

Loneliness experience through COVID-19 pandemic and lockdown is related with resting-state brain networks functional connectivity

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Abstract

Background: The reduction in social interactions often associated with old age frequently initiates or aggravates loneliness, increasing the risk of a number of diseases including depression and dementia (Mushtaq et al., *JCDR*. 2014;8(9):E01-WE4.). Loneliness has been related to particular patterns of brain resting-state networks (RSNs; Spreng et al., *Nat Commun*. 2020;11(1):6393). However, the role of RSNs in a resilient response to reductions of social interactions remains unknown and the COVID-19 pandemic provides a unprecedented opportunity to investigate it.

Method: Repeated loneliness assessments were collected by the Barcelona Brain Health Initiative (BBHI; www.bbhi.cat/en/) using the short UCLA Loneliness Scale (Russell et al., *J Pers Assess*. 1978; 42(3):290-294). Two timepoints were measured over two years prior to COVID-19 outbreak and four thereafter (March, April, June and October 2020). We used baseline resting-state functional magnetic resonance imaging (rs-fMRI), from 281 participants (mean age 53.91±7.35; 137 women), acquired within 1-2 years prior to the pandemic to compute resting-state functional connectivity (rs-FC) for each pair of nodes defined by the Schaefer-Yeo atlas. Then, we utilized partial least squares (PLS) analysis for the decomposition of two multivariate sets (i.e., rs-FC and loneliness scores) into latent variables of maximal covariation.

Result: We identified two latent trajectories significantly correlated with two latent connectivity patterns, each of them describing approximately opposite baseline rs-FC and loneliness levels during the months with the most severe restrictions (i.e., March and April). The first latent trajectory showed greater baseline loneliness improving during the pandemic, associated with higher within-network connectivity in the limbic and salience networks. The second trajectory captured individuals with baseline loneliness levels similar to the average population, improving in March, at the beginning of outbreak, and worsening in April, which was related to lower baseline within-network connectivity in the DMN and higher in the dorsal attention and visual circuits.

Conclusion: Present findings reveal specific associations between RSNs' functional connectivity and opposite changes in feelings of loneliness during an unanticipated

period of severe social restrictions. Specifically, lower rs-FC of limbic networks combined with high connectivity of salience system at baseline suggested greater resilience to the negative impact during the pandemic on loneliness.

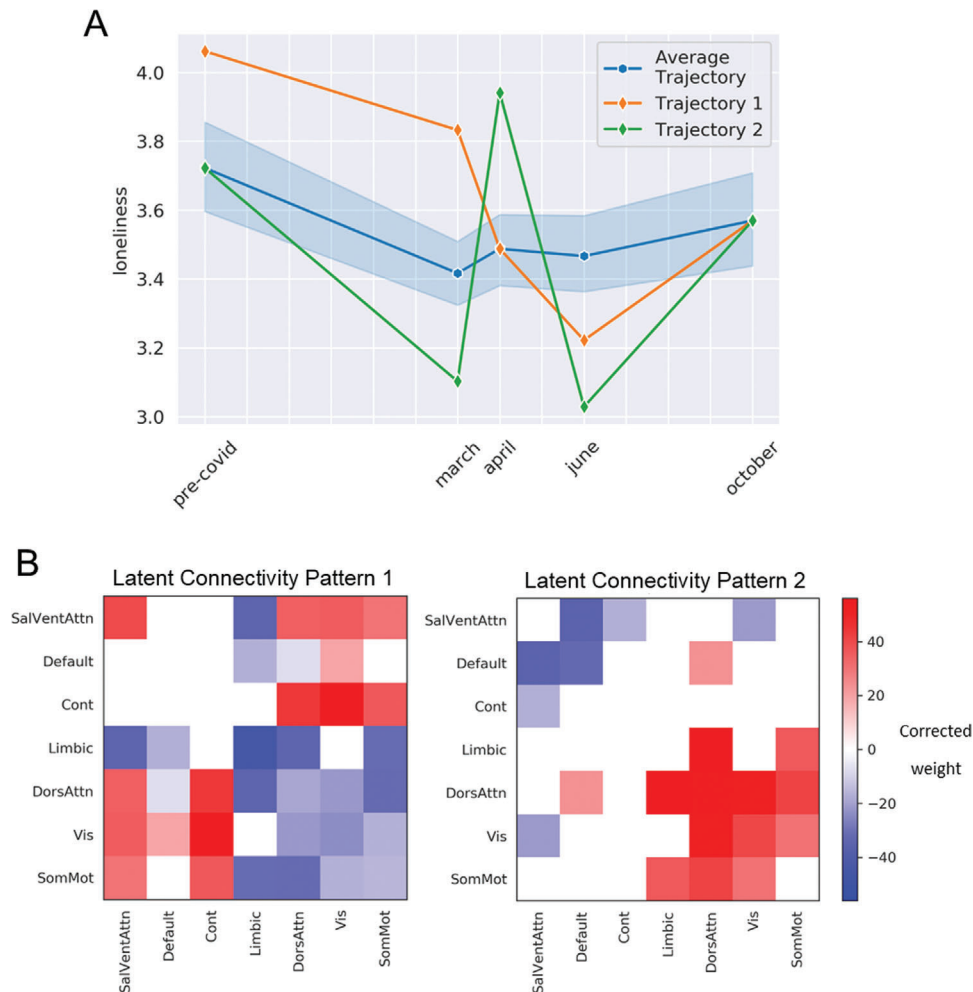


Fig. 1. A) Trajectories along the studied loneliness assessments (pre-covid, march, april, june and october). Particularly, pre-covid timepoint represent the mean loneliness of the two timepoints that were measured within the first two years prior to COVID-19 outbreak. Blue line depicts the average loneliness trajectory at the level of the whole population and shadowed blue area shows the confidence interval of 95%. Orange and green lines are, respectively, the first and second estimated latent trajectories, identified by PLS analysis, which are significantly correlated ($p < 0.05$) with the latent connectivity patterns shown in B. **B)** Heatmaps representing the corrected version of the weights that PLS assigns to each pair-wise rs-FC at the level of seven RSNs, from the Schaefer-Yeo atlas of 100 sub-ROIs (Schaefer et al., *Cereb Cortex*. 2018; 29:3095-3114). Due to the scalation of data prior to PLS analysis, corrected weights (i.e., divided by standard error estimated by bootstrapping resampling and thresholded at corrected-weight > 2) explain the amount of deviation from mean pair-wise rs-FC (for further details see Mwilambwe-Tshilobo et al., *Cogn Affect Neurosci*. 2019;14(4):423-433). In consequence, blue squares are interpreted as patterns of lower than average RSN functional connectivity and red ones as the opposite.

FIGURE 1