Beyond "Correlation vs. Causation": Multi-brain Neuroscience needs Explanation

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Recent advances in brain sciences have enabled the co-recording of multiple interacting brains (i.e. hyperscanning [1]). This technique has led to the discovery of inter-brain synchrony (IBS) between people involved in social and interactive scenarios. In a recent article, Novembre and Iannetti argued that studies using hyperscanning to understand social behaviors are crucial but limited to correlational analysis [2]. They further develop the idea that the causal role of IBS can only be apprehended through multi-brain stimulation (MBS). Although we agree with Novembre and Iannetti that MBS is one of the most promising methods for investigating inter-brain coupling in the future, we disagree on their radical claim that it constitutes "*the only validated empirical approach capable of teasing apart the mechanistic from the epiphenomenal interpretation of inter-brain synchrony*". In this letter, we aim at defending the idea that explaining IBS in terms of causal mechanisms is possible through adequate experimental designs and computational tools, with empirical approaches ranging from multi-brains (hyperscanning) to single-brain (classic social neuroscience) recordings, and even no-brain (i.e. in-silico computational social neuroscience) (see Fig. 1).

It is widely accepted that IBS relies partly on sensorimotor loops from at least two participants: the motor outputs of one participant being the sensory inputs of another. Hence, one can argue that the bidirectional exchange of sensorimotor information is already a non-interventional, but ecological, multi-brain stimulation. As explained by Novembre and Iannetti, the non-negligible advantage of brain stimulations —including their “Sensory MBS”— is a greater control of causal perturbation or enhancement of this natural phenomenon to study its impact on behavior. However, while hyperscanning is still at its early stage and faces important challenges, including going beyond correlational results, we advocate for the

development of new experimental designs and analytic pipelines. We believe that capitalizing on various tools, such as recent computational analyses and models, will allow future studies using hyperscanning, and even single-brain recordings, to make causal inferences.

First, multi-brain recordings can target the role of IBS beyond the solely observational level by linking behavioral and biometric channels [1], but also through multiple Brains-Computer-Interface [3] or multi-brain neurofeedback [4]. For example, in the case of dual-neurofeedback, Duan and colleagues [4] propose to use IBS as an independent variable and that "*observ[ing] the behavioral effect as a dependent variable [...] can provide more causal insights into the relationship between brain and behavior*". Hence, cross-channel feedback (Fig 1A) can place IBS as independent variables (without inducing it through stimulation) and thus pave the way for new socio-interactive experiments aiming to understand how IBS facilitates social interactions.

In addition, human-machine interaction using a responsive virtual partner, can also systematically explore the parameters space at the behavioral level, integrating well-controlled perturbations grounded in empirical observations [5]. Combined with brain recordings, such a paradigm allows tracking in real-time representation of self and other behavior [6]. Therefore, single-brain recordings can also demonstrate core structural causation at play in IBS by uncovering specific neural mechanisms implicated in the integration of the ongoing inter-personal coupling during social interaction (Fig. 1b).

Furthermore, mathematical models can also uncover counterfactual explanations and logical causation that remain useful for a mechanistic understanding of natural phenomena [7]. The recent development of computational neuroscience allows in-silico experiments with simulated virtual brains in interaction that highlight causal-mechanisms underlying IBS (Figure 1c). For example, the anatomical structure of the human connectome not only facilitates the integration of information across distant areas within one brain, but also appears to potentiate the propensity of two brains to enter in mutual entrainment [8]. Recently, similar computational models demonstrated how interpersonal coupling strategies rely on the balance between intra- and inter-brain synchrony patterns, with for example higher between-unit coupling than within-unit coupling during mutual adaptation [9, Fig. 1c].

Moreover, as noted by Novembre and Iannetti (see their Box 1, [2]), computational analyses and quasi-experimental methods can also bring causal inference in absence of intervention [10]. A crucial factor for those methods to infer causality is the proper assessment of generalizability, i.e. to what extent the results from a specific sample apply to the general population and context [7]. Interestingly, this issue of generalizability strongly applies to perturbation paradigms [11]. Indeed, artificial brain stimulations cannot mimic natural brain

stimulations and thus create "supernatural" brain states that would never occur in daily life. In fact, recent philosophical debates emphasize how neuroscience aiming at studying brain-behavior dynamics mainly focuses on the development of fancier tools to analyze and influence brain data, resulting in a (sometimes unwitting) reductionist approach of behavior [12].

Hence we argue, building on Novembre and Iannetti's perspective, that without a clear understanding of behavior and the influence of socio-cognitive factors, neural variables (correlational or causal) cannot lead to what (social) neuroscience needs: Explanation [7]. Explanation is to be understood here as a coherent theoretical framework describing the causal structure of a given occurrence, integrating behavioral dynamics with neural mechanisms, but also the causal sequence leading up to this phenomenon. Overall, as IBS remains widely misunderstood, we believe that it requires the development of a general model and that only methodological and conceptual plurality will contribute to this collective endeavor.

References

1 Montague, P.R. et al. (2002) Hyperscanning: Simultaneous fMRI during Linked Social Interactions. NeuroImage 16, 1159–1164

2 Novembre, G. and Iannetti, G.D. (2020) Hyperscanning Alone Cannot Prove Causality. Multibrain Stimulation Can. Trends Cogn. Sci. DOI: 10.1016/j.tics.2020.11.003

3 Bonnet, L. et al. (2013) Two Brains, One Game: Design and Evaluation of a Multiuser BCI Video Game Based on Motor Imagery. IEEE Trans. Comput. Intell. AI Games 5, 185–198

4 Duan, L. et al. (2013) Cross-Brain Neurofeedback: Scientific Concept and Experimental Platform. PLoS ONE 8, e64590

5 Dumas, G. et al. (2014) The Human Dynamic Clamp as a Paradigm for Social Interaction. Proc. Natl. Acad. Sci. U. S. A. 111, E3726–34. DOI: 10.1073/pnas.1407486111.

6 Dumas, G. et al. (2020) The Human Dynamic Clamp Reveals the Fronto-Parietal Network Linking Real-Time Social Coordination and Cognition. Cereb. Cortex DOI: 10.1093/cercor/bhz308

7 Craver, C.F. (2007) Explaining the Brain, Oxford University Press.

8 Dumas, G. et al. (2012) Anatomical Connectivity Influences both Intra- and Inter-Brain Synchronizations. PLoS ONE 7, e36414

9 Heggli, O.A. et al. (2019) A Kuramoto model of self-other integration across interpersonal synchronization strategies. PLOS Comput. Biol. 15, e1007422

10 Marinescu, I.E. et al. (2018) Quasi-experimental causality in neuroscience and behavioural research. Nat. Hum. Behav. 2, 891–898

11 Jazayeri, M. and Afraz, A. (2017) Navigating the Neural Space in Search of the Neural Code. Neuron 93, 1003–1014

12 Krakauer, J.W. et al. (2017) Neuroscience Needs Behavior: Correcting a Reductionist Bias. Neuron 93, 480–490

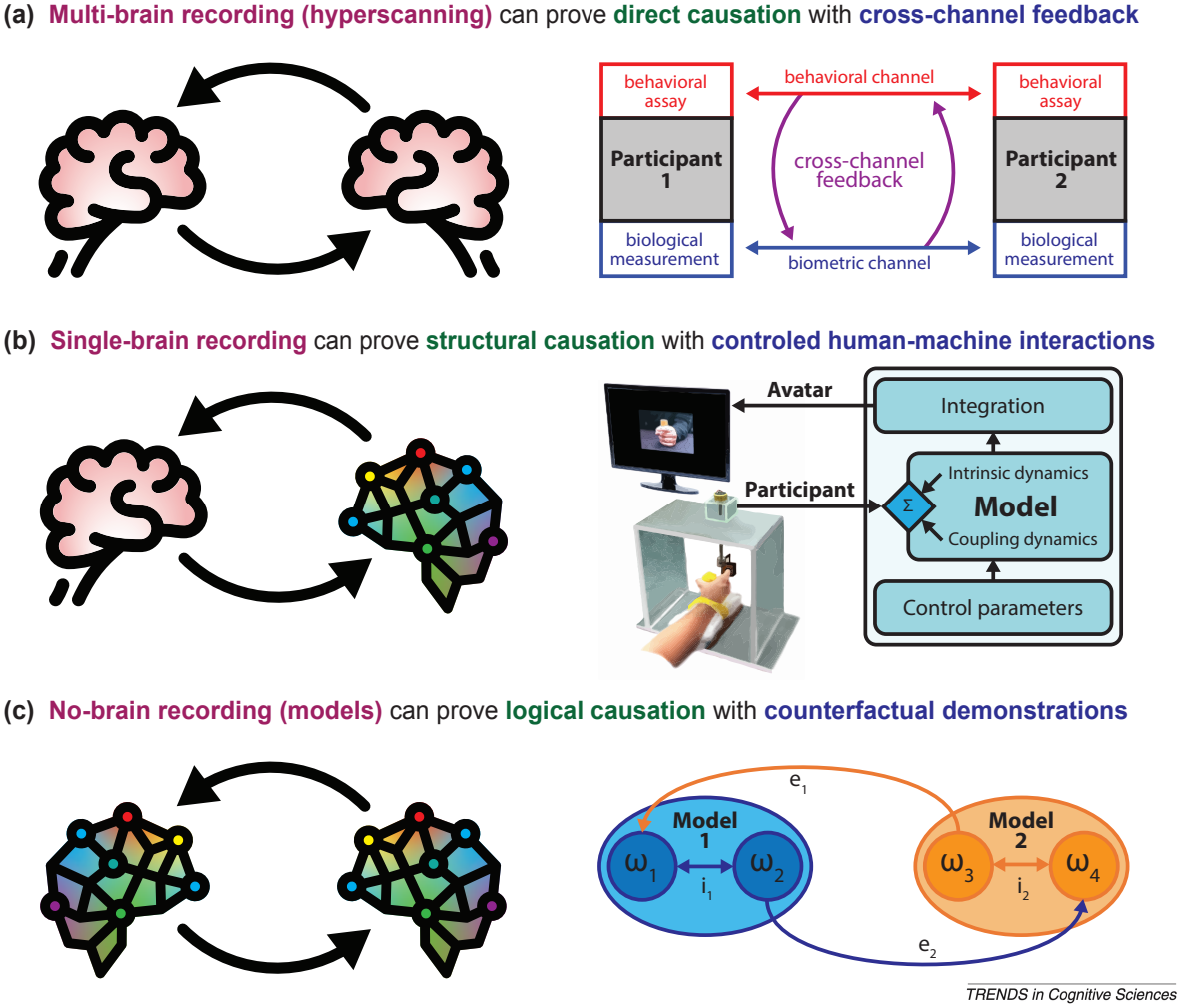

Figure 1. Illustration of three empirical designs that can provide explanation of causal mechanisms at play in the inter-brain synchronization phenomena without relying on multi-brain stimulation. Example of studies on the right, from top to bottom: [1,5,9].