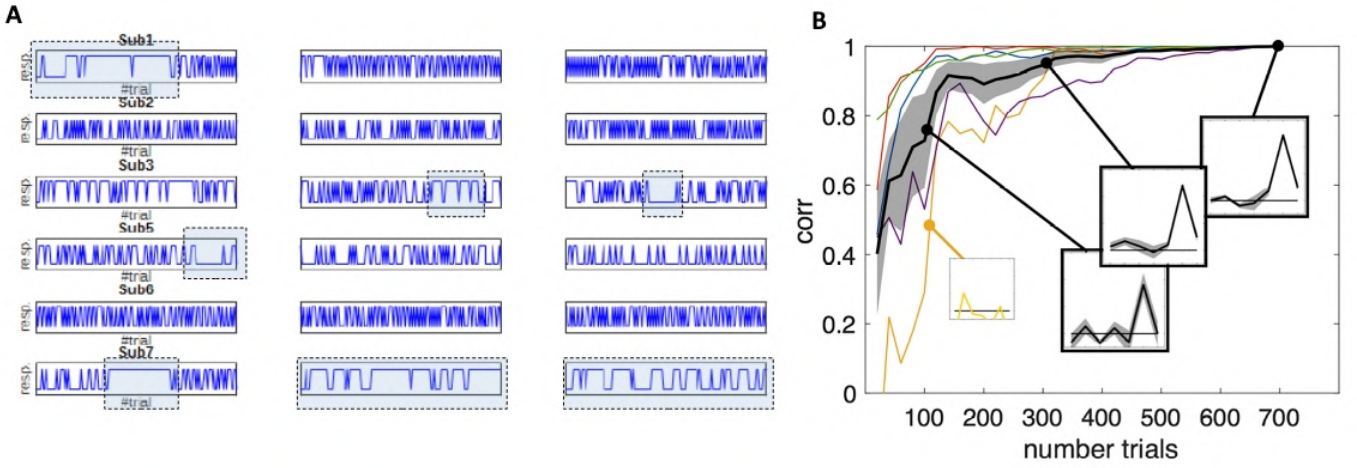


Figure 4: Computational modeling of trial-to-trial responses. ***A-left:*** *Example series of patient responses from pilot data (series of 150 successive trials; 2 response value corresponding to first or second sound in the pair), showing episodes of pathological choice perseverations, highlight in blue.* ***B-right****: Correlation between the mental representation derived using the n first trials of pilot data in healthy controls, and the mental representation derived using all trials (n = 700; compare with Figure 1). These curves reflect the "speed" at which our measure converges toward the final mental representation estimate. Insets show temporary kernels at stages n = 100, n = 300 and n = 700, averaged across subjects in black line, and for the subject with the slowest convergence in yellow. Figure adapted from Burred et al. 2019.*

Design and procedure: Secondary analysis of patient data collected in WP1

Analysis: To improve the robustness of the procedure, we will design an algorithm to detect perseverations in patient data (Figure 4-left). To do so, we will estimate the internal noise of the system (Neri, 2010) on successive time-windows and only include for analysis the windows for which internal noise is below a certain threshold, to be determined from data.

To improve the speed of the procedure to compute mental representations, we will use patient data to extract the smallest number of trials needed to obtain informative representations. To do so, we will compute the correlation of the representation extracted after trial #i for all i from 1 to 150 (the maximum number of trials collected in WP1), and use the average inflection point from the resulting curve as the optimal number of trials (Figure 4-right).

Novelty: While choice perseverations in value-based decision making have been studied for healthy controls (Senftleben et al. 2019), currently no procedure exists to model and detect pathological perservation in psychophysical data. Additionally, no procedure exists to optimize the duration of reverse-correlation tests for fatigable patients.

Feasibility: Feasibility is excellent, as the WP involves computational analyses with large degree of freedom on data that is already collected as part of WP1. Modeling efforts can be initiated before completion of WP1, on the basis of incomplete pilot data.

Expected results: A more robust and faster experimental procedure to estimate mental representations, to be used in the mobile application of WP3.

Potential difficulties and solutions: The analytical approaches listed above may not work, for instance because data analysis shows no clear cut-off to reject perseverations or stop the procedure early. Computational alternatives would be many, including using generalized linear models (Knoblauch & Maloney, 2008) and priors (Mineault, Barthelme & Pack, 2009) to estimate a final mental representation based on incomplete or noisy trial data.

Importance for the broad long-term objectives: Improving the speed/robustness of the procedure is important to make it acceptable for patients and facilitate its adoption into routine clinical speech therapy.

Ethics: Use of data for such analyses is covered by the WP1 ethical approval (CPP IDF5, Decision of 22/07/2020)

2) Symptom-lesion mapping

While many authors have proposed that prosodic functions are right-lateralized (Schirmer & Kotz, 2006), there is debate about what type of lesion explain what types of prosodic impairment (Sheppard et al. 2020). This objective aims to combine the patient data collected as part of WP1 with patient MRI records, in order to seek associations of representational abnormalities with specific temporo-frontal lesion sites.

Design and procedure: Secondary analysis of patient data collected in WP1

Analysis: We will use the voxel-based lesion–symptom mapping procedure (Bates et al. 2003) to analyze the relationship between tissue damage and behavior on a voxel-by-voxel basis. Patients' lesions will be reconstructed onto templates by a neurologist based on patient records collected at the acute stage of the stroke. For each voxel, patients will be divided into two groups according to whether they have or don't have a lesion affecting that voxel, and reverse-correlation metrics will be compared for these two groups, yielding a t-statistic (or chi-square) for each voxel. We will map several reverse-correlation metrics, including differences in the diagnostic criteria of WP1 (distance to controls), amount of internal noise, and occurrence of different morphologies in representations (e.g. rising pitch at the beginning vs at the end) as extracted by hierarchical clustering, as well as the other non-reverse-correlation metrics (e.g. MEC, amusia, etc.) measured in WP1.

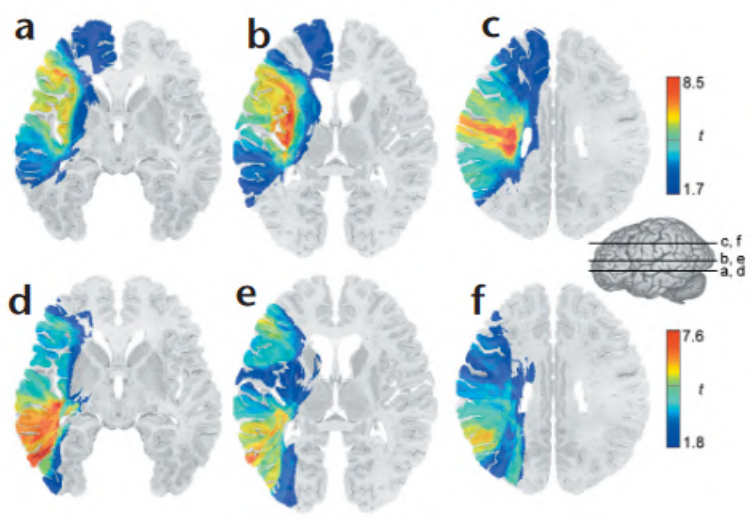


Figure 5: Example of voxel-based lesion–symptom mapping between left hemisphere lesions and measures of fluency (a–c) or auditory comprehension (d–f). High t-scores (red) indicate that lesions to these voxels have a highly significant effect on behavioural measures. Figure adapted from Bates et al. 2003.

Novelty: Only one study to our knowledge has attempted lesion-symptom mapping for prosodic impairments in right-hemisphere strokes, and has done so using a limited number of regions of interest and a custom test of emotional prosody recognition (Sheppard et al. 2020). The present study will be first to map reverse-correlation metrics, with a potential to highlight the mechanistic contribution of certain lesion sites.

Feasibility: Good feasibility, as the number of patients included for WP1 (N=60) is consistent with the sample size used in similar recent lesion-symptom studies (ex. N=63 in Faulkner & Wilshire, 2020; N=41 in Patel et al., 2018). Patients will systematically have MRI scans at inclusion for WP1. Ethical documents (CPP) foresees that the data from these examinations can be used as part of the study.

Expected results: Lesion maps showing correlation with reverse-correlation outcomes, expected to e.g. map the diagnostic criteria of WP1 to regions critical to prosodic comprehension.

Potential difficulties and solutions: One potential difficulty is statistical (lack of sensitivity, inflated false alarm rate), for which we can investigate nonparametric alternatives to the standard t-test or chi-square approaches (Rorden, Karnath & Bonilha, 2007). Another potential risk is that reverse-correlation metrics do not have clearly localised lesion associations, yielding non-significant maps. This risk will be alleviated by also studying lesion-symptom maps with the other non-data-driven metrics collected as part of WP1, such as the MEC gold standard which has never been studied with this technique either.

Importance for the broad long-term objectives: Localizing specific reverse-correlation outcomes to lesion sites will both advance our mechanistic understanding of the neural bases of prosodic comprehension, but also improve diagnosis at the acute stage of the strokes, when lesions identified in certain sites could be used to evaluate the risk and nature of subsequent prosodic impairments.

Ethics: Use of data for the study is covered by the WP1 ethical approval (CPP IDF5, Decision of 22/07/2020)

WP3. Mobile application development and testing.

A final objective of the project is to use the insights generated by WP1 and WP2 to develop a novel mobile audio-health platform to help the adoption of the procedure in clinical practice, and to collect remote patient data to assist medical decision-making.

Design: We will build a prototype Android application, available for both tablets and smartphone mobile platforms, able to administer the reverse-correlation test via headphones. The tool will use the optimizations for speed and robustness identified in WP2, in order to offer a quick procedure (<10min.). The sounds and user interface of the tool will be customizable to allow testing for more diverse reverse-correlation tasks (e.g. emotional prosody) than the sole word “vraiment” and the sole perception of interrogative prosody used for assessment in WP1. The tool will be designed to be used during speech therapy sessions (thus relaying the research apparatus used in the data collection of WP1, as soon as ready), or in autonomy by the patient in their home environment. The tool will also have the option to give performance feedback to the patients, thus acting both a tool for remote monitoring/evaluation and training/rehabilitation. Patient results (e.g. day-by-day profile of performance) will be made available remotely to their caregivers (e.g. speech therapists) via an online portal.

Figure 6: Mockup of the mobile application designed to administer the reverse-correlation test during speech therapy sessions (left) and remotely, in the patient’s home environment (right).

Procedure: The tool will be tested on a group of N=10 patient volunteers undergoing speech therapy at the Pitié-Salpêtrière rehabilitation center using the same inclusion criteria as WP1. Patients will be instructed to use the tool for evaluation everyday for a period of 4 weeks, encompassing at least 3 speech therapy sessions.

Analysis: We will collect evaluations of useability from the patients, as well as usefulness from the speech therapists. The performance of the tool will be tested as a proof of concept, but its formal clinical validation is outside the scope of the project and will be the object of subsequent applications for funding.

Novelty: While mobile tools for hearing health screening in the general-population have recently been introduced (incl. the FPA's own application Höra), no such mobile platform exists to measure profiles of recovery for prosodic comprehension in the patient's home environment.

Feasibility: Development of the application can start early, without waiting for completion of WP1 and WP2 and a first version non-optimized for speed will relay the research apparatus used for WP1 as soon as ready. Assessment of useability and usefulness will be conducted in collaboration with Romain Gombert, dir. Living Lab, Brain and Spine Institute, Pitié-Salpétrière Hospital (Paris), an expert in the design and assessment of health technologies and software user interfaces for rehabilitation.

Expected results: A prototype mobile application ready to graduate to formal clinical validation, and to form the basis of a subsequent commercialization plan in the form of a product or startup.

Potential difficulties and solutions: Development of the mobile application presents no difficulty, and will be able to rely on existing open-source packages for collecting experience-sampling data on mobile phones (e.g. mobileQ: Meers et al. 2020).

Importance for the broad long-term objectives: The tool will facilitate the adoption of the reverse-correlation procedure in clinical practice and foster the collection of additional patient data beyond the objectives of the project. In addition, remote monitoring of patient's recovery profiles (e.g. daily over the acute stroke period) will assist speech therapist for their medical decision-making and help the systematic evaluation of interventions for aprosodia, which often have delayed effects which are difficult to assess immediately after the intervention, and will benefit from continuous remote monitoring.

Ethics: The tool will be tested for useability, and non-interventionally, with patient volunteers on the basis of a simple consent form. Ethical clearance for a formal interventional study is beyond the scope of the project.

E. DELIVERABLES

WP1. Validation study

D1. Anonymized reverse-correlation data for N=60 patients, matched with standard assessment (MEC, MBEA, HADS, LAMA, AIRTAC2) and clinical record (incl. MRI scans for WP2)

D2. Report / research article on the diagnosticity of reverse-correlation distance to control group as a biomarker of prosodic perception deficits

WP2. Computational modeling

D3. Publication of a more robust and faster algorithm to estimate mental representations, to be used in the mobile application of WP3.

D4. Report / research article on lesion-symptom mapping of prosodic deficits

WP3. Mobile application development

D5. Version 1 of mobile application with no optimization, to relay the research apparatus used in WP1

D6. Version 2 of mobile application including the optimization of D3.

D7. Report / research article on useability evaluation of the mobile applications

F. LEADERSHIP PLAN

The project combines the computational and psychoacoustic expertise of PI JJ Aucouturier (FEMTO-ST Institute, Besançon) with the clinical expertise in neurology and speech therapy of co-PI L. Naccache and project personnel M. Villain (ICM/Hôpital Pitié-Salpêtrière, Paris).

JJA will coordinate the project, supervise the methodological developments in WP1, the computational analyses in WP2, and the application development in WP3. LN and MV will supervise clinical data collection in WP1 and the application testing in WP3.

Members of the project are highly complementary, with expertise in all key levels of the evaluation of prosodic processing in controls and patients (Ponsot et al., 2018; Goupil et al., 2021; Villain et al., 2016), and have a successful history of collaboration prior to the project, incl. the co-supervision of 3 MSc theses.

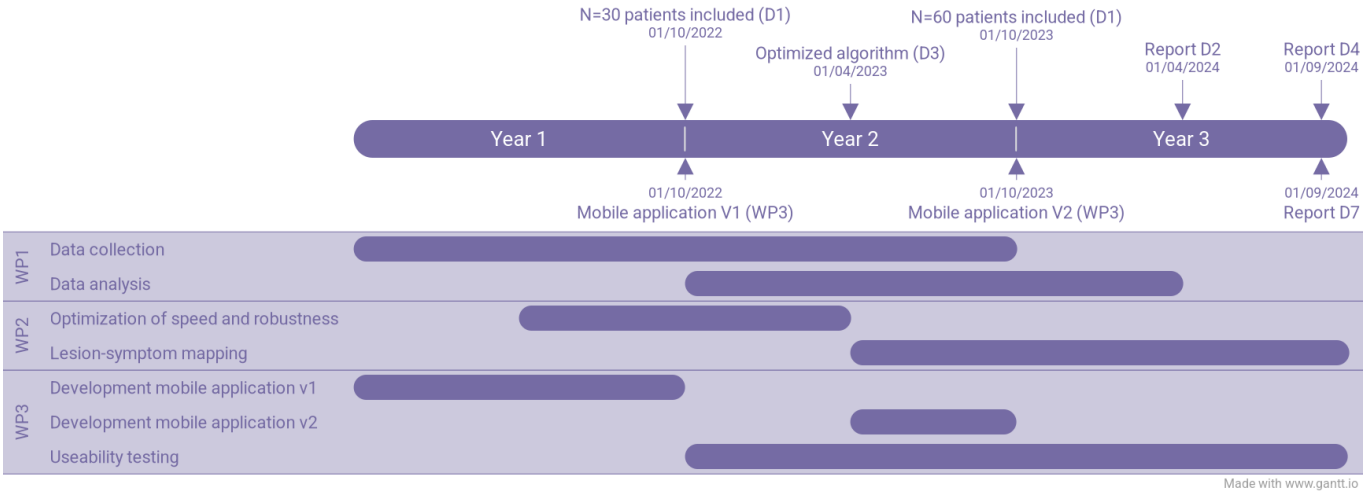
G. RESUBMISSION

The proposal is a new submission as a "*Laboratory*" proposal of a project previously accepted as part of the 2019 *PhD studentship* call (applicant: Mélissa Jeulin, co-supervised by Aucouturier and Villain), but which couldn't proceed for administrative reasons. We applied for ethical committee clearance (CPP) at the end of year 2019, but the application was delayed by the outset of SARS-Cov2 in the early months of 2020. This in turn delayed the start of the studentship to the point that the applicant had to decline it, cancelling the funding.

We are therefore resubmitting the project in the form of a 'laboratory" application. We are convinced that the project remains highly topical and even more feasible in its current form because (1) we have now obtained CPP clearance ahead of the present application (CPP IDF5, Decision of 22/07/2020), and (2) we have obtained ancillary funding from DGOS (PHRIP ProsAVC 2020-2023) covering the administrative part of data collection (patient management, ARC, insurance, etc.).

Finally, the present proposal is also new and improved from the 2019 studentship application in that (1) we have combined forces with neurologist Lionel Naccache, an expert in the physiological investigation of cognitive impairments and (2) the project coincides (as of Jan. 2021) with the relocating of Aucouturier's team to health-technology institute FEMTO-ST in Besançon, providing a new and improved context for the computational modeling aspects of the work, as well as its eventual *valorisation* in clinical technology at the end of the project.

H. TIMELINE



I. LITERATURE CITED

Publications co-authored by project members appear in bold.

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- **Benedetti, V., Reggio, E., Weill-Chounlamountry, A., Pradat-Diehl, P. & Villain, M. (2021) Assessment tools and rehabilitation treatments for aprosodia following acquired brain injury: a systematic review. International Journal of Language and Communication Disorders (in review)**
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- **Ponsot, E., Burred, JJ., Belin, P. & Aucouturier, JJ. (2018) Cracking the social code of speech prosody using reverse correlation, Proceedings of the National Academy of Sciences. Vol. 115 (15) 3972-3977.**
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REBUTTAL (if applicable)

The proposal is a new submission as a "*Laboratory*" proposal of a project previously accepted as part of the 2019 *PhD studentship* call (applicant: Mélissa Jeulin, co-supervised by Aucouturier and Villain), but which couldn't proceed for administrative reasons.

There was no reviewer comments to address from the initial submission. We nevertheless improved on the original project on several points, which are described in section **G. RESUBMISSION** above.

In addition, the following points were brought to our attention in the invitation letter issued on the basis of this year's pre-proposal, and we took great care to address them in the present document:

Clarify the prevalence of prosodic problems in stroke survivors and try to make some estimate of prevalence that will help establish significance of research

Previous studies reveal that prosodic disorders after stroke are frequent, in both expressive and/or receptive modes. A recent review by co-authored by project member Marie Villain estimates that between 50–78% of right hemisphere stroke survivors have one or more deficits in communication. As an example, in a study of N=28 patients with right-hemisphere lesions by Côté et al. (2007), 15 (54%) were found impaired in prosodic comprehension. Strikingly, among these 15 patients, 10 (35%) had otherwise relatively preserved discourse abilities, which explains that these symptoms, while frequent, often appear "invisible" and are less extensively studied than the more obvious symptoms of aphasia. These clarifications were provided on page 5 of the present proposal.

Document what is the excess of hearing disorders in stroke survivors compared with other people of the same age-match

With 100,000 cases per year in France, stroke is the most common cause of neurological disability (Lecoffre et al., 2017). Up to 86% of survivors are found to develop peripheral or central hearing impairments limiting their comprehension of speech and music (Koohi et al, 2017). This is a 38% excess compared to controls of the same age. These numbers also appear on page 5.

Provide more detail for the proposed rehabilitation program for WP3. "Proposed strategies" is not an acceptable phrase in a grant proposal.

We apologize for the brevity of our description for WP2 and WP3 in the pre-proposal. We have now fully expanded our proposal for both workpackages and, for each, committed to explicit analytical strategies (incl. alternative strategies to be used in case of difficulty).

The objectives of WP2 are:

1. to optimize the speed and robustness of the reverse-correlation procedure, on the basis of data collected in WP1, and in the perspective of the mobile platform to be built in WP3. Our proposed strategy to do so is described on page 9 of the present proposal.
2. To conduct a lesion-symptom study on the basis of data collected in WP1, combined with MRI scans of the lesion collected from the patient's clinical record. Our proposed analytical strategy to do so is described on page 10.

The objectives of WP3 have also been clarified: WP3 aims to develop a novel mobile audio-health platform (an Android application for tablets and smartphones) which is designed to be used

1. during speech therapy sessions (thus relaying the research apparatus used in the data collection of WP1, as soon as possible in the project), and
2. in autonomy by the patient in their home environment, for the remote monitoring of recovery from symptoms in between speech therapy sessions.

We have included a timeline for development of the application, as well as clear objectives for its evaluation, on page 12.

We thank you for these comments which, in our view, gave us the opportunity to clarify and strengthen our initial proposal.

PRINCIPAL INVESTIGATOR'S BIOGRAPHICAL SKETCH – TEAM A

Name & Degree: Jean-Julien AUCOUTURIER, PhD, HDR

Position: Directeur de recherche CNRS, Cognitive Science

A. Education, Training, Positions & Honors

Positions

- Since 2021: **Directeur de recherche CNRS** (section 7), FEMTO-ST Institute (UMR6174), CNRS/Université de Bourgogne-Franche-Comté/ENSMM/UTBM (Besançon, France).
- 2012-2020: **Chargé de recherche CNRS** (section 7), Sciences et Technologies de la Musique et du Son (STMS UMR9912), IRCAM/CNRS/Sorbonne Université (Paris, France).
- 2011–2012: **Ingénieur de recherche contractuel** au Laboratoire d'Etude de l'Apprentissage et du Développement (LEAD UMR5022), Université de Bourgogne (Dijon, France).
- 2008–2011: **Tenure-track Assistant Professor** (équiv. *maître de conférence*) à Temple University (Philadelphie, PA/ Tokyo/Japon).
- 2008–2011: **Chercheur contractuel** au Biolinguistics laboratory, RIKEN Brain Science Institute (Wako, Japon).
- 2006–2008: **Postdoctorant JSPS** à l'Institute of Physics, University of Tokyo (Japon).
- 2003–2006: **Chercheur assistant** au SONY Computer Science Laboratory (Paris, France).

Education

- 2017-2018: **Diplôme Inter-universitaire de Neurophysiologie Clinique**, Faculté de Médecine de Lille (France).
- Nov. 2017: **Habilitation à diriger des recherches**, Faculté d'Ingénierie de l'Université Pierre et Marie Curie (Paris, France). Titre : *"L'apport des sciences et technologies du son à la recherche en sciences cognitives"*.
- 2014–2015: **Certification postgraduate de neuroanatomie**, Neurocourses, King's College University of London (Londres, UK).
- 2001–2006: **Doctorat d'Informatique**,(mention très honorable) de l'Université Paris VI (Paris, France). Titre : *"Dix expériences sur la modélisation du timbre musical"*.
- 2000–2001: **MSc. Audio and Music Processing**, Dept. of Electrical and Electronic Engineering, King's College University of London (Londres, UK).
- 1998–2001: **Diplôme d'ingénieur**, Traitement du signal. École Supérieure d'Électricité (Supélec - Rennes, France).

Academic Prizes and distinctions

- **Prix scientifique :** Lauréat du Prix d'Émergence Scientifique, catégorie recherche fondamentale de la Fondation pour l'Audition, Nov. 2018. https://www.youtube.com/watch?v=toHbRQMHB-w
- **Best-paper awards**: International Conference on Music Information Retrieval (ISMIR), Porto, Portugal, Oct. 2012;Workshop on Music and Artificial Life, European Conference on Artificial Life (ECAL), Lisbon, Portugal, Sept. 2007.
- **Concours logiciel :** Première place (avec Elias Pampalk), MIREX evaluation, ISMIR 2006.
- **Bourses** : Association des Journalistes Scientifiques de la Presse d'Information (AJSPI), Bourse d'échange, 2014 ; Japanese Society for the Promotion of Science (JSPS) Postdoctoral Fellowship for Foreign Researcher, 2006-2008 ; Arts & Humanities Research Council Postdoctoral (UK) Fellowship, 2006 ; Agence Nationale de la Recherche et de la Technologie (ANRT), Bourse CIFRE, 2003-2006 ; British Council Foundation Graduate Scholarship, 2000-2001 ; Fondation Georges Besse, Bourse, 2000.

B. Peer-Reviewed Publications

1. Goupil, L., Ponsot, E., Richardson, D., Reyes, G. & Aucouturier, JJ. (**2021**) Listeners perception of certainty and honesty of another speaker is associated with a common prosodic signature. *Nature Communications*, in press.
2. Arias, P., Rachman, L., Liuni, M. & Aucouturier, JJ. (**2020**). Beyond Correlation: Acoustic Transformation Methods for the Experimental Study of Emotional Voice and Speech. *Emotion Review*, 1-13.
3. Arias, P., Soladié, C., Bouafif, O., Roebel, A., Séguier, R. & Aucouturier, JJ. (**2020**) Realistic manipulation of facial and vocal smiles in real-world video streams. *IEEE Transactions on Affective Computing*, Vol. 11(3)
4. Guerrier, G., Lellouch, L., Liuni, M., Vaglio, A. Rothschild, P-R., Baillard, C. & Aucouturier, JJ. (**2019**) Vocal markers of pre-operative anxiety: a pilot study, *British Journal of Anaesthesia,* Vol. 123, Issue 4, Pages e486–e488.
5. Burred, J. J., Ponsot, E., Goupil, L., Liuni, M., & Aucouturier, JJ. (**2019**). CLEESE: An open-source audio-transformation toolbox for data-driven experiments in speech and music cognition. *PLoS One*, 14(4), e0205943.
6. Goupil, L. & Aucouturier, JJ. (**2019**) Musical pleasure and musical emotions (Commentary on Ferreri et al., 2019). *Proceedings of the National Academy of Sciences*, Vol. 116 (9), 3364-336628.
7. Arias, P., Belin, P. & Aucouturier, JJ. (**2018**) Auditory smiles trigger unconscious facial imitations. *Current Biology*. Vol. 28 (4), PR782-R783.
8. Ponsot, E., Burred, JJ., Belin, P. & Aucouturier, JJ. (**2018**) Cracking the social code of speech prosody using reverse correlation, *Proceedings of the National Academy of Sciences*. Vol. 115 (15) 3972-3977
9. Rachman, L., Liuni, M., Arias, P., Lind, A., Johansson, P., Hall, L., Richardson, D., Watanabe, K., Dubal, S. and Aucouturier, J.J. (**2017**) DAVID: An open-source platform for real-time transformation of infra-segmental emotional cues in running speech. *Behaviour Research Methods*. Vol. 50 (1), pp 323–343..
10. Aucouturier, J.J., Johansson, P., Hall, L., Segnini, R., Mercadié, L. & Watanabe, K. (**2016**) Covert Digital Manipulation of Vocal Emotion Alter Speakers' Emotional State in a Congruent Direction. *Proceedings of the National Academy of Sciences*, vol. 113 no. 4

PERSONNEL INVOLVED in the PROJECT – TEAM A
TO BE FUNDED by the PROJECT

Name & Degree	Date of birth	Position	Institution	email
To be recruited	n/a	PhD student	CNRS	n/a

NOT FUNDED by the PROJECT

Name & Degree	Date of birth	Position	Institution	email
Aucouturier, Jean-Julien, PhD	14-06-1979	Directeur de recherche CNRS	CNRS / FEMTO-ST institute	aucouturier@gmail.com

PERSONNEL'S BIOGRAPHICAL SKETCH – TEAM A

The project will support the hiring in Team A of **one PhD student**, working on the methodological developments in WP1, the computational analyses in WP2, and the application development in WP3. The applicant, who is yet to be recruited, will typically hold a Master of Science in cognitive science, with expertise in computational modeling for psychophysics or cognitive neuroscience.

DESCRIPTION OF THE RESEARCH ENVIRONMENT – TEAM A

The FEMTO-ST Institute in Besançon (UMR6174, Université de Bourgogne Franche-Comté / CNRS) is one of the country's largest technological research unit, with 700 researchers spanning all fields of engineering and system science, and an internationally-recognized hub for health technology, incl. robotic medical devices, biomechanics and neuroscience. https://www.femto-st.fr/fr

The team of PI JJ Aucouturier is part of FEMTO-ST Dept. of Automatic control and Robotics (AS2M), which research activity encompasses research on innovative robotic architecture for e.g. medical applications, computational modeling for complex systems, and automatic pronostics for environmental and physiological systems.

The team offers an excellent environment for the project, incl. access to a complete EEG neurophysiology lab equipped with audiometry cabins, access to state-of-art computational modeling software, as well as an ecosystem of colleagues working on related system-science topics. FEMTO-ST also boasts excellent support for the eventual "*valorisation"* of clinical technology at the end of the project, with integration in the TEMIS Santé startup studio.

GLOBAL BUDGET – YEAR 1 – TEAM A

		Name	% Effort	Annual Base Salary (€)	Project Salary (€)	Project Fringe Benefits (€)	TOTAL (€)
	FPA	PhD student	100	40,585	40,585	-	40,585
	NON FPA	JJ Aucouturier	30	112,697	33,809	-	33,809
				SUBTOTALS:			74,394
SUPPLIES							215
EQUIPMENT							2500
TRAVEL							4000
TOTAL COSTS							81,109
REQUESTED FPA CONTRIBUTION			in Euros				**47300**
			in % of the TOTAL COSTS				58%

GLOBAL BUDGET – YEAR 2 (if applicable) – TEAM A

		Name	% Effort	Annual Base Salary (€)	Project Salary (€)	Project Fringe Benefits (€)	TOTAL (€)
	FPA	PhD student	100	40,585	40,585	-	40,585
	NON FPA	JJ Aucouturier	30	112,697	33,809	-	33,809
				SUBTOTALS:			74,394
SUPPLIES							215
EQUIPMENT							1,000
TRAVEL							10,000
TOTAL COSTS							85,609
REQUESTED FPA CONTRIBUTION			in Euros				**51,800**
			in % of the TOTAL COSTS				61%

GLOBAL BUDGET – YEAR 3 (if applicable) – TEAM A

		Name	% Effort	Annual Base Salary (€)	Project Salary (€)	Project Fringe Benefits (€)	TOTAL (€)
	FPA	PhD student	100	40,585	40,585	-	40,585
	NON FPA	JJ Aucouturier	30	112,697	33,809	-	33,809
				SUBTOTALS:			74,394
SUPPLIES							215
EQUIPMENT							2,100
TRAVEL							8,000
TOTAL COSTS							84,709
REQUESTED FPA CONTRIBUTION			in Euros				**50,900**
			in % of the TOTAL COSTS				60%

GLOBAL BUDGET SUMMARY – TEAM A

TEAM A		YEAR 1	YEAR 2	YEAR 3	ENTIRE PROJECT
PERSONNEL		74,394	74,394	74,394	223,182
SUPPLIES		215	215	215	645
EQUIPMENT		2500	1,000	2,100	5,600
TRAVEL		4000	10,000	8,000	22,000
TOTAL COSTS		81,109	85,609	84,709	251,427
REQUESTED FPA CONTRIBUTION	in Euros	**47300**	**51,800**	**50,900**	**150,000**
	in % of TOTAL COSTS	58%	61%	60%	60%

GLOBAL BUDGET JUSTIFICATION FORM – TEAM A

Personnel

The project will support the hiring in Team A of **one PhD student**, working on the methodological developments in WP1, the computational analyses in WP2, and the application development in WP3. Total CNRS cost, base 2021: 38,783.39 year 1; 40,579.05 year 2; 41,390.64 year 3 (2% yearly increase to cover for increase in social costs, as confirm to CNRS accounting practices).

PI JJA will devote 30% full-time to the coordination of the project and the supervision of the PhD student. His salary, charged 112,697€ annually (DR2 CNRS), will be supported by CNRS and is not part of budget requested to the FPA.

Supplies

Supplies include small audio equipment (cables, microphone, etc.) and small computer equipment (adapters, etc.), est. 215€ yearly

Equipment

Equipment in year 1 includes one laptop workstation for the PhD student (2,000€) and test equipment for the development of the mobile application (1 phone, 1 tablet; 500€); total: 2,500€
Equipment in year 2 includes3 tablets for the deployment of the mobile app in the test centers responsible for WP1 (1,000€)
Equipment in year 3 includes an additional 7 tablets to be let to patients, for the user tests of WP3 (2,100€)
Total project: 5,600€

Travel

Travel in year 1 includes coordination meetings in Paris for JJA and the PhD student (250€ x 2 people x 4 times yearly; 2,000€) and one 3-week research stay in Besançon for Marie Villain (2,000€). Total: 4,000€.
Travel in year 2 includes coordination meetings at the same rate (2,000€), a second 3-week research stay in Besançon (2,000€), as well as travel for 2 international conferences such as ARO 2023 and EAN 2023 (1500€ x 2 people 2 meetings; 6,000€). Total: 10,000€
Travel in year 3 includes coordination meetings (2,000€) and travel for 2 international conferences such as ARO 2024 and EAN 2024 (1500€ x 2 people 2 meetings; 6,000€). Total: 8,000€

CO-INVESTIGATOR'S BIOGRAPHICAL SKETCH – TEAM B

Name & Degree: Lionel NACCACHE, M.D., PhD, HDR

Position: Professor (1st Class PU-PH) of Physiology, head of the PICNIC Lab team (ICM)

A. Education, Training, Positions & Honors

Positions

- Since2015– **Head of Clinical Neurophysiology Department** – Pitié Salpêtrière Hospital, Paris, France
- Since 2014 – **Head of PICNIC** (Physiological Investigations of Clinically Normal and Impaired Cognition) **Lab research team** at the ICM (UMRS, INSERM U1127), Paris, France
- Since 2013 – **Member of the French National Ethical Committee** (CCNE)
- Since 2010 – **Professor of Physiology** in the Department of Physiology, Faculty of Medicine, Paris 6 University, Paris, France
- Since 1999 – **Consulting neurologist** at the Clinical Neurology Department – Pitié Salpêtrière Hospital, Paris, France

Education

Scientific studies

- 2005 **HDR** (Habilitation to Conduct Researches), Paris 6 University, Paris, France
- 2002 **PhD of Neuroscience** with cum laude - Paris 6 University, Paris, France
- 1996 **Master of Neurobiology** (former DEA) – Paris 6 University, Paris, France
- 1988-1992 **Scholarship at the Ecole Normale Supérieure** (Ulm/Sciences), Paris, France

Medical Studies

- 1998 Certification of Neurologist - Paris 5 University, Paris, France
- 1998 Medical Degree (MD) - Paris 5 University, Paris, France
- 1994-1998 Residency in Neurology - Paris 5 University, Paris, France

Academic Prizes and distinctions

- Nominated **member of the Dana Alliance for Brain Initiatives** (DABI) (2019)
- **Prize of Ethics** Pierre Simon "Ethique et réflexion" (2017)
- **Grand Prize Lamonica of Neurology**, French Academy of Sciences (2016)
- **Prize Le Goff**, Lemonon, Houry, Laveran, French Academy of Sciences (2011)
- **Prize Diderot-Curien** of A.M.C.S.T.I. (2011)
- **Recipient of the Research Investment Reward** since 2010
- **Invited Professor at the Royal Academy of Science**, Bruxelles, Belgium (2009)
- **Nominated « Rising Star of Psychology »** by the Association of Psychological Science, USA
- **Fellowship at the Summer Institute in Cognitive Neuroscience** (Dartmouth, USA ,1999)
- **FRM fellowship** for DEA (Master) in Neuroscience (1996)

- **Fellowship at MICEFA Exchange Program**: Summer research work at UCSF, USA (1989)

B. Peer-Reviewed Publications

1. Rozier, C., T. Seidel Malkinson, D. Hasboun, M. Baulac, C. Adam, K. Lehongre, S. Clemenceau, V. Navarro, and L. Naccache. (**2020**) Conscious and unconscious expectancy effects: A behavioral, scalp and intracranial electroencephalography study. *Clin Neurophysiol*, 2020. **131**(2): p. 385-400.
2. Demertzi, A., E. Tagliazucchi, S. Dehaene, G. Deco, P. Barttfeld, F. Raimondo, C. Martial, D. Fernandez-Espejo, B. Rohaut, H.U. Voss, N.D. Schiff, A.M. Owen, S. Laureys, L. Naccache, and J.D. Sitt. (**2019**) Human consciousness is supported by dynamic complex patterns of brain signal coordination. *Sci Adv,* 5(2):p. Eaat7603.
3. Bourdillon, P., B. Hermann, M. Guenot, S. J.D., H. Bastuji, J. Isnard, and L. Naccache, (**2019**) Slow cortico-cortical connectivity (2-5Hz) is a new robust signature of conscious states*. BioRxiv*.
4. Axelrod, V., C. Rozier, T.S. Malkinson, K. Lehongre, C. Adam, V. Lambrecq, V. Navarro, and L. Naccache. (**2019**), Face-selective neurons in the vicinity of the human fusiform face area. *Neurology*, 2019. **92**(4): p. 197-198
5. Bourdillon, P., B. Hermann, S. J.D., and L. Naccache,(**2019**) Electromagnetic brain stimulation in patients with disorders of consciousness*. Frontiers in Neuroscience*, **13**.
6. Velly, L., V. Perlbarg, T. Boulier, N. Adam, S. Delphine, C.E. Luyt, V. Battisti, G. Torkomian, C. Arbelot, R. Chabanne, B. Jean, C. Di Perri, S. Laureys, G. Citerio, A. Vargiolu, B. Rohaut, N. Bruder, N. Girard, S. Silva, V. Cottenceau, T. Tourdias, O. Coulon, B. Riou, L. Naccache, R. Gupta, H. Benali, D. Galanaud, and L. Puybasset (**2018**) Use of brain diffusion tensor imaging for the prediction of long-term neurological outcomes in patients after cardiac arrest: a multicentre, international, prospective, observational, cohort study*. The Lancet. Neurology*, **17**(4): p. 317-326.
7. Naccache, L. (**2018**), Why and how access consciousness can account for phenomenal consciousness*. Philos Trans R Soc Lond B Biol Sci*, **373**(1755).
8. Naccache, L. (**2018**), Minimally conscious state or cortically mediated state? *Brain*, **141**(4): p. 949-960.
9. Raimondo, F., B. Rohaut, A. Demertzi, M. Valente, D.A. Engemann, M. Salti, D. Fernandez Slezak, L. Naccache, and J.D. Sitt (**2017**) Brain-heart interactions reveal consciousness in noncommunicating patients. *Ann Neurol*, 82(4): p. 578-591.
10. Sergent, C., F. Faugeras, B. Rohaut, F. Perrin, M. Valente, C. Tallon-Baudry, L. Cohen, and L. Naccache (**2017**) Multidimensional cognitive evaluation of patients with disorders of consciousness using EEG: A proof of concept study*. Neuroimage Clin*, 13: p. 455-469.

PERSONNEL INVOLVED in the PROJECT – TEAM B

TO BE FUNDED by the PROJECT

Name & Degree	Date of birth	Position	Institution	e-mail
Marie Villain, PhD	18/03/85	Postdoctoral fellow	Institut du Cerveau	marie.villain@aphp.fr

NOT FUNDED by the PROJECT

Name & Degree	Date of birth	Position	Institution	e-mail
Lionel Naccache, PhD	27/03/1969	PUPH	Institut du Cerveau	lionel.naccache@gmail.com

PERSONNEL'S BIOGRAPHICAL SKETCH – TEAM B

The project will support two years of postdoctoral training for speech therapist Marie Villain, who will take an unpaid sabbatical (*disponibilité*) from her full-time clinical position to devote her time to the project.

Name & Degree: Marie VILLAIN, PhD

Education :

- 2016 : Qualification aux fonctions de Maître de Conférence en Neurosciences
- 2013 – 2016: Doctorat en Neurosciences au sein du laboratoire « Neuroimagerie et Cognition Humaine » (INCIA Bordeaux, CNRS 5287)
- 2005 – 2009: Ecole d'orthophonie, UPMC

Positions :

- Since 2017 : **Orthophoniste** service de Médecine Physique et Réadaptation (Pitié-Salpêtrière)
- Since 2013 : **Chargée d'enseignement** à l'école d'orthophonie de Paris et Bordeaux et M2 Recherche et Organisation en Santé
- 2016 – 2018 **Orthophoniste** en cabinet libéral à Levallois-Perret
- 2013 – 2016 **Orthophoniste** service de Médecine Physique et Réadaptation (CHU Bordeaux)
- 2010 – 2013 **Orthophoniste** pôle neurologie (Unité de Soins Intensifs Neuro-Vasculaires et service de neurologie) hôpital de Poissy (78)

Peer-Reviewed Publications

1. A. BEN SALAH, P-F. PRADAT, M. VILLAIN, A. BALCERAC, P. PRADAT-DIEHL, F. SALACHAS, L. LACOMBLEZ, E. BAYEN **(2020)** Anosognosia in amyotrophic lateral sclerosis: a cross-sectional study of 85 individuals and their relatives. *Annals of physical and rehabilitation medicine*
2. H. ROBERT, M. VILLAIN, C. PREVOST-TARABON, M. COCQUELET-BUNTING, B. GLIZE, P. PRADAT-DIEHL, E. BAYEN **(2020)** Ecological assessment of numerical skills in adults suffering from left stroke. *Annals of physical and rehabilitation medicine*. S1877-0657
3. M. VILLAIN, I. SIBON, M. POLI, P. RENOU, J. SWENDSEN **(2020)** Depression and routinization following stroke. *Revue Neurologique*.

4. E. BAYEN, F. STEFANESCU, H. ROBERT, A. WEILL-CHOUNLAMOUNTRY, M. VILLAIN, C. GOURIOU, P. PRADAT-DIEHL **(2020)** Will participation restrictions related to the COVID-19 lockdown boost inclusivity? *Annals of Physical and Rehabilitation Medicine.*
5. B. BULLIER, H. CASSOUDESALLE, M. VILLAIN, M. COGNE, C. MOLLO, I. DE GABORY ... & B. GLIZE **(2020)** New factors that affect quality of life in patients with aphasia. *Annals of physical and rehabilitation medicine*. 63(1), 33-37
6. B. GLIZE, A. BIGOURDAN, M. VILLAIN, *et al.* (**2019**) Motor evoked potential of upper-limbs is predictive of aphasia recovery. *Aphasiology*, vol. 33, no 1, p. 105-120.
7. M. VILLAIN, C. COSIN, B. GLIZE, S. BERTHOZ, J. SWENDSEN, I. SIBON, W. MAYO (**2016**) Affective prosody and depression after stroke: a pilot study. *Stroke*. 47(9):2397-400
8. B. GLIZE, M. VILLAIN, L. RICHERT, M. VELLAY, I. DE GABORY, J.M. MAZAUX, P. DEHAIL, M. LAGANARO P.A. JOSEPH (**2016**) Language features in the acute phase of post-stroke severe aphasia could predict the outcome. *European J of Physical and Rehabilitation Medicine.*
9. M. VILLAIN, I. SIBON, P. RENOU, M. POLI, J. SWENDSEN (**2016**) Very early social support following mild stroke is associated with emotional and behavioral outcomes three months later. *Clin Rehab*. 1-7.
10. M. VILLAIN, C. TARABON-PREVOST, E. BAYEN, H. ROBERT, B. BERNARD, E. HURTEAUX, P. PRADAT-DIEHL (**2015**) Ecological Assessment Battery for Numbers (EABN) for brain-damaged patients: Standardization and validity study. *Annals of physical and rehabilitation medicine*, 58(5), 283-288.

DESCRIPTION OF THE RESEARCH ENVIRONMENT – TEAM B

The Brain and Spine Institute (Institut du cerveau et de la moelle épinière; ICM) hosts more than 600 researchers, engineers and technicians conducting basic or clinical research on the brain and neurological (Alzheimer's disease, Parkinson's disease, epilepsy, stroke, etc.) or psychiatric diseases (Dementia, depression, etc.) as well as on the spinal cord (paraplegia, quadriplegia, etc.).It has been housed since 2010 on the site of the Pitié-Salpêtrière Hospital in Paris. https://institutducerveau-icm.org/en/

The PICNIC lab (Physiological investigation of clinically normal and impaired cognition), codirected by Laurent Cohen, Lionel Nacache and Paolo Bartolomeo, explores the neural bases of cognitive functions in humans. They work with both healthy and brain-damaged persons, using behavioral methods and brain imaging (anatomical, functional and diffusion-based MRI, EEG, MEG, intracerebral recordings).

The team offers excellent environment for the project, incl. access to a full panel of brain imaging techniques, as well as close interaction with the clinical units of Hôpital Pitié-Salpétrière such as the Service de Médecine Physique et de Réadaptation, where patients for WP1 and WP3 will be included.

GLOBAL BUDGET – YEAR 1 – TEAM B

		Name	% Effort	Annual Base Salary (€)	Project Salary (€)	Project Fringe Benefits (€)	TOTAL (€)
	FPA	Marie VILLAIN	100	59,500	59,500	-	59,500
	NON-FPA	Lionel NACCACHE	20	152,994	30,599	-	30,599
				SUBTOTALS:			90,099
SUPPLIES							200
EQUIPMENT							9,400
TRAVEL							7,000
TOTAL COSTS							106,699
REQUESTED FPA CONTRIBUTION			in Euros				**76,100**
			in % of the TOTAL COSTS				71%

GLOBAL BUDGET – YEAR 2 (if applicable) - TEAM B

		Name	% Effort	Annual Base Salary (€)	Project Salary (€)	Project Fringe Benefits (€)	TOTAL (€)
	FPA	Marie VILLAIN	100	59,500	59,500	-	59,500
	NON-FPA	Lionel NACCACHE	20	152,994	30,599	-	30,599
				SUBTOTALS:			90,099
SUPPLIES							200
EQUIPMENT							0
TRAVEL							7,000
TOTAL COSTS							97,299
REQUESTED FPA CONTRIBUTION			in Euros				**66,700**
			in % of the TOTAL COSTS				68%

GLOBAL BUDGET – YEAR 3 (if applicable) - TEAM B

		Name	% Effort	Annual Base Salary (€)	Project Salary (€)	Project Fringe Benefits (€)	TOTAL (€)
	FPA	-	-	-	-	-	0
	NON-FPA	Lionel NACCACHE	20	152,994	30,599	-	30,599
				SUBTOTALS:			30,599
SUPPLIES							200
EQUIPMENT							0
TRAVEL							7000
TOTAL COSTS							37,799
REQUESTED FPA CONTRIBUTION			in Euros				7,200
			in % of the TOTAL COSTS				19%

GLOBAL BUDGET SUMMARY – TEAM B

TEAM B		YEAR 1	YEAR 2	YEAR 3	ENTIRE PROJECT
PERSONNEL		90,099	90,099	30,599	**210,797**
SUPPLIES		200	200	200	**600**
EQUIPMENT		9,400	0	0	**9400**
TRAVEL		7,000	7,000	7000	**21,000**
TOTAL COSTS		106,699	97,299	37,799	241,797
REQUESTED FPA CONTRIBUTION	in Euros	**76,100**	**66,700**	**7,200**	**150,000**
	in % of TOTAL COSTS	71%	68%	19%	62%

GLOBAL BUDGET JUSTIFICATION FORM – TEAM B

Personnel

The project will support the hiring in Team B of one postdoctoral fellow (Marie Villain), for two years. Villain will supervise the patient studies in WP1 and WP3, as well as co-supervise Team A's PhD student with PI JJA. Total ICM cost (3-5 years experience): 59,500€.

Co-PI LN will devote 20% full-time to the supervision of the postdoctoral fellow. His salary, charged 152,994€ annually (PUPH Classe Exceptionnelle), will be supported by APHP and is not part of budget requested to the FPA.

Supplies

Supplies include small audio equipment (cables, microphone, etc.) and small computer equipment (adapters, etc.), est. 200€ yearly

Equipment

Equipment in year 1 includes one laptop workstation for the postdoctoral fellow (2,000€), 3 laptops fitted with the reverse-correlation test (6,000€) and 3 audio set-up (research-grade headphones, audio sound card; 1,400€) for the patient study in WP1; total: 9,400€
No equipment cost for Team B in year 2 and 3
Total project: 9,400€

Travel

Travel in all 3 years for Team B includes coordination meetings in Besançon for Naccache and Villain (250€ x 2 people x 2 times yearly; 1,000€) and travel for 2 yearly international conferences such as ARO and EAN (1500€ x 2 people x 2 meetings; 6,000€). Total: 7,000€
Total project: 21,000€

OVERALL GLOBAL BUDGET

		YEAR 1	YEAR 2	YEAR 3	ENTIRE PROJECT
TEAM A		81,109	85,609	84,709	251,427
TEAM B		106,699	97,299	37,799	241,797
TOTAL COSTS		187,808	182,908	122,508	493,224
REQUESTED FPA CONTRIBUTION	in Euros	**123,400**	**118,500**	**58,100**	**300,000**
	in % of TOTAL COSTS	66%	65%	47%	61%

LAY SUMMARY *(in English and French)*

See guidelines

Les Accidents Vasculaires Cérébraux (AVC) sont la première cause de handicap acquis chez l'adulte et peuvent entraîner à différents niveaux, une altération du traitement auditif. Dans les suites d'un AVC droit, on observe fréquemment des difficultés de perception de la prosodie, correspondant aux variations de rythme, d'intensité et de hauteur du son qui permettent de transmettre des informations au-delà des mots. C'est par exemple, ce qui permet de comprendre qu'on est en train de nous poser une question, de percevoir l'ironie de notre interlocuteur ou encore de sentir que la personne qui nous parle est en colère. Ces troubles sont encore mal connus et nous manquons d'outils d'évaluation et rééducation efficaces. Pourtant, les conséquences pour les patients souffrant de tels troubles peuvent être importantes puisque ces habiletés sont essentielles dans les relations sociales et peuvent ainsi limiter la reprise d'activité professionnelle notamment. Nous disposons actuellement de données concernant les représentations mentales de la prosodie chez les sujets sains et nous avons débuté des évaluations similaires auprès de patients ayant subi un AVC. Cette première étude a permis d'observer des différences importantes entre les perceptions des patients et celles des sujets témoins. Il s'agit donc d'une perspective intéressante pour un meilleur dépistage. L'objectif de ce projet est de poursuivre les évaluations auprès des patients dans le but de mieux comprendre d'où viennent leurs difficultés, d'analyser les différents profils de performances afin de pouvoir proposer des rééducations orthophoniques ciblées et efficaces dans la mesure où nous manquons d'outils d'évaluation et de moyens thérapeutiques à l'heure actuelle.

Strokes are the first cause of acquired disability in adults and can lead to a variety of hearing impairments. Following a right-hemisphere stroke, we frequently observe difficulties in perception of prosody, corresponding to variations in rhythm, intensity, and pitch of the sound that make it possible to transmit information beyond words. For example, this allows us to understand that we are asking ourselves a question, to perceive the irony of our interlocutor or to feel that the person who speaks to us is angry. These disorders are still poorly understood and we lack effective assessment and rehabilitation tools. However, the consequences for patients suffering from such disorders can be significant since these skills are essential in social relations and can thus limit the return to job. We currently have data on the mental representations of prosody in healthy subjects and we have started similar assessments with stroke patients. This pilot study found significant differences between patient and control perceptions. This is an interesting prospect for better screening. The aim of this project is to continue the assessments with stroke patients in order to better understand the mechanism underlying their difficulties, to analyze the variety of performance profiles in order to be able to offer targeted and effective speech therapy assessments and interventions.

RESEARCH SUPPORT – TEAM A

See guidelines

1. ACTIVE, APPROVED or COMPLETED GRANTS related to the present proposal

n/a

2. PENDING GRANTS related to the present proposal

n/a

3. GRANTS UNRELATED to the present proposal

Agence Nationale de la Recherche
Intitulé : Rétroaction faciale et linguistique et États de stress traumatiques (REFLETS)
Rôle : Responsable scientifique, partenaire (coord. : Catherine Soladié, CentraleSupélec).
Durée, financement : 2017-2020, 650k€
Partenaires : CentraleSupélec (Rennes, France), IRCAM (Paris, France), IRBA (Paris, France), Chanel (Paris, France).

ERC Starting Grant
Intitulé : Cracking the Emotional Code of Music (CREAM n.335536)
Rôle : Coordinateur / PI
Durée, financement : 2014-2019, 1500k€
Partenaires : STMS (Paris, France) ; Brain and Spine Institute (Paris, France).

PEPS IDEX/CNRS
Intitulé : Voice morphing (MaVOIX)
Rôle : Responsable scientifique, partenaire (coordinateur : Jean-Luc Rouas, LaBRI)
Durée, financement : 2013, 15k€
Partenaire : *LaBRI (Bordeaux, France), STMS (Paris, France)*

Agence Nationale de la Recherche
Intitulé : Sensory & Emotional Processing in Autism (SEPIA)
Rôle : Responsable scientifique, partenaire (coord. : Marie Gomot, Tours).
Durée, financement : 2020-2024, 450k€
Partenaires : iBrain (Tours, France), IRCAM (Paris, France)

ERC Proof of Concept
Intitulé : Amplifying the commercial value of conversation with voice technology (ACTIVATE)
Rôle : Coordinateur / PI
Durée, financement : 2020-2021, 150k€
Partenaires : *STMS (Paris, France)*

RESEARCH SUPPORT – TEAM B

1. ACTIVE, APPROVED or COMPLETED GRANTS related to the present proposal

Direction Générale de l'Offre de Soins (DGOS)
Intitulé : PHRIP ProsAVC : Evaluation de la prosodie réceptive suite à un AVC droit
Rôle : Investigateur principal (Marie Villain)
Durée, financement : 2020-2022, 170k€
Partenaires : Jean-Julien Aucouturier

2. PENDING GRANTS related to the present proposal

n/a

3. GRANTS UNRELATED to the present proposal

Templeton Foundation research funding:
Intitulé: « Testing Global Neuronal Workspace and Integrated Information theories of consciousness in animal models »
Durée, **financement**: 2021-2023, 200k€

UNIM ALLIANZ grant
Durée, **financement**: 2018-2022 : 200k€

Académie des Sciences Grand Prix Lamonica Neurologie
Durée, **financement**: 2017 : 110k€

Equipe FRM:
Durée, **financement**: 2015-2017, 380k€

James S. McDonnell Foundation
***Durée, financement**: 2013-2017: 150k$/an*

COMITE DE PROTECTION DES PERSONNES

ILE DE FRANCE V

Hôpital Saint-Antoine - 184 rue du Faubourg Saint-Antoine - 75012 PARIS
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☎ 01 49 28 20 25

Présidente :
A. KURTZ

Vice-Président :
J.J. BOFFA

Paris, le 22 Juillet 2020

Le Comité avait été saisi en date, **du 4 juin 2020**, d'une demande d'avis portant sur le projet de recherche mentionné ci-dessous:

20.06.04.59700 Catégorie 2 Hors produit de santé (produit non mentionné à l'article L.5311-1 du code de la santé publique)
Domaine thérapeutique: Autre
Titre: Validation d'un outil de diagnostic et d'évaluation de la prosodie réceptive dans les suites d'un AVC droit : Utilisation du paradigme de « reverse correlation »
Promoteur: Assistance Publique-Hôpitaux de Paris /DRCI
Investigateur : Marie VILLAIN
N° National : 2020-A01668-31
Rapporteurs : Dr RADENNE- Mme KURTZ

Le Comité avait examiné les informations relatives à ce projet lors de la séance **du jeudi 9 juillet 2020** et demandé d'apporter des modifications.

Le Comité a examiné les réponses envoyées le 20 juillet 2020 et a pris la décision suivante : **AVIS FAVORABLE, les modifications demandées ayant été faites.**

La Présidente
Annie KURTZ

C.P.P. Ile de France V
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184, Rue du Fbg Saint Antoine
75571 PARIS CEDEX 12

Le Vice-Président
Jean Jacques BOFFA

COMITE DE PROTECTION DES PERSONNES

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☎ 01 49 28 20 25

Présidente :
A. KURTZ

Vice-Président :
J.J. BOFFA

Annexe :

Liste des documents soumis :

- Le dossier administratif
  - le courrier de demande d'avis daté
  - le formulaire de demande d'avis daté
  - le document additionnel daté,
- Le dossier sur la recherche
  - le protocole de la recherche, version n°1.0 du 21/04/2020
  - le résumé du protocole, version n°1.0 du 21/04/2020
  - la(les) note(s) d'information et le(s) formulaire(s) de recueil
- du consentement destinés aux personnes qui se prêtent à la
- recherche, version n°1.0 du 21/04/2020
  - la copie de l'attestation d'assurance
  - la justification de l'adéquation des moyens humains,
- matériels et techniques au projet de recherche

COU - 20/07/20 - réponses remarques cpp proavc pdf
Documents liés à la recherche
INF - 20/07/20 - note information volontaire sain sans modification
INF - 20/07/20 - note d information volontaire sain avec modification
INF - 20/07/20 - note d information patient sans modification
INF - 20/07/20 - note d information patient avec modification
PRO - 20/07/20 - protocole sans modification version 1 0
PRO - 20/07/20 - protocole avec modification version 1 0

Ont participé à la délibération :

Premier Collège :
Recherche biomédicale : Pr Victor Georges LEVY (T), Mme Alexandra ROUSSEAU (T), Pr Jean Jacques BOFFA (T),
Médecin généraliste : Dr Simone RADENNE (S)

Deuxième Collège :
Psychologue : Mme Annie KURTZ (T)
Compétence Ethique : Mme Jacqueline DAUXOIS, Mme Jeanne ZILBERBERG

Grille des coûts salariaux annuels des contractuels, contrats > à un an

Montants donnés à titre indicatif

En vigueur au 01/01/2021

Fonctions (Niveau)	Zone de résidence	Expérience	BRUT	Charges salariales	NET	TSS	Total Charges Patronales dont TSS	BRUT CHARGE	TOTAL BRUT CHARGE avec PPE ANR	TOTAL BRUT CHARGE avec PPE
Travaux scientifiques (Niveau Chercheur)	**1**	>= 20 ans	51 887,64	9 890,00	41 997,64	5 606,00	24 108,38	75 996,02	78 097,47	80 095,15
		>= 15 et < 20 ans	51 694,32	9 857,37	41 836,95	5 581,00	24 014,76	75 709,08	77 802,70	79 792,93
		>= 10 et < 15 ans	50 708,16	9 690,90	41 017,26	5 454,00	23 537,67	74 245,83	76 299,51	78 251,77
		>= 7 et < 10 ans	48 680,88	9 348,69	39 332,19	5 192,00	22 555,98	71 236,86	73 208,44	75 082,65
		>= 2 et < 7 ans	46 575,36	8 993,28	37 582,08	4 920,00	21 536,52	68 111,88	69 998,19	71 791,34
		< 2 ans (max)	37 748,16	7 410,06	30 338,10	3 780,00	17 256,09	55 004,25	56 533,05	57 986,36
		< 2 ans (min)	32 739,00	6 426,75	26 312,25	3 132,00	14 819,82	47 558,82	48 884,75	50 145,20
	2	>= 20 ans	50 880,12	9 719,93	41 160,19	5 476,00	23 620,71	74 500,83	76 561,48	78 520,36
		>= 15 et < 20 ans	50 690,52	9 687,93	41 002,59	5 452,00	23 529,41	74 219,93	76 272,89	78 224,48
		>= 10 et < 15 ans	49 723,56	9 524,70	40 198,86	5 327,00	23 061,14	72 784,70	74 798,50	76 712,86
		>= 7 et < 10 ans	47 735,64	9 189,14	38 546,50	5 070,00	22 098,42	69 834,06	71 767,36	73 605,18
		>= 2 et < 7 ans	45 671,04	8 840,63	36 830,41	4 803,00	21 098,49	66 769,53	68 619,21	70 377,54
		< 2 ans (max)	37 015,20	7 266,18	29 749,02	3 685,00	16 899,43	53 914,63	55 413,74	56 838,83
		< 2 ans (min)	32 103,24	6 301,95	25 801,29	3 050,00	14 510,86	46 614,10	47 914,28	49 150,25
	3	>= 20 ans	50 376,36	9 634,90	40 741,46	5 411,00	23 376,88	73 753,24	75 793,48	77 732,97
		>= 15 et < 20 ans	50 188,68	9 603,21	40 585,47	5 387,00	23 286,25	73 474,93	75 507,57	77 439,84
		>= 10 et < 15 ans	49 231,32	9 441,61	39 789,71	5 263,00	22 822,39	72 053,71	74 047,58	75 942,98
		>= 7 et < 10 ans	47 263,08	9 109,37	38 153,71	5 009,00	21 869,67	69 132,75	71 046,90	72 866,53
		>= 2 et < 7 ans	45 218,88	8 764,30	36 454,58	4 745,00	20 879,97	66 098,85	67 930,22	69 671,15
		< 2 ans (max)	36 648,72	7 194,24	29 454,48	3 638,00	16 721,59	53 370,31	54 854,59	56 265,56
		< 2 ans (min)	31 785,48	6 239,57	25 545,91	3 009,00	14 356,42	46 141,90	47 429,21	48 652,95
Travaux techniques hautement spécialisés (Niveau 1 - IR)	**1**	>= 20 ans	38 329,20	7 524,12	30 805,08	3 855,00	17 538,52	55 867,72	57 420,06	58 895,73
		>= 15 et < 20 ans	37 886,16	7 437,15	30 449,01	3 797,00	17 322,36	55 208,52	56 742,91	58 201,53
		>= 10 et < 15 ans	36 824,88	7 228,82	29 596,06	3 660,00	16 806,48	53 631,36	55 122,77	56 540,53
		>= 5 et < 10 ans	34 702,92	6 812,27	27 890,65	3 386,00	15 774,94	50 477,86	51 883,33	53 219,39
		>= 3 et < 5 ans	32 335,68	6 347,57	25 988,11	3 080,00	14 623,84	46 959,52	48 269,11	49 514,04
		< 3 ans	30 128,88	5 914,37	24 214,51	2 795,00	13 551,01	43 679,89	44 900,11	46 060,07
	2	>= 20 ans	37 584,96	7 378,02	30 206,94	3 759,00	17 176,83	54 761,79	56 283,98	57 731,00
		>= 15 et < 20 ans	37 150,56	7 292,75	29 857,81	3 702,00	16 964,75	54 115,31	55 619,91	57 050,20
		>= 10 et < 15 ans	36 109,80	7 088,44	29 021,36	3 568,00	16 459,20	52 569,00	54 031,45	55 421,67
		>= 5 et < 10 ans	34 029,00	6 679,98	27 349,02	3 299,00	15 447,35	49 476,35	50 854,53	52 164,64
		>= 3 et < 5 ans	31 707,84	6 224,33	25 483,51	2 999,00	14 318,70	46 026,54	47 310,71	48 531,46
		< 3 ans	29 543,88	5 799,54	23 744,34	2 720,00	13 267,17	42 811,05	44 007,57	45 145,01
	3	>= 20 ans	37 212,84	7 304,97	29 907,87	3 710,00	16 994,98	54 207,82	55 714,94	57 147,64
		>= 15 et < 20 ans	36 782,76	7 220,55	29 562,21	3 655,00	16 786,45	53 569,21	55 058,91	56 475,04
		>= 10 et < 15 ans	35 752,32	7 018,27	28 734,05	3 522,00	16 285,58	52 037,90	53 485,87	54 862,33
		>= 5 et < 10 ans	33 692,16	6 613,86	27 078,30	3 256,00	15 284,10	48 976,26	50 340,79	51 637,94
		>= 3 et < 5 ans	31 393,92	6 162,70	25 231,22	2 959,00	14 166,63	45 560,55	46 832,00	48 040,67
		< 3 ans	29 251,44	5 742,13	23 509,31	2 682,00	13 124,76	42 376,20	43 560,89	44 687,07
Travaux d'études et de conception (niveau 2 - IE)	**1**	>= 20 ans	32 976,96	6 473,46	26 503,50	3 163,00	14 935,77	47 912,73	49 248,30	50 517,91
		>= 15 et < 20 ans	32 017,44	6 285,10	25 732,34	3 039,00	14 469,23	46 486,67	47 783,37	49 016,04
		>= 10 et < 15 ans	30 938,28	6 073,26	24 865,02	2 900,00	13 944,97	44 883,25	46 136,25	47 327,37
		>= 5 et < 10 ans	29 064,60	5 705,45	23 359,15	2 658,00	13 034,06	42 098,66	43 275,78	44 394,77
		>= 3 et < 5 ans	27 267,24	5 352,63	21 914,61	2 425,00	12 159,40	39 426,64	40 530,97	41 580,76
		< 3 ans	25 815,72	5 067,69	20 748,03	2 238,00	11 454,21	37 269,93	38 315,47	39 309,37
	2	>= 20 ans	32 336,64	6 347,76	25 988,88	3 080,00	14 624,18	46 960,82	48 270,45	49 515,42
		>= 15 et < 20 ans	31 395,72	6 163,06	25 232,66	2 959,00	14 167,27	45 562,99	46 834,52	48 043,25
		>= 10 et < 15 ans	30 337,56	5 955,34	24 382,22	2 822,00	13 652,51	43 990,07	45 218,74	46 386,74
		>= 5 et < 10 ans	28 500,24	5 594,67	22 905,57	2 585,00	12 759,59	41 259,83	42 414,09	43 511,34
		>= 3 et < 5 ans	26 737,80	5 248,70	21 489,10	2 357,00	11 902,39	38 640,19	39 723,08	40 752,48
		< 3 ans	25 314,48	4 969,30	20 345,18	2 173,00	11 210,27	36 524,75	37 549,99	38 524,59
	3	>= 20 ans	32 016,48	6 284,92	25 731,56	3 039,00	14 468,88	46 485,36	47 782,03	49 014,67
		>= 15 et < 20 ans	31 084,92	6 102,05	24 982,87	2 919,00	14 016,32	45 101,24	46 360,18	47 556,95
		>= 10 et < 15 ans	30 037,20	5 896,38	24 140,82	2 783,00	13 506,28	43 543,48	44 759,99	45 916,42
		>= 5 et < 10 ans	28 218,12	5 539,29	22 678,83	2 548,00	12 621,87	40 839,99	41 982,82	43 069,22
		>= 3 et < 5 ans	26 473,08	5 196,73	21 276,35	2 323,00	11 773,89	38 246,97	39 319,13	40 338,34
		< 3 ans	25 063,92	4 920,11	20 143,81	2 141,00	11 088,82	36 152,74	37 167,83	38 132,79

Grille des coûts salariaux annuels des contractuels, contrats > à un an

Montants donnés à titre indicatif

En vigueur au 01/01/2021

Travaux d'études techniques (Niveau 3 - AI)	**1**	>= 20 ans	29 208,60	5 733,72	23 474,88	2 676,00	13 103,47	42 312,07	43 495,02	44 619,55
		>= 15 et < 20 ans	28 926,84	5 678,41	23 248,43	2 640,00	12 966,88	41 893,72	43 065,26	44 178,94
		>= 10 et < 15 ans	28 184,64	5 532,72	22 651,92	2 544,00	12 605,92	40 790,56	41 932,03	43 017,14
		>= 5 et < 10 ans	26 808,00	5 262,48	21 545,52	2 366,00	11 936,46	38 744,46	39 830,18	40 862,29
		>= 3 et < 5 ans	25 486,08	5 002,98	20 483,10	2 195,00	11 293,53	36 779,61	37 811,80	38 793,01
		< 3 ans	23 865,24	4 684,81	19 180,43	1 986,00	10 505,89	34 371,13	35 337,67	36 256,48
	2	>= 20 ans	28 641,48	5 622,39	23 019,09	2 603,00	12 828,01	41 469,49	42 629,47	43 732,17
		>= 15 et < 20 ans	28 365,12	5 568,14	22 796,98	2 567,00	12 693,35	41 058,47	42 207,26	43 299,31
		>= 10 et < 15 ans	27 637,44	5 425,30	22 212,14	2 473,00	12 339,57	39 977,01	41 096,32	42 160,36
		>= 5 et < 10 ans	26 287,44	5 160,29	21 127,15	2 299,00	11 683,62	37 971,06	39 035,70	40 047,76
		>= 3 et < 5 ans	24 991,20	4 905,84	20 085,36	2 131,00	11 052,86	36 044,06	37 056,20	38 018,36
		< 3 ans	23 401,80	4 593,83	18 807,97	1 926,00	10 280,44	33 682,24	34 630,02	35 530,98
	3	>= 20 ans	28 357,92	5 566,73	22 791,19	2 566,00	12 689,78	41 047,70	42 196,19	43 287,97
		>= 15 et < 20 ans	28 084,32	5 513,02	22 571,30	2 531,00	12 557,10	40 641,42	41 778,84	42 860,08
		>= 10 et < 15 ans	27 363,84	5 371,59	21 992,25	2 438,00	12 206,89	39 570,73	40 678,97	41 732,47
		>= 5 et < 10 ans	26 027,28	5 109,22	20 918,06	2 265,00	11 556,74	37 584,02	38 638,12	39 640,17
		>= 3 et < 5 ans	24 743,88	4 857,29	19 886,59	2 099,00	10 932,57	35 676,45	36 678,57	37 631,21
		< 3 ans	23 170,20	4 548,37	18 621,83	1 896,00	10 167,76	33 337,96	34 276,35	35 168,41
Travaux de réalisation (Niveau 4 - T)	**1**	>= 20 ans	23 016,48	4 518,19	18 498,29	1 876,00	10 092,88	33 109,36	34 041,53	34 927,67
		>= 15 et < 20 ans	22 806,60	4 476,99	18 329,61	1 849,00	9 990,96	32 797,56	33 721,22	34 599,28
		>= 10 et < 15 ans	22 760,52	4 467,95	18 292,57	1 843,00	9 968,51	32 729,03	33 650,83	34 527,11
		>= 5 et < 10 ans	21 990,24	4 316,74	17 673,50	1 744,00	9 594,52	31 584,76	32 475,36	33 321,98
		>= 3 et < 5 ans	21 080,88	4 138,23	16 942,65	1 626,00	9 151,87	30 232,75	31 086,53	31 898,14
		< 3 ans	19 943,64	3 914,99	16 028,65	1 479,00	8 598,88	28 542,52	29 350,24	30 118,07
	2	>= 20 ans	22 569,60	4 430,47	18 139,13	1 819,00	9 876,35	32 445,95	33 360,02	34 228,95
		>= 15 et < 20 ans	22 363,80	4 390,07	17 973,73	1 792,00	9 775,88	32 139,68	33 045,41	33 906,42
		>= 10 et < 15 ans	22 318,56	4 381,19	17 937,37	1 786,00	9 753,73	32 072,29	32 976,19	33 835,45
		>= 5 et < 10 ans	21 563,28	4 232,93	17 330,35	1 689,00	9 387,09	30 950,37	31 823,68	32 653,87
		>= 3 et < 5 ans	20 671,56	4 057,88	16 613,68	1 573,00	8 952,75	29 624,31	30 461,51	31 257,36
		< 3 ans	19 556,40	3 838,97	15 717,43	1 429,00	8 410,63	27 967,03	28 759,07	29 511,99
	3	>= 20 ans	22 346,16	4 386,61	17 959,55	1 790,00	9 767,58	32 113,74	33 018,76	33 879,09
		>= 15 et < 20 ans	22 142,40	4 346,61	17 795,79	1 763,00	9 667,84	31 810,24	32 707,00	33 559,49
		>= 10 et < 15 ans	22 097,64	4 337,82	17 759,82	1 758,00	9 646,86	31 744,50	32 639,45	33 490,21
		>= 5 et < 10 ans	21 349,80	4 191,02	17 158,78	1 661,00	9 282,88	30 632,68	31 497,35	32 319,31
		>= 3 et < 5 ans	20 466,96	4 017,72	16 449,24	1 547,00	8 853,70	29 320,66	30 149,58	30 937,55
		< 3 ans	19 362,84	3 800,97	15 561,87	1 404,00	8 316,53	27 679,37	28 463,57	29 209,04
Travaux d'exécution (Niveau 5 - AJT)	**1**	>= 20 ans	20 462,40	4 016,82	16 445,58	1 546,00	8 851,08	29 313,48	30 142,20	30 930,01
		>= 15 et < 20 ans	20 384,04	4 001,44	16 382,60	1 536,00	8 813,10	29 197,14	30 022,70	30 807,48
		>= 10 et < 15 ans	20 166,00	3 958,64	16 207,36	1 508,00	8 707,26	28 873,26	29 689,99	30 466,38
		>= 5 et < 10 ans	19 393,68	3 807,03	15 586,65	1 408,00	8 331,54	27 725,22	28 510,67	29 257,32
		>= 3 et < 5 ans	19 142,04	3 757,63	15 384,41	1 376,00	8 209,71	27 351,75	28 127,00	28 863,97
		< 3 ans	19 027,20	3 735,09	15 292,11	1 361,00	8 153,71	27 180,91	27 951,51	28 684,06
	2	>= 20 ans	20 065,08	3 938,83	16 126,25	1 495,00	8 658,23	28 723,31	29 535,95	30 308,45
		>= 15 et < 20 ans	19 988,28	3 923,75	16 064,53	1 485,00	8 620,82	28 609,10	29 418,62	30 188,17
		>= 10 et < 15 ans	19 774,44	3 881,77	15 892,67	1 457,00	8 516,48	28 290,92	29 091,78	29 853,10
		>= 5 et < 10 ans	19 017,12	3 733,11	15 284,01	1 360,00	8 149,11	27 166,23	27 936,43	28 668,58
		>= 3 et < 5 ans	18 770,28	3 684,65	15 085,63	1 328,00	8 028,99	26 799,27	27 559,47	28 282,12
		< 3 ans	18 657,72	3 662,56	14 995,16	1 313,00	7 973,81	26 631,53	27 387,16	28 105,49
	3	>= 20 ans	19 866,48	3 899,84	15 966,64	1 469,00	8 561,33	28 427,81	29 232,41	29 997,27
		>= 15 et < 20 ans	19 790,40	3 884,90	15 905,50	1 459,00	8 524,17	28 314,57	29 116,08	29 878,01
		>= 10 et < 15 ans	19 578,72	3 843,35	15 735,37	1 432,00	8 421,60	28 000,32	28 793,26	29 547,04
		>= 5 et < 10 ans	18 828,84	3 696,15	15 132,69	1 335,00	8 056,90	26 885,74	27 648,30	28 373,21
		>= 3 et < 5 ans	18 584,52	3 648,19	14 936,33	1 304,00	7 938,67	26 523,19	27 275,87	27 991,37
		< 3 ans	18 473,04	3 626,30	14 846,74	1 289,00	7 883,88	26 356,92	27 105,07	27 816,29
Doctorant			25 620,00	5 029,27	20 590,73	2 213,00	11 359,34	36 979,34	38 016,95	39 003,32
Doctorant multi-activités		(min)	25 620,00	5 029,27	20 590,73	2 213,00	11 359,34	36 979,34	38 016,95	39 003,32
		(max)	30 920,40	6 069,75	24 850,65	2 897,00	13 935,58	44 855,98	46 108,26	47 298,69

Sent at: 02/04/2021 09:44:25

Fw: RE: Projet Fondation pour l'Audition

From: JJ Aucouturier <aucouturier@gmail.com>
To: JJ Aucouturier <aucouturier@gmail.com>

From: grants <grants@icm-institute.org>

Date: 25/03/2021 10:21:17
Subject: RE: Projet Fondation pour l'Audition
To: VILLAIN Marie <marie.villain@aphp.fr>
Cc: NACCACHE Lionel (502764) <lionel.naccache@gmail.com>, JJ Aucouturier <aucouturier@gmail.com>, grants <grants@icm-institute.org>

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