2019 PhD STUDENTSHIP APPLICATION

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

AMOUNT REQUESTED (€): 120,000 €

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

STUDENT: ENT resident ☐ Speech therapy student ☒ Audiology student ☐

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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ABSTRACT

This proposal aims to support the PhD research of speech therapist *Mélissa Jeulin (MSc)*, for a project aiming to study speech prosodic perception in brain-stroke survivors. The project combines the clinical background of both the applicant and co-supervisor Marie Villain (Hôpital Pitié-Salpêtrière, Paris) with the computational and cognitive expertise of co-supervisor Jean-Julien Aucouturier (IRCAM/CNRS, Paris), and has both methodological, theoretical and clinical objectives.

From a **methodological** point of view, the project will pioneer the application of a novel data-driven technique, the reverse correlation paradigm (Ponsot, Burred, Belin, & Aucouturier, 2018) to the context of prosodic perception in brain-stroke patients. 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 random stimuli. Based on encouraging pilot data gathered by the applicant during her recent Master research, the present project will evaluate the relevance of reverse-correlation as a marker of prosodic impairments in speech therapy practice.

From a **theoretical** point of view, the project 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 statistical 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, the project will provide a new paradigm able to (1) diagnose prosody impairments beyond existing gold standards, (2) provide a prognosis metric to quantify how well a patient reacts to speech therapy week after week and (3) inspire new audio-based health technology to rehabilitate prosody perception in these patients all of this thanks to the forces of computational modelling.

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, and between one half and two thirds of survivors are expected to develop hearing impairments limiting their comprehension of speech and music (Hirel 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. Beyond stroke, the project will provide a case-study for the application of reverse-correlation to general speech therapy practice, and will benefit patients across the whole spectrum of hearing impairments.

RATIONALE

The main novelty of the project is to apply a psychoacoustical paradigm recently developed in the supervisor's team to the novel context of speech therapy for brain-stroke patients. In Ponsot et al. (PNAS, 2018), we demonstrated that we could use reverse-correlation to uncover healthy participant's mental representation of a dominant or trustworthy prosody. It was the first time this innovative technique was used to study high-level speech perception, and the technique has never yet been used in a clinical context, aside from the recent pilot data motivating the present application.

Adapting this technique to brain-stroke patients is highly relevant, because impairments of prosodic perception are a major component of cognitive impairments following right-hemisphere strokes, and yet there are no good tools to evaluate and rehabilitate these deficits, which receive less clinical attention than left-hemisphere aphasia. With its ability to extract mental representations at the level of the individual, reverse-correlation techniques have the potential to build computational models of a patient's specific difficulties, improve diagnosis and prognosis, and even provide new personalized strategies for rehabilitation.

Beyond strokes, the project as a whole is a case-study for a computational turn in speech therapy, and an important step towards personalized treatment strategies based on modern psychophysics and audio-technologies. As such, the project will benefit patients across the whole spectrum of hearing impairments, and may find extensions to e.g. the personalized fitting of hearing aids. Because preserving hearing should not be restricted to low-level auditory skills, it is crucially important to develop tools to better characterize, assess and rehabilitate 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 Fondation pour l'Audition.

From an institutional perspective, the proposed project will also impact the community by promoting the research training of the applicant. Melissa Jeulin, a speech therapist who graduated summa cum laude with a MSc. from a Sorbonne University last year, is one of a rare breed of clinician-scientists who no doubt constitute the future of French research excellence in hearing science but who, yet, because of their initial professional training, are a difficult match for the usual doctoral funding channels. Through the example of Melissa, the project will therefore offer a reflection on good practices, and an institutional precedent to encourage scientific careers for future hearing health professionals, positively impacting the field for years to come.

LAY SUMMARY

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 travail de thèse 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 thesis work 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.

List sources of funding for this project:

The project will be able to use overhead funding from the supervisor's ERC project (CREAM 335536), which ends Oct. 2019 but which overheads run for another 3 years (expected funding < 20,000€). In addition, funding will be sought by co-supervisor Marie Villain from the ARS PHRIP scheme.

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

The applicant, a speech therapist who graduated summa cum laude with a MSc. from a Sorbonne University last year, is one of a rare breed of clinician-scientists who no doubt constitute the future of French research excellence in hearing science but who, because of their initial professional training, are a difficult match for the usual doctoral funding channels. Support from Fondation pour l'Audition will be critical for the student to support herself while on *disponibilité* from her permanent speech therapist position in APHP, and will constitute an ideal institutional context to develop her scientific and professional skills as a future academic-clinical researcher. Through the example of Melissa, the project will offer a reflection on good practices on how to provide doctoral training for speech therapists, and an institutional precedent to encourage scientific careers for future applicants with the same profile, positively impacting the field for years to come.

RESEARCH PLAN

Specific Aims

The proposed research has both methodological, theoretical and clinical objectives. From a methodological point of view, the project aims to adapt the reverse-correlation paradigm of Ponsot et al.(2018) to the context of the speech therapy management of stroke patients with impairments of prosody perception. Specifically, we will collect reverse-correlation data for 40 right-hemisphere stroke patients and evaluate its relevance as a marker of prosodic impairments in comparison to the gold-standards of current clinical practice. From a theoretical point of view, the project aims to characterize the morphological (ex. patients attending to the wrong part of a word) and statistical abnormalities (ex. correct mental representations, but large amounts of sensory noise) in patients' mental representations of prosody, and relate them to the type and location of the stroke. From a clinical point of view, the project aims to provide a new paradigm able to (1) diagnose prosody impairments beyond existing gold standards, (2) provide a prognosis metric to quantify how well a patient reacts to speech therapy week after week and (3) inspire new audio-based health technology to rehabilitate prosody perception in these patients.

Background and Significance

a. Strokes, hearing deficits and speech prosody

With 100,000 cases per year in France, stroke is the most common cause of neurological disability, and the first cause of handicap and loss of autonomy (Lecoffre et al., 2017). Both ischaemic and haemorrhagic strokes may disturb all levels of the auditory pathway and lead to hearing deficits that could concern 50% to 80% of patients (Hirel et al., 2017; Savva & Stephan, 2010). Hearing deficits, especially when they extend to language comprehension, have a negative impact on social function and mental health, and may prevent access to healthcare (Brown, Worrall, Davidson, & Howe, 2010). Yet, possibly due to the "invisible" nature of this impairment, hearing deficits after stroke have not been as extensively investigated as the more obvious symptoms of aphasia or motor loss.

Consciously or not, we convey emotional 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. Besides words, the sole sound of our voice is rich in information about our emotional states: higher fundamental frequency/pitch when happy than sad (Scherer, 1987), faster speech rate when excited, raising intonation/prosody when surprised (Banse & Scherer, 1996). Following a stroke, our capacity to produce and perceive linguistic or emotional prosody may be altered (Uekermann, Abdel-Hamid, Lehmkaemper, Vollmoeller, & Daum, 2008; Villain et al., 2016). While aphasia and impairments of lexical/syntactic comprehension are traditionally associated with lesions of the left-hemisphere, many authors have proposed that prosodic functions are right lateralized (Schirmer & Kotz, 2006). However, there is considerable debate about the cognitive models that may explain different types of prosodic impairments (impairments of production may correspond to right anterior lesions, and perception to right posterior lesions), 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 develop tools to better characterize the mechanistic basis of prosodic impairments after stroke, and relate them to the type and location of the lesions. This is the theoretical objective of the current project.

Unfortunately, because of common symptoms of anosognosia (a patient's failure to detect their own cognitive deficits), the screening of prosodic perception impairments cannot reliably rely on self-report. 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 battery is plagued with a high-rate of false negative, and does not allow a fine characterization of the impairments. (Aura, 2012) ; in addition, the MEC battery has good inter-rater reliability for all subtests, but the one devoted to prosodic perception (Côté, Payer, Giroux, & Joanette, 2007). 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 both more sensitive and more versatile to assess prosodic impairments in this population of patients.

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

The paradigm of reverse-correlation was initially developed for neurophysiology (Ringach & Shapley, 2004) and visual cognition (Murray, 2011) In Ponsot et al. (PNAS, 2018), we demonstrated that we could use reverse-correlation to uncover healthy participant's mental representation of specific prosodic judgements.
To this aim, 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, Ponsot, Goupil, Liuni, & Aucouturier, 2018). We then use 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 ask 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 are 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.

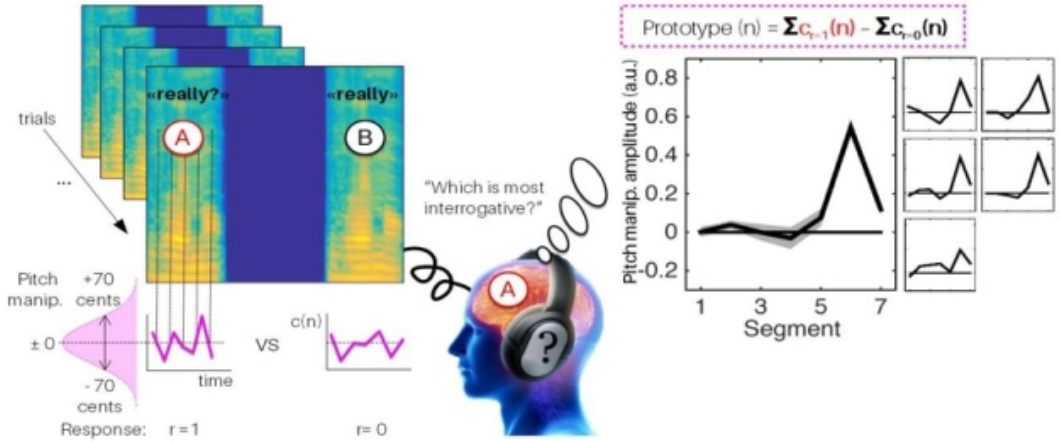


Figure 1. Accessing mental representations of interrogative prosody by using reverse correlation. (Left) Utterances of the same word "vraiment" ("really") were digitally manipulated to have random pitch contours. Participants were presented pairs of manipulated words and judged which was most interrogative. (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 this paradigm present several important advantages for its clinical application. First, 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. Second, they can be measured at regular intervals, allowing the prognostic study of symptom evolution. Finally, they offer a qualitative insight into the patient's cognitive process, revealing if a patient e.g. pays attention to parts of a word that are different then the prosodic representations of healthy controls. This information can be used to construct personalized rehabilitation strategies, in which e.g. unattended parts of words for a given patient can be acoustically emphasized to increase comprehension. The purpose of our project is to unlatch the clinical potential of the reverse-correlation paradigm, and improve the evaluation and treatment of prosodic processing in stroke survivors.

Preliminary Data

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 recently conducted a pilot study on a group of n=9 right hemisphere stroke patients, and n=11 controls paired in age, sex and audiogram, recruited by the applicant in the context of her MSc research. 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-AVC 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).

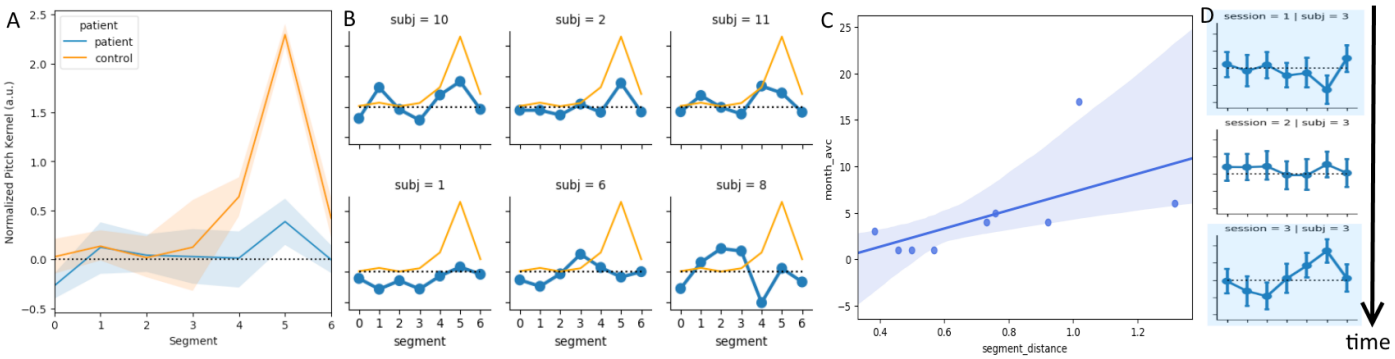


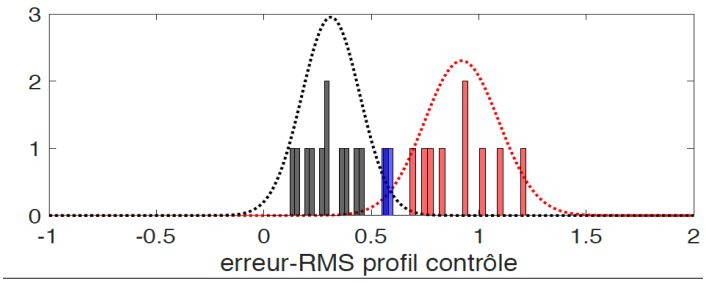
Figure 2: Preminary data on the mental representations of interrogative prosody extracted by reverse-correlation in a group of n=11 controls (orange), and n=9 stroke patients (blue). A : group averaged of the representations. B : individual patient data, compared to control group, for a subset of 6 patients. 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-AVC at the time of inclusion. D : Weekly representations for patient 3, measured on three consecutive weeks.

Research Design and Methods

1) WP1. Validation study

The first, and principal, 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. To do so, the applicant will conduct a prospective diagnostic research study, in a national multicentric manner, non-randomized, with a control group.

Main outcome: 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.
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.



The objective of the study is 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. The following figure shows the distribution of the criteria in a group of healthy controls (grey) and a group of right-hemisphere stroke patients (red), from our preliminary data. Data suggests good discriminative power between groups on the basis of this criteria, even though it will be necessary to include more patients and controls to confirm these results and establish a pathological threshold. We will use the MEC inguistic and emotional prosody comprehension and production subtasks as references, despite their known limitations.

Secondary outcomes

One major issue regarding the characterization of auditory perception deficits caused by neurological disorders concerns their origins, i.e. where they arise in the auditory system. Indeed, many factors can underlie impaired pitch processing, even in the absence of measurable loss of audibility using typical audiometric tests in quiet (e.g. Russo et al., 2008 for ASDs patients). The problem will be likely even more complex with the stroke patients, as they will mainly be aged >40 yrs. and therefore will additionally exhibit audibility problems. Even if this project will mainly focus on the inefficiencies of high-level, cognitive template-matching operations in stroke patients, we are well aware of these problems and will run a careful step-by-step characterization of pitch disorder at the different stages of the auditory system, including freq. thresholds of constant tones as well as for gliding tones (extending the paradigms of Liu, Patel, Fourcin, & Stewart, 2010 used for congenital amusia), all of this both quiet and in noise.

For this reason, we will also use the following tools, which are normed, standardized, and used in regular practice but rarely used systematically and in a combined manner : Musical perception (Montreal Battery for the Evaluation of Amusia - MBEA, Peretz, Champod, & Hyde, 2003), anxiety and depression (Hospital Anxiety and Depression Scale - Zigmond & Snaith, 1983), auditory attention (LAMA, Logiciel d'Attention en Modalité Auditive, Ambert-Dahan et al., 2013), central auditory deficits (AIRTAC2, Del Fabro & Desmons, 2014; Weill-Chounlamountry, Tessier, Soyez-Gayout, & Pradat-Diehl, 2010), auditory threshold (audiograms).

Inclusion criteria	Exclusion 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	- 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 (hearing loss > 40dB HL)

Recruitment

Recruitment will be conducted at the Service de Medecine 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.

2) WP2. Computational modeling

A secondary, and subsequent objective of the proposed PhD project will use data collected as part of the validation study of WP1 as a basis for a series of theoretical investigations aiming to derive computational models of prosodic processing in patients and controls. Several directions of research are anticipated, including:

- computational modeling of trial to trial responses to account for drifts of attention and perseverations
- symptom – lesion mapping, using patient MRI scans, seeking associations of representational abnormalities with specific temporo-frontal sites in the patient group.

Work in WP2 will be conducted in collaboration with Dr Emmanuel Ponsot (Ecole Normale Supérieure), an expert in computational modeling of reverse-correlation data.

3) WP3. Therapeutic application

A final objective of the proposed PhD project is to use the insights generated y WP1 and WP2 to build a prototype of software application targeting the personalized rehabilitation of brain-stroke patients.
Possible strategies will include:
- designing speech-therapy training to emphasize morphological aspects of words that are processed abnormally, given the prior assessment of a patient's mental representation (ex. learning to pay attention to the end of words, instead of the beginning)
- using audio-signal processing software to emphasize aspects of a word's prosody in order to compensate for the abnormal morphology of the patient's representation (ex. emphasizing the final rise of the word, for representations that put less emphasis than necessary on this part of the word).

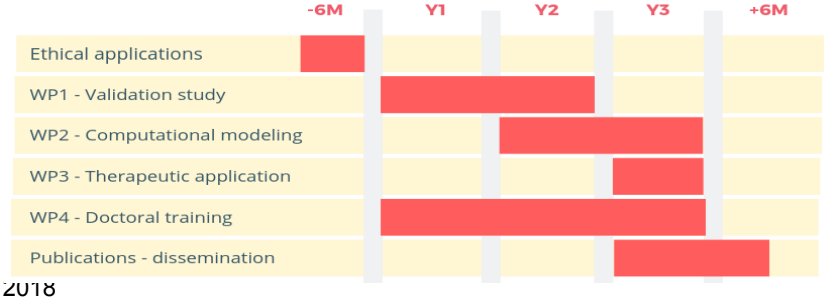
Work in WP3 will be conducted in collaboration with Romain Gombert, dir. Living Lab, Brain and Spine Institute, Pitié-Salpétrière Hospital (Paris), an expert in the development of health technologies and software user interfaces for rehabilitation. The application will be tested on a few patient volunteers, for a proof of concept. The formal clinical validation of the tool is outside the scope of this project, and will be the object of subsequent applications for funding.

4) WP4. Doctoral training
The project recognizes the unusual academic background of the applicant (a speech therapist), and will carefully assist her in developing the scientific and professional skills required by the project, and later by a successful career in academic/clinical research. Training will be sought from the project host institutions IRCAM and CNRS, as well as academic summer schools, in basic skills such as computer programming for psychology (Python) and statistical analysis (Python, R), as well as professional development skills such as English for oral and written scientific presentations. The supervision team will also ensure that the applicant gets sufficient experience attending academic meetings, presenting her work, and managing research projects and Master students. All costs incurred by this training program will be supported by the supervisor's other sources of funding.

Feasability: We estimate the recruitment in WP1 of ca. 20 patients per year meeting our inclusion criteria, 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.
Notices of approval from the ethics committees for all the exp. described here has been approved and are provided in Appendix. Upon acceptance an addendum for this project will be filed.
The project's supervision team is highly complementary, with expertise in all key levels of the evaluation of prosodic processing in controls and patients, have already published on the topic (Aucouturier et al., 2016; Ponsot et al., 2018; Villain et al., 2016), and have a successful history of collaboration, incl. On the supervision of the applicant's own Msc. Research project in 2017-2018. Finally, we collected preliminary data that confirmed the feasibility of the task with brain stroke patients, and yielded encouraging preliminary results concerning the diagnostic power of the reverse-correlation metrics.

Deliverables: The results of WP1 will be published first in the form of a preprint on the bioRxiv plateforme, circulated for comments in the community, and then submitted for publication in international scientific journals such as Brain or Cortex (see e.g. Särkämö et al., 2008). Results of the computational experiments of WP2 will be submitted for publication in psychology journals, such as Attention & Psychophysics, or neuroscience journals such as Journal of Cognitive Neurosciences. Results of the WP3 experimentations will be published in health tech journals, such as IEEE Transactions on Biomedical Engineering.

Timeline:



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Särkämö, T., Tervaniemi, M., Laitinen, S., Forsblom, A., Soinila, S., Mikkonen, M., … Laine, M. (2008). Music listening enhances cognitive recovery and mood after middle cerebral artery stroke. *Brain*, *131*(3), 866-876.

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Schirmer, A., & Kotz, S. A. (2006). Beyond the right hemisphere: brain mechanisms mediating vocal emotional processing. *Trends in cognitive sciences*, *10*(1), 24-30.

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Uekermann, J., Abdel-Hamid, M., Lehmkaemper, C., Vollmoeller, W., & Daum, I. (2008). Perception of affective prosody in major depression: a link to executive functions? *Journal of the International Neuropsychological Society*, *14*(4), 552-561.

Villain, M., Cosin, C., Glize, B., Berthoz, S., Swendsen, J., Sibon, I., & Mayo, W. (2016). Affective prosody and depression after stroke: a Pilot Study. *Stroke*, *47*(9), 2397-2400.

Weill-Chounlamountry, A., Tessier, C., Soyez-Gayout, L., & Pradat-Diehl, P. (2010). Quand le cerveau trompe l'oreille: De la surdité centrale à l'amusie.

Zigmond, A. S., & Snaith, R. P. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica*, *67*(6), 361-370. https://doi.org/10.1111/j.1600-0447.1983.tb09716.x

STUDENT'S BIOGRAPHICAL SKETCH

Name & Degree: Mélissa JEULIN, Speech therapist, MSc.

Current laboratory affiliation:

A. Education, Training, Positions & Honors

Since August 2018 : Speech therapist, University Hospital Saint-Louis – Lariboisière – Fernand Widal, Physical Medecine and Rehabilitation sector, Paris France

August 2017- July 2018 : Speech therapist, Physical Medecine and Rehabilitation's Center COS Bobigny, France

February 2018-June 2018 : internship at UMR9912 STMS lab (CNRS, UPMC, IRCAM) Paris, France

September 2017-July 2018 : Msc Health Research and Organization, subject Rehabilitation Research, obtained with honors, Sorbonne University Paris, France

October 2016-July 2017 : Speech Therapist, University Hospital Robert Debré, Paris, France

September 2012-October 2016 : Speech Therapist's studies, obtained with honors, University of Bordeaux, France

B. Peer-Reviewed Publications

M. Jeulin, E. Ponsot, P. Pradat-Diehl, JJ. Aucouturier, M. Villain. Etude de la prosodie réceptive après un Accident Vasculaire Cérébral : Utilisation du paradigme de « Reverse Correlation ». Poster. ICM days (Janvier 2019, Paris)

C. Studentships

February 2018-June 2018 : Master of science internship at IRCAM/CNRS (STMS UMR9912), supported by ERC STG CREAM 335536 .

CAREER DEVELOPMENT PLAN

Speech therapist since 2016, Mélissa Jeulin has completed Msc Recherche et Organisation en Santé parcours recherche en réadaptation at Sorbonne University in Paris, in order to acquire scientific skills in clinical research, not only to develop her professional practice, but also to pursue a university career. During this Master, she completed a five-month internship at IRCAM. This work, resulting from the meeting between Marie Villain (PhD and speech therapist) and Mélissa Jeulin, two speech-language therapists who are keen to participate in the evolution of their professional practices, and Jean-Julien Aucouturier and Emmanuel Ponsot, Researchers in computer and cognitive sciences, offers an innovative and transdisciplinary perspective on the understanding of prosodic mechanisms. Before and during this internship, Melissa participated in adapting the paradigm of reverse correlation to brain-injured patients, then proceeded to recruit patients and control group. Finally, she wrote and submitted a research thesis, for which she scored 16.5 / 20. Preliminary data was published in a poster at the ICM days (Janvier 2019, Paris). This project, with promising preliminary results, highlights the contribution of speech therapists to hearing research.
During this Phd, Melissa will acquire essential skills that she could not acquire without a transdisciplinary framework as proposed in this project. First, she will continue to learn how to conduct research and bibliographic reviews, which will allow her to base her practice on scientific evidences. She will also learn basic skills such as computer programming for psychology (Python) and statistical analysis (Python, R) and professional development skills such as English for oral and written scientific presentations. At least, the supervision team will ensure that the applicant gets sufficient experience attending academic meetings, presenting her work, and managing research projects and Master students.

The contribution of computational sciences in the study of hearing is promising and gives a new light in this area. Thanks to Marie Villain, a speech therapist who also has a university background, Mélissa will have the clinical supervision necessary to carry out this project.
The aim of this Ph.D. is to allow Mélissa Jeulin to combine her clinical skills with pure and applied research expertise in acoustic and neuroscience. She will be able to continue her career as a part-time speech therapist in a University Hospital Center and obtain a teaching-researcher position in a speech-language pathology department.

This profile of bi-owned paramedical researcher, still rare in France, is gradually developing. It seems essential to be closer to the issues of patients and speech therapists, and to develop assessment and rehabilitation tools, adapted and based on Evidence-Based-Practice, and particularly prosodic impairment that remain unrecognized and not much reeducated.

SUPERVISOR'S BIOGRAPHICAL SKETCH

See instructions

Name & Degree: Jean-Julien AUCOUTURIER, PhD Position: Chargé de recherche CNRS

A. Education, Training, Positions & Honors

Positions

- Since 2012 : **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

- Depuis 2017 : **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).

Prix et bourses académiques

- **Prix scientifique :** Lauréat du Prix d'Émergence Scientifique, catégorie recherche fondamentale de la Fondation pour l'Audition, Nov. 2018.

- **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 (2018-2013)

1. Burred, J.J., Ponsot, E., Goupil, L., Liuni, M. & Aucouturier, JJ. (2018) *CLEESE : An opensource audio-transformation toolbox for data-driven experiments in speech and music cognition*, PLOS One (in press)
2. Arias, P., Belin, P. & Aucouturier, JJ. (2018) *Auditory smiles trigger unconscious facial imitations*. Current Biology, vol.28(14), R782-R783.
3. 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.
4. Arias, P., Soladié, C., Bouafif, O., Roebel, A., Séguier, R. & Aucouturier, JJ. (2018) *Realistic manipulation of facial and vocal smiles in real-world video streams*. IEEE Transactions on Affective Computing (in press).
5. Ponsot, E., Arias, P. & Aucouturier, JJ. (2018) Uncovering mental representations of smiled speech using reverse correlation. Journal of the Acoustical Society of America, 143 (1).
6. Rachman, L., Liuni, M., Arias, P., Lind, A., Johansson, P., Hall, L., Richardson, D., Watanabe, K., Dubal, S. & Aucouturier, JJ. (2017) *DAVID : An open-source platform for real-time emotional speech transformations*. Behavior Research Methods vol. 50(1), pp 323–343
7. Aucouturier, JJ. & Canonne, C. (2017) *Musical friends and foes : the social cognition of affiliation and control in musical interactions*. Cognition, vol. 161, 94-108.
8. Aucouturier, JJ., 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 Science, 113(4).
9. Boidron, L., Boudenia, K., Avena, C., Boucheix, J.M. & Aucouturier, JJ. (2016) *Emergency medical triage decisions swayed by manipulated cues of physical dominance in caller's voice*, Scientific Reports, 6, 3021
10. Aucouturier, JJ., Fujita, M., & Sumikura, H. (2015). *Experiential response and intention to purchase in the cocreative consumption of music : The Nine Inch Nails experiment*. Journal of Consumer Behaviour.
11. Canonne, C. & Aucouturier, JJ. (2015). *Play together, think alike : Shared mental models in expert music improvisers*. Psychology of Music, 44(3).
12. Lagrange, M., Lafay, G., Defreville, B., & Aucouturier, JJ. (2015). *The bag-of-frames approach : a not so sufficient model for urban soundscapes, after all*. Journal of the Acoustical Society of America, 138
13. Mercadié, L., Caballe, J., Aucouturier, JJ., & Bigand, E. (2014). *Effect of synchronized or desynchronized music listening during osteopathic treatment : An EEG study*. Psychophysiology, 51(1), 52-59.
14. Hemery, E., & Aucouturier, JJ. (2014). *One hundred ways to process time, frequency, rate and scale in the auditory cortex : a pattern-recognition meta-analysis*. Frontiers in Computational Neuroscience, 9(80).
15. Aucouturier, JJ. (2013) *All class communication, public : Using Twitter in lieu of LMS*, International Journal on Learning and Media, 4 (1), 1-7.
16. Aucouturier, JJ. & Bigand, E. (2013) *Seven problems that keep MIR from attracting the interest of cognition and neuroscience*, Journal of Intelligent Information Systems, 41 (3), 483-497
17. Ferreri, L., Aucouturier, JJ., Muthalib., M., Bigand, E. & Bugaiska, A. (2013) *Music improves verbal memory encoding while decreasing prefrontal cortex activity : a fNIRS study*, Frontiers in Human Neuroscience 7.
18. Lüthy, M., & Aucouturier, JJ. (2013). *Content Management for the Live Music Industry in Virtual Worlds : Challenges and Opportunities*. Journal For Virtual Worlds Research, 6(2).

Complete list of publication available on https://scholar.google.fr/citations?user=jnST06UAAAAJ.

SUPERVISOR'S RESEARCH SUPPORT

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

ERC Starting Grant
Intitulé : Cracking the Emotional Code of Music (CREAM n.335536)

Rôle : Coordinateur / PI
Durée, financement : 2014-2019, 1500ke
Partenaires : STMS (Paris, France) ; Brain and Spine Institute (Paris, France).

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, 650ke
Partenaires : CentraleSupélec (Rennes, France), IRCAM (Paris, France), IRBA (Paris, France), Chanel (Paris, France).

PEPS IDEX/CNRS
Intitulé : Voice morphing (MaVOIX)
Rôle : Responsable scientifique, partenaire (coordinateur : Jean-Luc Rouas, LaBRI)
Durée, financement : 2013, 15 000e
Partenaire : LaBRI (Bordeaux, France), STMS (Paris, France)

2. PENDING GRANTS related to the present proposal

n/a

3. GRANTS UNRELATED to the present proposal

Agence Nationale de la Recherche
Intitulé : Musical Interaction and Collective Action (MICA)
Rôle : Responsable scientifique, partenaire (coord. : Clément Canonne, STMS).
Durée, financement : 2017-2020, 430ke
Partenaires : STMS (Paris, France).

Fondation Fyssen
Intitulé : Behavioural plateform for mouse cognition (MOUSECOG)
Rôle : Responsable scientifique, partenaire (coordinateur : Brice Bathelier, UNIC)
Durée, financement : 2014, 35 000e
Partenaires : STMS (Paris, France), UNIC (Gif/Yvette, France).

Seed Research Initatives, Temple University
Rôle : co-PI, avec Ron Carr, Irene Herrera
Durée, financement : 2010, 50 000 USD

Grant-in-aid of Scientific Research, Japanese Society for the Promotion of Science
Rôle : Coordinateur / PI
Durée, financement : 2007-2008, 1,6M JPY, c. 15,000 USD

CO-SUPERVISOR'S BIOGRAPHICAL SKETCH

Name & Degree: Marie VILLAIN, PhD Position: Speech Therapist

A. Education, Training, Positions & Honors

Positions :
Since 2017 Orthophoniste service de Médecine Physique et Réadaptation (Pitié-Salpêtrière)
2016 – 2018 Orthophoniste en cabinet libéral à Levallois-Perret
2013 – 2016 Orthophoniste service de Médecine Physique et Réadaptation (CHU Bordeaux)
2013 – 2019 Chargée d'enseignement à l'école d'orthophonie de Paris et Bordeaux et M2 Recherche et Organisation en Santé
2010 – 2013 Orthophoniste pôle neurologie (Unité de Soins Intensifs Neuro-Vasculaires et service de neurologie) hôpital de Poissy (78)

Education :
2016 : Obtention de la 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

B. Peer-Reviewed Publications (2018-2013)

1. 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.
2. C. DEBARLE, V. PERLBARG, L. PUYBASSET, E. CARON, B. LESIMPLE, M. VILLAIN, P. PRADAT-DIEHL (2017) Long term outcome after severe traumatic brain injury (TBI) and correlation with volumetry and fractional anisotropy. Annals of Physical and Rehabilitation Medicine.60:83-84
3. TARABON-PREVOST, M. VILLAIN (2017) B.E.N.Q : Batterie d'Evaluation des Nombres au Quotidien. Présentation des épreuves et étude auprès d'une population adulte cérébro-lésée. Rééducation Orthophonique. 270
4. 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
5. G. PYTHON, M. VILLAIN, A.C. GAY, M. LAGANARO (2016) Semantic context effects on picture naming in aphasia. Frontiers in Psychology.
6. 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 PRM.
7. 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. DOI: 10.1177/0269215515623600
8. 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.
9. M. VILLAIN, O. HEINZLEF (2013) Validation française du DYMUS : questionnaire de dépistage des troubles de déglutition dans la Sclérose en Plaques destiné aux neurologues. Glossa. 113 (13-26)
10. H. ROBERT, C. TARABON-PREVOST, M. VILLAIN, P. PRADAT-DIEHL. Evaluation écologique des troubles du calcul par la BENQ, en MPR. Poster congrès SORMER (Reims, octobre 2013)
11. M. VILLAIN, C. TARABON-PREVOST, H. ROBERT, P. PRADAT-DIEHL. Ecological Assessment Battery for Numbers: validation study. Communication orale, congrès international de réhabilitation neuropsychologique (WFNR) (Maastricht, juillet 2013)
12. M. VILLAIN, O. HEINZLEF. D'une difficulté à identifier la dysphagie dans la sclérose en plaques à la validation d'un questionnaire de dépistage destiné aux neurologues. Communication orale, congrès de l'UNADREO (Paris, décembre 2013)

13. M. VILLAIN, L. NGOUDJO-DEUTOU, A. DIAWARA, O. HEINZLEF. Validation française d'un questionnaire de dépistage des troubles de déglutition dans la sclérose en plaques, étude DY-MUS. Poster, Journées de Neurologie de Langue Française (Montpellier, avril 2013)

C. ACTIVE, APPROVED or COMPLETED GRANTS unrelated to the present proposal

- Ligue Française contre la Sclérose en Plaques (2011) : étude sur le dépistage des troubles de déglution dans la Sclérose en Plaques. Bourse de recherche de 15000€

- Société Française de NeuroVasculaire (2013) : étude des déterminants des troubles de l'humeur après un Accident Vasculaire Cérébral. Bourse paramédicale de 10000€

- Fondation pour la Recherche Médicale (2015) **:** financement de fin de thèse (10000€)

FACILITIES AND RESOURCES OF THE HOST INSTITUTION

The applicant will be hosted primarily at **STMS** (UMR9912, IRCAM/CNRS/Sorbonne Université) in the PDS/CREAM research team (http://cream.ircam.fr). **STMS** (Sciences and Technology of Music and Sound**)** is the country's only laboratory fully devoted to the science and technologies of voice and music, located in Institut de Recherche/Coordination en Acoustique et Musique (IRCAM) in Paris. It brings to the project high expertise in psychoacoustics, reverse-correlation and emotional speech, and a technical environment consisting of an EEG/EMG lab and audiometric cabins for psychophysics.

Jean-Julien Aucouturier (PhD 2006, HDR 2017), neuroscientist, CR CNRS and PI of ERC StG CREAM (2014-2019), will be the applicant's main PhD supervisor. From 2012 to 2019, JJA has been the main supervisor of 2 PhD students (defended, 2018), 5 postdocs, and 7 MSc. students. The applicant will be enrolled in the Brain, Cognition and Behaviour Graduate School (ED3C) of Sorbonne Université. In addition, through its affiliation with IRCAM and CNRS, the host institution will provide the applicant with training opportunities, via the continuing education program of CNRS, and the doctoral training institute of Sorbonne Université.

Throughout the project, the applicant will also have a secondary affiliation with Physical and Rehabilitation Medicine Unit, Pitié-Salpêtrière Hospital, Paris. The Unit will provide facilities for patient testing, speech therapy booths, assessment tools and softwares and access to the ICM Living Lab for application development and testing in WP3. Two interns in speech therapy's studies (5th year) will welp Melissa in assessing patients. Marie Villain (PhD 2016), speech therapist, neuroscientist, will be the applicant's PhD co-supervisor. MV works at Physical and Rehabilitation Medicine Unit, Pitié-Salpêtrière and has been the main supervisor of 6 MSc students.

Marie Villain, Emmanuel Ponsot and JJ Aucouturier have co-supervised the research project of the applicant's Master of Science in 2017-2018.

In addition to the supervision team, the project builds on the collaboration with Dr Emmanuel Ponsot (Ecole Normale Supérieure, Paris), for the computational modeling studies of WP2, and Romain Gombert (Brain and Spine Institute, Paris) for the therapeutic application development of WP3.