

# The gendered self: Evidence for differences in whole-brain dynamics

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### Abstract

How the brain constructs gender identity is largely unknown, but some neural differences have recently been discovered. Here, we used an intrinsic-ignition framework to investigate if gender identity changes the propagation of the neural activity across the whole-brain network and within resting-state networks. Studying 29 transmen and 17 transwomen with gender incongruence, 22 ciswomen, and 19 cismen, we computed the capability of a given brain area in space to propagate activity to other areas (mean-ignition) and its variability across time (node-metastability). We found that both measures differentiated all four groups across the whole-brain network. Furthermore, at the network level, we found that compared to the other groups, cismen showed higher mean-ignition of the dorsal attention network and node-metastability of the dorsal and ventral attention, executive control, and temporal parietal networks. We also found mean-ignition differences between cismen and ciswomen within the executive control network, but higher in ciswomen than cismen and transmen for the default-mode network. For the node-metastability, this was higher in cismen compared to ciswomen in the somatomotor network, while both mean-ignition and node-metastability were higher for cismen than transmen in the limbic network. Finally, we computed correlations between both measures and their body image scores. Transmen dissatisfaction, cismen, and ciswomen satisfaction towards their own body image were distinctively associated with specific networks per group. Overall, the study of the whole-brain network dynamical complexity discriminates binary gender identity groups, and functional connectivity dynamics approaches are needed to disentangle the complex understanding of the gendered self.

**Keywords**— whole-brain dynamics, dynamical complexity, ignition, transgender, cisgender, sex/gender differences



## Significance statement

The study of sex/gender differences may be enriched by the heterogeneity of other gender minority groups, such as transgender. Functional connectivity measures capturing the spatio-temporal oscillations of the brain can provide insights on how the brain cooperates. This is the first study investigating how the whole-brain network propagates information across the brain, spatially and temporally, in binary gender groups (cisgender and transgender) by means of the intrinsic-ignition framework. We found four whole-brain unique phenotypes pertaining to each gender group, namely cismen, ciswomen, transmen and transwomen. Novel functional connectivity dynamics frameworks can contribute to disentangle the complex experience of a *gendered*-self.

## Introduction

A significant number of studies have explored sex-related differences in brain connectivity (Biswal et al., 2010; Ritchie et al., 2018; de Lacy et al., 2019; Eliot et al., 2021). However, the proposed sexual dimorphism, as observed in the reproductive organs, has been rejected in terms of psychological sex differences in the brain (Hyde et al., 2019; Eliot et al., 2021) and a meta-analysis informed about probable excessive significance reports, i.e., inducing a positive reporting bias (David et al., 2018). Furthermore, when investigating the brain differences between *females* and *males*, the heterogeneity of the sex/gender construct and its less prevalent forms, such as the transgender groups, have usually been overlooked. Gender identity can be defined as a complex multifactorial trait that may or may not be binary and that may correspond either to one's sex assigned at birth, i.e., cisgender, or to a discrepant type, i.e., transgender (Polderman et al., 2018).

Understanding gender incongruence in transgender people has been a growing focus of interest, although it is important to note that not all transgender people present such incongruence. Recently, intrinsic brain functional connectivity have differentiated gender groups (Nota et al., 2017; Clemens et al., 2020; Uribe et al., 2020b). However, as the brain networks are constantly interacting (Menon, 2011; Chen et al., 2013), the understanding of their interplay across the whole-brain underlying the complex construction of gender (Uribe et al., 2020b) is something worth exploring.

The study of the brain network interactions is enriched by investigating its spatio-temporal fluctuations in response to internal and external stimuli. Whole-brain dynamics differences between cismen and ciswomen have been described using a sliding window approach (de Lacy et al., 2019), and more recently, with a small dataset of transmen (Uribe et al., 2021). This latter study mainly differentiated cismen from transmen and ciswomen, while these last groups had statistically equivalent fluidity and range dynamism (Uribe et al., 2021). On the other hand, the brain dynamics of transwomen remain elusive. Although differences in the interactions among large-scale networks

25 between cis- and transgender groups have been described (Uribe et al., 2020b), it remains unclear how such networks cooperate to build gender identity.

In recent years, a growing number of data-driven approaches have been proposed to describe the spatiotemporal brain dynamics (Allen et al., 2014; Hansen et al., 2015; Deco et al., 2017a). Among them, the novel intrinsic ignition framework has been lately developed to investigate the propaga-  
30 tion of activity over time across the whole-brain (Deco and Kringelbach, 2017). This data-driven method was conceived to capture the influence of local activity on the global brain computation by describing the broadness of communication (Deco and Kringelbach, 2017). In particular, the concept of intrinsic ignition reflects a degree of global integration induced by the capability of a given brain area to propagate neural activity across the whole-brain network.

35 In this work, we explored gender-related differences in whole-brain functional dynamics. Specifically, we investigated the dynamical complexity of four gender groups (transmen and transwomen with gender incongruence, cismen, and ciswomen) by looking at the effects of spontaneously occurring local activation (i.e., events) on global integration (Deco et al., 2015) through the intrinsic ignition framework (Deco and Kringelbach, 2017; Deco et al., 2017b). While large samples are  
40 needed to capture gender effects in the brain (Ritchie et al., 2018), we studied a well-characterized group of cisgender and transgender people beyond the assumed self-identification to a cisgender identity.

Second, we were also interested in exploring the associations of the functional connectivity dynamics with the degree of satisfaction towards body parts. Although it may not be the case  
45 for all transgender people, they frequently report gender nonconformity towards the sex assigned at birth, especially when they still have not gone through a gender-affirmative hormone treatment (GAHT) (Selvaggi and Bellringer, 2011). The transgender participants of this study presented with such disconformity, and they were candidates to initiate GAHT.

## Methods and materials

### 50 Participants and instruments

Twenty-nine transmen with no GAHT initiated participants (age: mean(SD) = 24.7(6.2), range = 17 — 39; education: mean(SD) = 11.7(1.7), range = 9 — 15), 17 transwomen with no GAHT (age: mean(SD) = 21.4(3.9), range = 18 — 34, education: mean(SD) = 13.1(1.8), range = 10 — 16), 19 cismen (age: mean(SD) = 22.2(4.4), range = 18 — 32, education mean(SD) = 14.4(3.0), range  
55 = 10 — 20), and 22 ciswomen (age: mean(SD) = 19.6(2.4), range = 18 — 27, education: mean(SD) = 13.3(1.6), range = 12 — 17) were enrolled. All participants explicitly stated to have a binary identity, thus transmen and cismen identified themselves as a man, and transwomen and ciswomen

as a woman. Detailed demographic information such as age and education, and information of the protocol assessment and recruitment can be found in the data article (Uribe et al., 2020a).

60 All transmen and transwomen met diagnostic criteria for gender identity disorder according to the DSM-IV-TR and ICD-10 when recruited. Nonetheless, the diagnosis was relabeled to gender incongruence as per the ICD-11 and recommended by EPATH and WPATH v7 (Bouman et al., 2017).

Participants answered the Body Image Scale (Lindgren and Pauly, 1975). This auto-administered  
65 questionnaire has a total averaged score that includes: the nose, shoulders, chin, calves, hands, adam's apple, eyebrows, face, feet, height, hips, figure, waist, arms, buttocks, biceps, appearance, stature, muscles, weight, thighs, breasts, chest, body hair, facial hair, hair, voice, penis/vagina, scrotum/clitoris, and testicles/uterus. Participants scored each body part on a Likert scale ranging from 1 (Very satisfied) – 2 (Satisfied) – 3 (Neutral) – 4 (Dissatisfied) – 5 (Very dissatisfied). Written  
70 informed consent was obtained from all participants after a full explanation of the procedures. The study was approved by the ethics committee of the Hospital Clinic of Barcelona.

## MRI acquisition and preprocessing

Raw and processed imaging data are available online (Uribe et al., 2020a). MRI data were acquired with a 3T scanner (MAGNETOM Trio, Siemens, Germany). Briefly, T1-weighted images  
75 were acquired in the sagittal plane, TR = 2,300 ms, TE = 2.98 ms, TI = 900 ms, 240 slices, FOV = 256 mm; matrix size = 256 x 256; 1 mm isotropic voxel. A total of 240 T2\* weighted images were acquired with a TR = 2,500 ms, TE = 28 ms, flip angle = 80°, slice thickness = 3 mm, FOV = 240 mm. Participants were instructed not to fall asleep and not to focus in any specific thought, keeping their eyes closed. Basic preprocessing was conducted with AFNI using an in-house shell  
80 script. ICA-AROMA was applied for the automatic removal of motion-related artifact. No motion parameter differed between groups (Uribe et al., 2020a).

We extracted the timeseries of the 1,000 nodes parcellation in Schaefer et al. (2018) from Yeo's resting-state networks (Thomas Yeo et al., 2011) with the *fslmeants* tool from FSL v5.0.10 (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/>). The 17-network Schaefer parcellation was used to define  
85 networks by grouping, for example, the A, B, and C components of the default-mode or the executive control networks as one. We chose the 17 partition as there was the unique temporal parietal network, otherwise subdivided by several other networks in the 7-network partition, namely the default-mode, ventral attention, and somatomotor networks. For a comprehensive description of the method we refer readers to Schaefer et al. (2018) and Thomas Yeo et al. (2011).

## 90 Intrinsic ignition framework

We applied the intrinsic ignition framework to characterize gender-related differences in the spatiotemporal transmission of information across the entire brain over time (Deco and Kringelbach, 2017; Deco et al., 2017b). This framework has been used to successfully discriminate between different brain states, such as sleep (Deco et al., 2017b) and meditation (Escrichs et al., 2019), to explore  
95 differences in the healthy elderly brain (Escrichs et al., 2020), in depression (Alonso Martínez et al., 2020; Mayneris-Perxachs et al., 2021), and even in preterm children (Padilla et al., 2020). It allows computing the effect of spontaneous local activation on the whole-brain integration using the phase space of the signals. First, we filtered the blood-oxygen-level-dependent (BOLD) time-series parcellated in 1,000 brain regions within the narrowband 0.04 — 0.07 Hz to avoid artifacts (Glerean  
100 et al., 2012) (Figure 1.1A). Then, we calculated the instantaneous phase of the BOLD signals by computing the Hilbert Transform of the filtered time-series (Figure 1.1B).

Figure 1.2 gives a graphical representation of the algorithm used to compute the ignition value for each brain area evoked for an event within a fixed time window of 4-TR (TR = 2.5s). In brief, a binary event was defined by transforming the time series into z-scores,  $z_i(t)$ , and by fixing a  
105 threshold  $\theta$  (Tagliazucchi et al., 2012; Deco et al., 2017b). Then, the phase lock matrix  $P_{jk}(t)$  was calculated, representing the state of pair-wise phase synchronization at each time-point  $t$  between regions  $j$  and  $k$ , as given by:

$$P_{jk}(t) = e^{-3|\varphi_j(t) - \varphi_k(t)|} \quad (1)$$

where  $\varphi_j(t)$  and  $\varphi_k(t)$  represent the obtained phase at time  $t$  of the regions  $j$  and  $k$ . Given the fixed threshold  $\theta$ , the symmetric phase lock matrix  $P_{jk}(t)$  was binarized (Figure 1.2B) such that  
110  $\sigma(t)=1$  if  $z_i(t) > \theta$  and 0 otherwise. We computed the integration value as the length of the connected component (i.e., the largest subcomponent) considered as an adjacent graph (Figure 1.2C). Finally, we obtained the average integration value (i.e., ignition) by averaging across all events and the variability (i.e., node-metastability) by calculating the standard deviation, reflecting the spatial diversity across the whole-brain network and the level of variability over time for each brain region,  
115 respectively. The framework was applied to the whole-brain network parcellated into 1,000 brain areas and to each resting-state network separately: the dorsal and ventral attentional, executive control, default-mode, somatomotor, limbic, visual, and temporal parietal networks (Schaefer et al., 2018; Thomas Yeo et al., 2011).

## Statistical analyses

120 A general linear model and Monte Carlo permutation testing (1,000 iterations) to control for Family-Wise Error (FWE) rate were applied to perform group comparisons. Cohens's  $d$  effect sizes

were also calculated. Age and education were entered as covariates when comparing transmen and ciswomen, and the education variable alone when comparing transmen and cismen. Spearman correlations and 95% confidence interval were computed between the quantitative functional connectivity dynamics metrics and the body image scale total score per group. We did not include the visual network in the correlations, as there were no group differences within this network in ignition or node-metastability.

## Results

### Ignition across nodes

There were significant differences (FWE corrected  $p = 0.0042$ ) between all gender groups when computing the intrinsic ignition framework across the whole-brain functional network in both mean-ignition and node-metastability (Figure 2A and Table 1). There was a gradual progression in the mean-ignition, i.e., cismen>ciswomen>transmen>transwomen. On the other hand, the average node-metastability was the highest in the ciswomen group, and the lowest average was observed in the transmen group.

Figure 2B shows rendered brains, where the hot colors represent those regions with the highest ignition and node-metastability per group, while cold and dark tonalities represent the lowest values. The regional distribution of the highest ignition and node-metastability measures included regions across the whole-brain from all networks. There was no hemisphere predominance among the 100 areas with the highest ignition in any group (left/right: cismen 54/46 —out of the 100 regions—, ciswomen 43/57, transmen 51/49, transwomen 38/62,  $\chi^2=6.472$ ;  $p = 0.091$ ). Nodes in the right hemisphere were more frequent for the node-metastability measures except in the transwomen group (left/right: cismen 41/59, ciswomen 47/53, transmen 48/52, transwomen 61/39,  $\chi^2=8.512$ ;  $p = 0.037$ ).

### Ignition across participants

**Whole-brain.** There were no group differences that survived FWE correction (Figure 2C). When computing the intrinsic ignition framework by networks, group differences were present in all networks except for the visual network (Table 2, Figures 3 and 4). **Attentional network.** In the dorsal attention network, the ignition (Figure 3.1C and 3.2C) and node-metastability (Figure 4.1B and 4.2B) measurements were higher in the cismen's group with respect to ciswomen, transmen, and transwomen. Regarding the ventral subdivision of the attentional network, only the node metastability mean of cismen was higher than the other three gender groups, namely ciswomen, transmen, and transwomen (Figure 4.1C and 4.2C). **Executive control network.** Cismen's ig-

155 nition was significantly higher than ciswomen (Figure 3.1A and 3.2A). Cismen also had higher node-metastability than ciswomen, transmen, and transwomen (Figure 4.1A and 4.2A). **Default-mode network.** Ciswomen had higher ignition than cismen and transmen (Figure 3.1B and 3.2B). **Limbic network.** Both ignition and node-metastability measurements were higher within the cismen group with respect to transmen (Figures 3.1D, 3.2D, and 4.1D and 4.2D). **Somatomotor.** Cismen showed higher node-metastability than ciswomen (Figure 4.1E and 4.2E). **Temporal pari-**  
160 **etal.** Cismen had greater mean igniton than ciswomen, transmen, and transwomen (Figure 3.1E and 3.2E).

### Body image satisfaction correlations

The degree of dissatisfaction towards body parts was significantly higher in the two transgender groups in comparison to both cismen and ciswomen groups. On the other hand, satisfaction in the  
165 two cisgender groups was not statistically different (Figure 5A). The satisfaction/dissatisfaction with the body image within each gender group was associated distinctively with intrinsic ignition measures in specific networks. Cismen were the group with the highest overall mean satisfaction with their body, and this correlated negatively with the ignition in the executive control network and positively with node-metastability in the limbic network (Figure 5B). On the other hand, body  
170 image satisfaction in ciswomen correlated with the ignition in the default-mode network, which was reported to be higher in the ciswomen groups comparisons, and the temporal parietal's node-metastability (Figure 5C). Ventral attentional ignition was positively associated with the global score of the body image scale in transmen (Figure 5D).

Data of mean-ignition and node-metastability matrices per gender group and group comparisons  
175 stats are publicly available (<https://doi.org/10.6084/m9.figshare.14622564>).

## Discussion

For the first time, we characterize the spatio-temporal whole-brain dynamics of binary gender identities, cisgender and transgender. Our findings corroborate the existence of four brain phenotypes (Guillamon et al., 2016; Uribe et al., 2020b) beyond the classical, lately under questioning,  
180 conception that the human brain can be split into two configurations, the *male* and the *female* (Legato, 2018). We also demonstrate the need to study whole-brain networks in discriminating gender groups, untangling a complex phenomenon as the experience of a gendered self. To characterize the propagation of information and measure the degree of integration of spontaneously occurring events while at rest, we applied the intrinsic ignition framework (Deco and Kringelbach,  
185 2017; Deco et al., 2017b). Such a framework was very sensitive in detecting functional connectivity

differences between young adults grouped by gender. Some of these group functional connectivity differences had been elusive when using stationary functional MRI measurements (Uribe et al., 2020b), and sliding-windows approaches to study brain connectivity states (Uribe et al., 2021). In addition, spatial and temporal brain dynamics measures were uniquely related to the satisfaction  
190 towards body parts for cismen, ciswomen, and transmen.

The mean intrinsic ignition is an informative measure of the spatial diversity and broadness of communication across the brain. On the other hand, node-metastability captures the variability over time across the whole brain. Both the spatial and temporal variability that defined each gender group were widespread across the whole brain, including nodes from all functional networks.  
195 Likewise, when using a support vector machine algorithm inputting stationary group independent component maps and clinical data as features, four gender groups were obtained predicted by different patterns of brain connectivity (Clemens et al., 2020). In addition, our results stress the importance of using fine-grained connectivity measures to study spatio-temporal oscillations over grand averaged functional connectivity measurements, these latter enabling a more narrowed  
200 investigation of differences accountable for gender, and the incongruence felt in the transgender community.

Group differences in both subdivisions of the attentional networks and the executive control were in line with previous findings of functional connectivity differences, both stationary (Uribe et al., 2020a) and dynamic (Uribe et al., 2021). The particular group differences in the dorsal and the  
205 ventral subdivisions of the attentional network underline the need to study them separately. More relevant, the spatial broadness of communication of nodes in the default-mode network was higher in ciswomen with respect to cismen and transmen. Increased functional connectivity in default-mode regions has been reported in ciswomen in contrast with cismen (Biswal et al., 2010; Ritchie et al., 2018; de Lacy et al., 2019). Also, in the transgender literature, decreased connectivity in  
210 this network regions were found in the transmen group in contrast to cismen (Feusner et al., 2017; Uribe et al., 2020a) and ciswomen (Feusner et al., 2017) while it is not a generalized finding, as other studies had negative reports (Nota et al., 2017; Clemens et al., 2017).

On the other hand, the cismen reported pattern of activation relies on sensory-motor regions (Ritchie et al., 2018). The somatomotor network in the Schaefer parcellation included areas of  
215 motor action and sensory inputs of the external world, thus it is the most direct network interacting with our environment. Despite the previous relevance given to such functional network in understanding the own body perception and subsequently explaining the incongruence in transgender people (Manzouri et al., 2017; Burke et al., 2019), the intrinsic ignition framework only differentiated both cisgender groups in terms of temporal variability. Indeed, in our previous work  
220 of functional connectivity dynamics (Uribe et al., 2021), a sensorimotor state was found, although



no differences between trans and cisgender groups were captured (Uribe et al., 2021).

The spatial and temporal dynamism of the limbic network was greater in the cismen group than in transmen. On the other hand, increased limbic connectivity in transgender individuals has been reported when viewing "ambiguous, androgynous images of themselves morphed toward their gender identity" (Majid et al., 2020). Such findings should be further explored. Different functional MRI measurements do not allow further discussion, and greater integration, broadness of communication, and temporal variability do not necessarily translate to increased averaged connectivity.

The superior parietal cortex has been previously linked to gender differences when comparing cismen with ciswomen and transgender groups, structurally (Zubiaurre-Elorza et al., 2013) and functionally (Uribe et al., 2020a). The choice of the Schaefer parcellation (Schaefer et al., 2018) depicted a high representation of the temporal parietal network in terms of brain dynamics in agreement with temporoparietal junction findings in transmen with respect to cisgender groups (Manzouri et al., 2017). The spatial diversity and broadness of communication of temporal parietal regions were greater in cismen than in the other three gender groups, namely ciswomen, transmen, and transwomen.

The fact that cismen present higher brain dynamism than other gender groups, especially ciswomen and transmen, would be in line with previous brain states occupancy where cismen occupied more combinations of connectivity patterns over time than ciswomen (Yaesoubi et al., 2015). Nonetheless, such results have not consistently been replicated, like other brain flexibility measures through brain states using sliding windows reported regional brain dynamism for both cismen and ciswomen differentially (Mao et al., 2017). In addition, the increased spatial and temporal variability of brain oscillations in cismen was not homogeneous for all networks, as in the default-mode network.

Transwomen presented a lateralized predominance in the regions with the highest node-metastability in the left hemisphere. The discussion of such findings is limited due to the scarce literature investigating gender differences in brain dynamism. To the best of our knowledge, previous reports of the gender effects in the lateralization of brain connectivity patterns were mostly comparable between a large sample of cis men and women, with two marginal findings that did not survive false discovery rate correction and were considered a trend-level effect (Agcaoglu et al., 2015; Eliot et al., 2021), and marginal leftwards lateralization in ciswomen only in the inferior frontal cortex (Tomasi and Volkow, 2012). Given these and the small sample of individuals investigated, especially in the transwomen group, our results should be taken carefully.

Finally, the (dis)satisfaction towards the own body parts is not simply associated with a specific network, but differently according to the group, which suggests a different way to understand and accept the body depending on gender. The transmen group image (dissatisfaction) relied on the

ventral attentional, i.e., salience network. If one key element in the construction of gender is the perception of our own body (Peelen and Downing, 2007; Burke et al., 2019), the salience network has been highly related to trans and cisgender differences that may explain the gender incongruence (Uribe et al., 2020a, 2021). However, such a landmark is not helpful for the functional correlates of cisgender groups. These differences in the networks correlates could be driven by the fact that the transmen group scores were within the range of the unconformity towards the body parts —4-5 points in the Likert scale of Lindgren and Pauly (1975)—, while cisgender groups would range mainly within the neutral-satisfaction scores (1 to 3 points). Thus, the cismen group’s satisfaction and/or neutrality were positively associated with the limbic network and negatively with the executive control. On the other hand, the network with higher spatial dynamical complexity, i.e., the default-mode, was also associated with body parts satisfaction in ciswomen. Our works provide evidence that the construction of a gendered self, i.e., an inner self with maleness, femaleness, or other variants endowed, is a complex phenomenon characterized by the whole-brain network interplay in terms of spatial and temporal variability that exceed the rather specific correlates of the degree of satisfaction towards the own body.

Some shortcomings should be addressed in future works. First, the aforementioned need to increase the sample size that would add more power to the findings. Collaborative initiatives currently ongoing are trying to overcome such a persistent limitation in the neuroimaging field as for the ENIGMA initiative on transgender health (Mueller et al., 2021). However, it lacks standard acquisition protocols to reduce the variability accounted for sites that may hamper group discrimination. Second, the menstrual cycle of ciswomen and transmen was not accounted as a variable of interest, while there is growing evidence pointing out there are functional connectivity dynamics differences across the menstrual cycle (De Filippi et al., 2021). Likewise, the sexual orientation of all participants was not systematically assessed.

Including minority gender groups when investigating the gender phenomenon in the brain are imperative to understand the complexity of the gender experience. Nonetheless, future studies should include other gender groups, such as nonbinary or other genderqueer identities. Our exploratory work could potentially impact awareness, the development of healthcare guidelines, societal and political evidence-based changes accounting for such heterogeneity, and improving the quality of life while raising visibility that can help fight stigma (Janssen and Voss, 2020).

## Conclusion

First, we propose a gendered brain perspective of spatio-temporal whole-brain communications across networks that characterize four binary gender groups, namely cis- and trans- men and women. Second, we stress the need to study the brain as a whole complex system beyond the localizationism

290 paradigm when investigating complex phenomena such as the unique construction of gender. Third, taking advantage of novel brain dynamics techniques to understand network cooperation and the brain's dynamical complexity, we confirm and expand previous findings relating to the attentional network as the cornerstone of gender differences. However, the default-mode, executive control, limbic, somatomotor, and temporal parietal networks also presented differences in information  
295 propagation between cis and transgender identities. Fourth, we propose a unique brain network experience in perceiving satisfaction towards the own body parts according to each gender group. Finally, novel cutting-edge frameworks in studying brain dynamics are needed to untangle the complex and very intimate experience of a gendered self.

## Authors contributions

300 **Carne Uribe:** Designed research, Analyzed data, Investigation, and Writing - Original draft preparation. **Anira Escrichs:** Designed research, Analyzed data, Software and Writing - Original draft preparation. **Eleonora de Filippi:** Visualization and Writing - Original draft preparation. **Yonatan Sanz-Perl:** Software and Writing - Reviewing and Editing. **Carne Junque:** Supervision and Writing - Reviewing and Editing. **Esther Gomez-Gil:** Investigation and Writing -  
305 Reviewing and Editing. **Morten Kringelbach:** Methodology, Software and Writing - Reviewing and Editing. **Antonio Guillamon:** Funding acquisition and Writing - Reviewing and Editing. **Gustavo Deco:** Methodology, Software and Writing - Reviewing and Editing.

## Data accessibility statement

Imaging raw and processed data used for this study and demographical variables are publicly avail-  
310 able in Data Mendeley repositories (Uribe et al., 2020a): <https://doi.org/10.17632/hjmfvr6vmg.2>, <https://doi.org/10.17632/rw2yhtpj96.3>, <https://doi.org/10.17632/bgyzz94mz9.3>. The data that support the findings of this study are openly available in <https://doi.org/10.6084/m9.figshare.14622564>.

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455 **Figures**

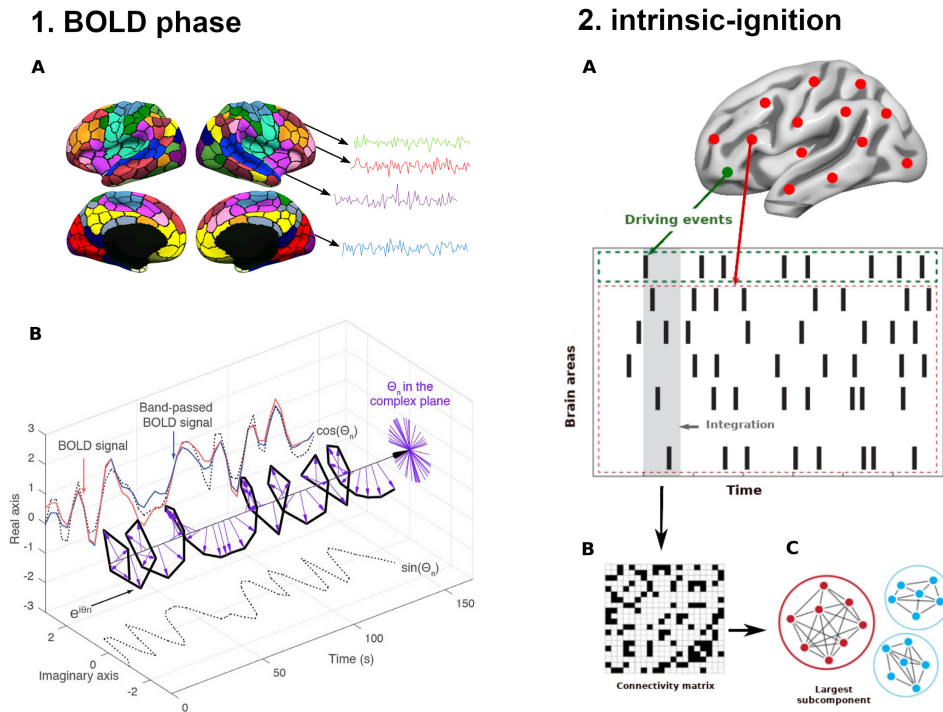


Figure 1: Intrinsic ignition framework. **(1)** We extracted the BOLD time series for each of the 1,000 brain areas and computed the phase space of the BOLD signal. **(1A)** We obtained the time series of each parcellation using the resting-state Schaefer atlas (Schaefer et al., 2018). **(1B)** Then, we measured the phase space of the BOLD signal through the Hilbert transform for each region. The BOLD signal (red) was band-pass filtered between 0.04 — 0.07 Hz (blue) and using the Hilbert transform. The phase dynamics can be represented in the complex plane as  $e^{i\varphi}$  (black bold line), the real part as  $\cos \varphi$  and the imaginary part as  $\sin \varphi$  (black dotted lines). The purple arrows represent the Hilbert phases at each TR (2.5s). **(2)** Intrinsic ignition measurements. **(2A)** Events were captured applying a threshold method (Tagliazucchi et al., 2012) (see green node). For each event elicited, the activity in the rest of the network (see red stippled region) was measured in the time-window of 4-TR (4x2.5s) (gray area). **(2B)** A binarized phase lock matrix was obtained from the time-window. **(2C)** From this phase-lock matrix, we obtained the integration measure by computing the largest subcomponent, i.e., by applying the global integration measure (Deco et al., 2015, 2017b). Repeating the procedure for each driving event, we obtained the ignition and node-metastability of the intrinsic-driven integration for each brain region across the whole-brain network. Figure adapted from (Deco and Kringelbach, 2017; Deco et al., 2019; Escrichs et al., 2020).

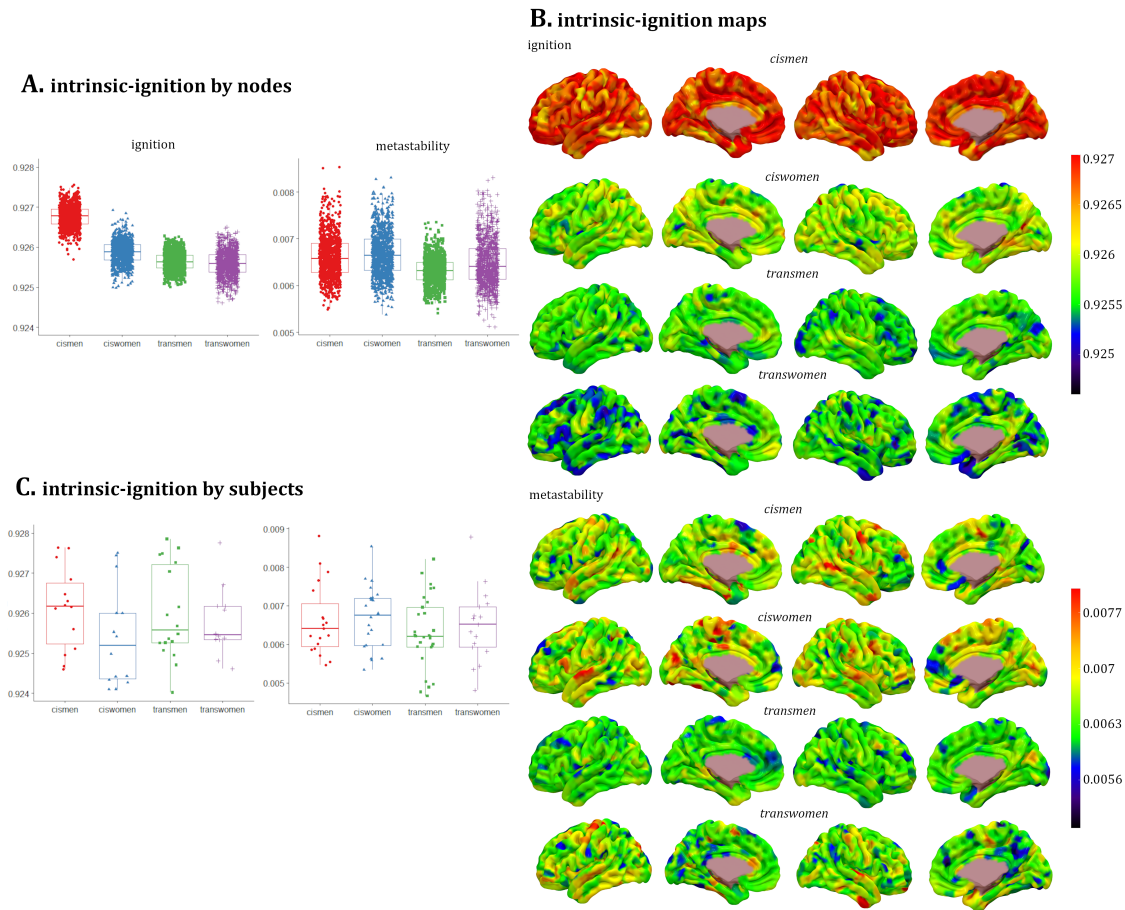


Figure 2: Whole-brain ignition and node-metastability measures for each of the 1,000 brain regions by each group. **(A)** The boxes in the plots indicate the second and third quartile (IQR), and middle lines are medians. Each dot represents a brain region. Means and standard deviations can be found in Table 1. There were significant differences between all groups' contrasts with Monte-Carlo 1,000 permutations and Bonferroni correction  $p = 0.0004$ . **(B)** Rendered brains show the distribution of ignition and node-metastability values per each brain region by group. Red warm regions had the highest ignition and node-metastability values, and dark blue ones the lowest. **(C)** Ignition and node-metastability measures with averaged regions for each participant by groups. Each dot represents a participant. No group comparison reached the significance threshold after Bonferroni correction. Metadata can be downloaded at <https://doi.org/10.6084/m9.figshare.14622564>.

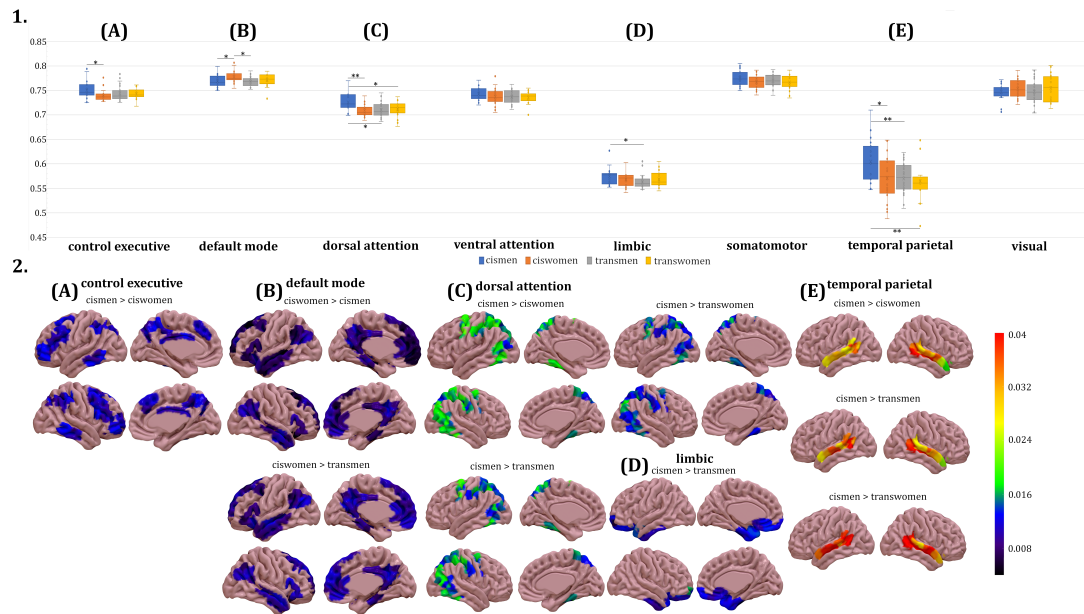


Figure 3: Ignition measures by networks. **(1)** Group ignition values by networks. The boxes in the plots indicate the second and third quartile (IQR), middle lines are ignition medians, and X are ignition means. Legend: \*  $p \leq 0.05$ ; \*\*  $p < 0.01$ . **(2)** Rendered brains represent the differences in ignition between groups, and were plotted with the SurfIce software. There were group differences in the **(A)** executive control, **(B)** default-mode, **(C)** dorsal attentional, **(D)** limbic, and **(E)** temporal parietal networks. Metadata can be downloaded at <https://doi.org/10.6084/m9.figshare.14622564>.

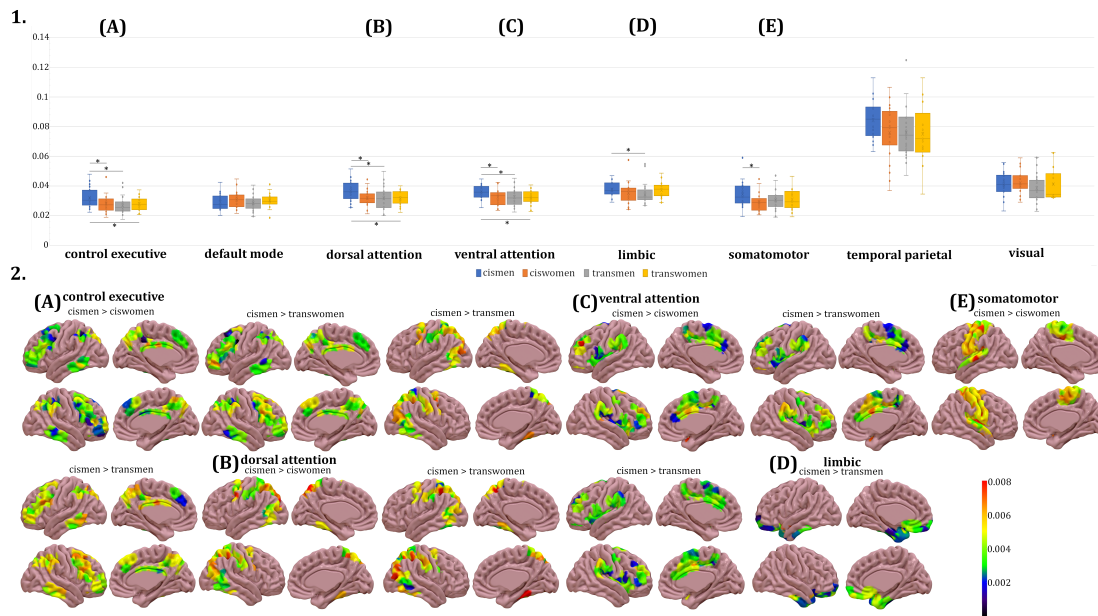


Figure 4: Node-metastability measures by networks. **(1)** Group node-metastability values by networks. The boxes in the plots indicate the second and third quartile (IQR), middle lines are ignition medians, and X are node-metastability means. Legend: \*  $p \leq 0.05$ ; \*\*  $p < 0.01$ . **(2)** Rendered brains depict the node-metastability difference between groups, and were plotted with the SurfIce software. There were group differences in the **(A)** executive control, **(B)** dorsal attention, **(C)** ventral attention, **(D)** limbic, and **(E)** somatomotor networks. Metadata can be downloaded at <https://doi.org/10.6084/m9.figshare.14622564>.

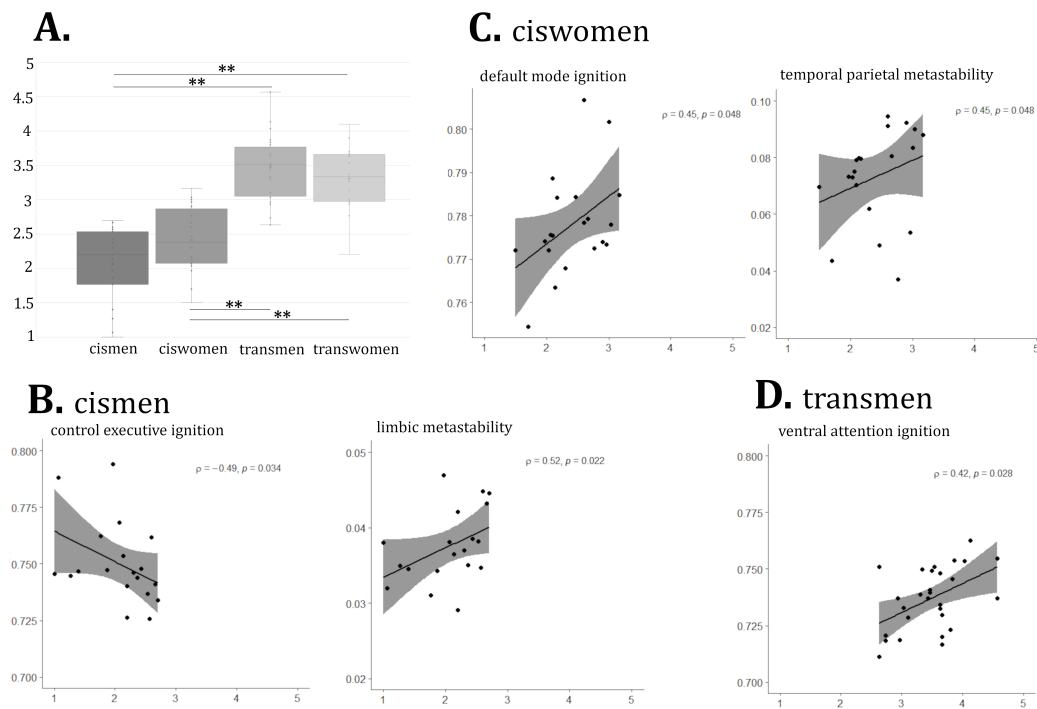


Figure 5: Correlations between network-based ignition and metastability measures and body image satisfaction scores. (A) Group comparisons of the body image scale scores. A general linear model with 1,000 permutation testing and Bonferroni was applied. Legend: \*  $p \leq 0.05$ ; \*\*  $p < 0.01$ . Correlations within (B) the cismen group, (C) the ciswomen, and (D) the transmen. There were no significant correlations within the transwomen group. Correlations are Spearman's  $\rho$  and shadowed areas are 95% confidence interval.

contrast	ignition - mean (SD)	t stat	uncorr-p	FWE-p	metastability - mean (SD)	t stat	uncorr-p	FWE-p
<i>cismen vs ciswomen</i>	cismen: 0.9268 (0.0003)	72.459	0.001	<0.004	cismen: 0.0066 (0.0005)	-3.194	0.002	<0.004
<i>cismen vs transmen</i>	ciswomen: 0.9259 (0.0003)	91.394	0.001	<0.004	ciswomen: 0.0067 (0.0005)	15.656	0.001	<0.004
<i>cismen vs transwomen</i>	transmen: 0.9259 (0.0002)	95.284	0.001	<0.004	transmen: 0.0063 (0.0003)	6.912	0.001	<0.004
<i>ciswomen vs transmen</i>	transwomen: 0.9256 (0.0003)	18.936	0.001	<0.004	transwomen: 0.0065 (0.0005)	18.850	0.001	<0.004
<i>ciswomen vs transwomen</i>		22.826	0.001	<0.004		10.106	0.001	<0.004
<i>transmen vs transwomen</i>		3.890	0.001	<0.004		-8.744	0.001	<0.004

Table 1: Stats from whole-brain intrinsic ignition framework by nodes. Data are means and standard deviations. There were significant differences between all contrasts groups with Monte-Carlo 1,000 permutations and family-wise error (FWE) correction.

measure	contrast	t stat	uncorr-p	corrected-p	Cohen's d
<b>dorsal attention network</b>					
ignition	<i>cismen vs ciswomen</i>	3.463	0.002	0.002	1.1
	<i>cismen vs transmen</i>	2.784	0.005	0.016	0.94
	<i>(education as covariate)</i>	no-cov: 3.368	no-cov: 0.001	no-cov: 0.007	
metastability	<i>cismen vs transwomen</i>	2.666	0.008	0.016	0.79
	<i>cismen vs ciswomen</i>	2.515	0.006	0.015	0.8
	<i>cismen vs transmen</i>	2.476	0.006	0.025	0.71
	<i>(education as covariate)</i>	no-cov: 2.681	no-cov: 0.008	no-cov: 0.023	
	<i>cismen vs transwomen</i>	2.407	0.007	0.030	0.86
<b>ventral attention network</b>					
metastability	<i>cismen vs ciswomen</i>	2.269	0.010	0.024	0.74
	<i>cismen vs transmen</i>	2.455	0.010	0.026	0.66
	<i>(education as covariate)</i>	no-cov: 2.252	no-cov: 0.022	no-cov: 0.048	
	<i>cismen vs transwomen</i>	2.190	0.016	0.044	0.82
<b>control executive network</b>					
ignition	<i>cismen vs ciswomen</i>	2.379	0.008	0.021	0.71
metastability	<i>cismen vs ciswomen</i>	2.100	0.015	0.037	0.61
	<i>cismen vs transmen</i>	2.875	0.004	0.012	0.8
	<i>(education as covariate)</i>	no-cov: 2.895	no-cov: 0.008	no-cov: 0.018	
	<i>cismen vs transwomen</i>	2.092	0.019	0.055	0.68
<b>default mode network</b>					
ignition	<i>cismen vs ciswomen</i>	-2.246	0.019	0.042	-0.67
	<i>ciswomen vs transmen</i>	2.050	0.020	0.055	0.91
	<i>(age &amp; education as covs)</i>	no-covs: 2.863	no-covs: 0.003	no-covs: 0.009	
<b>somatomotor network</b>					
metastability	<i>cismen vs ciswomen</i>	2.442	0.007	0.019	0.72
<b>limbic network</b>					
ignition	<i>cismen vs transmen</i>	2.869	0.003	0.012	0.75
	<i>(education as covariate)</i>	no-cov: 2.551	no-cov: 0.014	no-cov: 0.032	
metastability	<i>cismen vs transmen</i>	2.257	0.016	0.039	0.54
	<i>(education as covariate)</i>	no-cov: 1.75	no-cov: 0.05	no-cov: 0.105	
<b>temporal parietal network</b>					
ignition	<i>cismen vs ciswomen</i>	2.625	0.007	0.013	0.74
	<i>cismen vs transmen</i>	3.479	0.001	0.002	0.94
	<i>(education as covariate)</i>	no-cov: 2.896	no-cov: 0.007	no-cov: 0.018	
	<i>cismen vs transwomen</i>	2.954	0.002	0.005	0.91

Table 2: Intrinsic ignition by networks of averaged nodes across groups. General linear model with 1,000 permutations and family-wise error correction were applied. Cohen's d effect sizes were computed. The *cismen vs. transmen* contrast was tested with and without (no-cov) education as covariate, and the comparison between *ciswomen* and *transmen* with and without (no-covs) age and years of education.