

(April 2021)



Latest news from

1

General

Dear All,

Please take the time to find the latest news and updates of our R-LiNK project at the beginning of 2021.

- The recent R-LiNK consortium meeting successfully took place on 18th and 19th March. Due to the ongoing pandemic instead of meeting in Milan in person, the R-LiNK consortium members met virtually. Around 70 people participated and joined the lively discussions or listened to presentations from the nine workpackages.
- Fortunately, the implementation of Li7-Magnetic Resonance Spectroscopy in 6 different sites has been realized by WP5.
- Meanwhile the study is approved in all sites (except for Gothenburg, see below) and study initiating visits have been performed in almost all sites.
- Even though recruitment is faced with a lot of challenges, **46** patients have been included in the study in 11 sites!
- We are happy to announce that a new project manager has been recruited: Welcome Antoine Campagne!

Below, you will find a short overview from each work package.

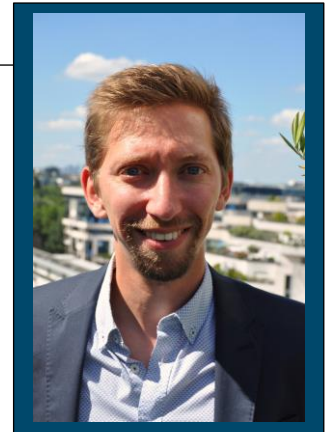
All the best

WP leaders and Project Management Team

NOTABLE. Remember if you need important documents such as SOPs, reports, ExCom Minutes, Protocol etc. you will find them on the project website and extranet <https://rlink.eu.com/collaborative-research-project/>

2

WP1



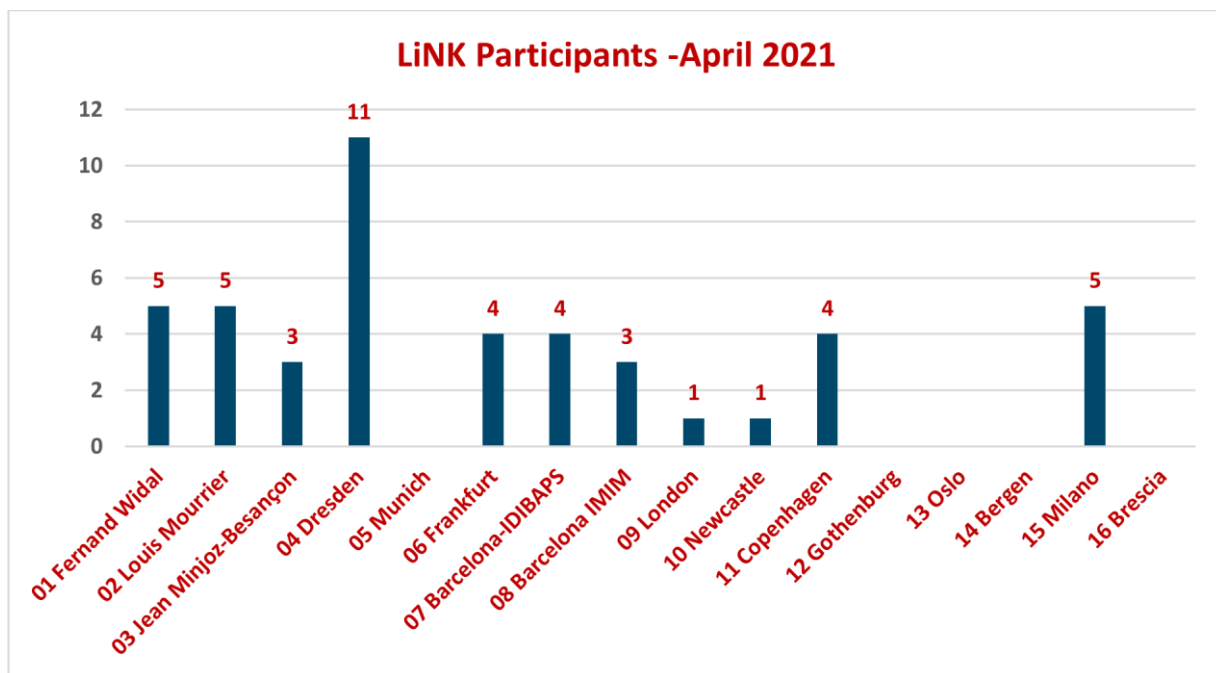
Once again we would like to cordially welcome our new project manager: Antoine Campagne (antoine.campagne@inserm-transfert.fr) has joined INSERM Transfert and is replacing Barbara Cagniard. Delphine Smagge will continue to follow the project, but Antoine will take the lead from now on.

Thank you Delphine for your great effort during the last months!

The amendment of the Grant Agreement was accepted on February 16th. It includes the addition of the University of Greenwich (UG), following the move of Professor Paul McCrone from KCL to UG. WP 1 is also still working on the finalization of the second periodic report (1 July 2019-31 Dec 2020). Antoine Campagne and colleagues will continue to organize the monthly telephone conferences for the Executive Committee and plan the next annual meeting in October 2021.

3

WP2 / WP3



3

WP2 / WP3

46 patients have been included in 11 sites, among them 5 dropped out so far. Munich, Bergen and Oslo are open and ready for the first participants. Brescia is awaiting the study initiation visit. The Swedish partners in Gothenburg are required to provide a new ethics approval (since two years have past since the beginning of the study), which delays even more the start of recruiting. Additionally, important payment and funding issues need to be resolved.

The general delay in recruiting has a substantial effect on the follow up period that covers two years from the point of inclusion. The coordinator is currently working with all WP leaders and consortium members to establish a new realistic calendar with regard to the impact of the ongoing COVID-pandemic.

The consortium meeting offered a great opportunity to share some experiences from the different recruiting sites (Paris, Dresden, Frankfurt, Barcelona, Newcastle): The participants agreed that the amount of questionnaires presents a considerable burden for the participants, discussed challenges when recruiting inpatients, shared their struggles regarding the organisation of MRI which proved difficult in some locations, and stressed the differences in Lithium dosage (morning and evening) that have an impact on the organisation of the scanning appointments. It became clear that staying in touch with the participants obtains priority and requires considerable flexibility in these days.

4

WP4

MRI data was so far acquired in Paris, Besançon, Dresden, Frankfurt, Barcelona, Newcastle and Milan. WP4 is responsible for data collection, sanity check and quality control. At the moment, WP4 is working on the finalization of the MRI SOP for the centralized database – consequently the first data should be transferred to the centralized database in the near future (in collaboration with WP7). The data that has been collected so far includes 27 data sets of MRI data from the first visit with satisfactory data quality and 13 MRI post Lithium data sets. In the light of some misunderstandings, the WP4 leaders would like to stress that both WP4 acquisitions (baseline and follow-up) are mandatory and WP5 acquisitions do not replace any WP4 sequence. What is more is that the order of the acquisitions cannot be modified. To be short, protocol adherence is required in the scanning sites during the post-lithium scans. WP4 will continue to closely monitor within and between centre consistency regarding the collection of MRI data.

5

WP5

Important milestones have been achieved by WP5 that deserve to be pointed out: The classical MRI harmonization was achieved in order to be able to analyse neuroimaging data generated by 15 different platforms from three different brands (Siemens, GE and Phillips) and the implementation of lithium MRI in Dresden, Milan and Paris.

As mentioned before, during the post-lithium visit it is important to establish both WP4 and WP5 protocols and to stick to the sequence. At single scanner sites, WP4 data should be acquired first. Additionally, WP5 data should be as best acquired 12 hours post-dose and Lithium levels should be taken at the time of scanning. So far, month 3 WP5 data has been acquired from Dresden, Milan and Paris. The timing of the scan raised some discussion, since it is ideally realized two hours post-dose. This is considered to be achievable in UNEW, CEA, TUD, UMIL and UCo. Munich are constrained by clinical activity on their scanner and only have afternoon sessions. If consistent, this may be addressed systematically or through timing of dose. Once daily dosing is standard in UNEW and Uco. Twice daily possible or probable at other centres. David Cousins will soon grant access to an updated set of frequently asked questions (FAQs).

6

WP6

WP6 experiences a delay in identification of biomarkers associated with response in the R-LiNK samples. During the consortium meeting, Annamaria Cattaneo reminded the sites that the blood samples from each recruiting centre will be shipped both to IRCCS and to LMU. The shipment will be organized once blood samples from 10 patients (B and FW) have been collected.

7

WP7

WP 7 is working on the transport of the different types of data to the central database and controls the quality of the data. Regarding MRI data and Lithium MRI data, the quality is almost satisfactory (some details remain with Lithium MRI). For OMICs data (WP4), the SOPs for methylation are fine, whereas those for miRNA are still work in progress. The SOPs that provide a guideline for the collection of actigraphy data are almost finalized, some minor issues need to be resolved. The SOPs for the smartphone assessment are currently in preparation as well, whereas for the eCRF, the SOPs and the data upload to the data base are being finalized.

8

WP8 / WP9

These two workpackages continue to create four internal newsletter together every year and present news on the R-LiNK website. Furthermore, a set of slides that withholds some crucial information on the study and its current status for World Bipolar Day and international conferences in the future are being created. This way, interested parties will be provided with contact information and a short summary of the study background. Since eleven sites are recruiting now, the teams are invited to try out the messenger service Flock that was established to solve practical problems with the help of the experience of other teams.