**Consciousness Study and Technology** 

# Workshop: Studying, Measuring and Altering Consciousness

Dates: 21/11/2019 Venue: Merton College, University of Oxford

Luminous Studying, Measuring and Altering Consciousness through information theory in the electrical brain.

Studying Consciousness in the electrical brain

luminous

### Studying, Measuring and Altering Consciousness 21 November 2019 Merton College, University of Oxford



### 8:30 - 9:00 Registration



**Welcome - Irene Tracey** Warden of Merton College and Nuffield Chair in Anaesthetic Science, University of Oxford; <u>irene.tracey@ndcn.ox.ac.uk</u>



## Aureli-Soria Frisch - Luminous: A study of consciousness in the electrical brain

Starlab Barcelona, Barcelona, Spain; aureli.soria-frisch@starlab.es

9:30 -



Keynote Speaker: Anil Seth - A higher state of consciousness? Neural dynamics in the psychedelic brain Professor of Cognitive and Computational Neuroscience and Co-Director, Sackler

Centre for Consciousness Science, University of Sussex, UK; A.K.Seth@sussex.ac.uk

10:10 10:10 -10:30



#### **Wim Pinxten - The ethical imperative of studying Consciousness** Prof. dr. at the Faculty of Medicine and Life Sciences, Hasselt University, Belgium; <u>wim.pinxten@uhasselt.be</u>

Julien Modolo - Can we use computer models of brain activity to

for Health and Research in Medicine, France; julien.modolo@gmail.com

understand how consciousness emerges and vanishes?

#### Refreshments

10:30 -11:00 11:00 -



11:20 11:20 -



12:00 12:00 -



Director, Oxford Immune Algorithmics, Oxford; Lab Leader, Algorithmic Dynamics Lab, Center for Molecular Medicine, Karolinska Institute, Stockholm; Head of Group, Algorithmic Nature Lab, LABORES for the Natural and Digital Sciences, Paris; hector.zenil@ox.cs.ac.uk

Keynote Speaker: Hector Zenil - Algorithmic Complexity and Cognition

Laboratoire Traitement du Signal et de l'Image (Rennes), INSERM / National Institute

**Giulio Ruffini - KT: an algorithmic information theory of consciousness** Starlab Barcelona, <u>http://starlab.es</u> and Neuroelectrics, <u>http://neuroelectrics.com</u>, Barcelona, Spain; <u>giulio.ruffini@starlab.es</u>

#### 12:20 - Flash talks 12:40 1. Michele

- Michele Farisco The ethical relevance of the unconscious Centre for Research Ethics and Bioethics, Uppsala University, Sweden; <u>michele.farisco@crb.uu.se</u>
  - 2. Rodika Sokoliuk Investigating top-down conscious awareness using auditory speech entrainment School of Psychology & Centre for Human Brain Health, University of Birmingham; R.Sokoliuk@bham.ac.uk
  - 3. Riku Ihalainen Computational modelling of posterior hot zone in anaesthesia-induced loss of consciousness School of Computing, University of Kent, Kent; rji4@kent.ac.uk
  - 4. Angus Stevner Large-scale brain networks and transition dynamics during fluctuations between wakefulness and sleep in humans Department of Psychiatry, University of Oxford; Center for Functionally Integrative Neuroscience & Center for Music in the Brain, Aarhus University, Denmark; angus.stevner@psych.ox.ac.uk

### 12:40 - Lunch & E-posters

1:40



## 1:40 - 2:20Keynote Speaker: Claire Sergent - From subjective experience to brain<br/>activity, and return

Associate Professor, Integrative Neuroscience and Cognition Center, Université Paris Descartes & CNRS, Paris, France; <u>claire.sergent@parisdescartes.fr</u>



**Hubert Preissl - Are there signs for conscious processing in the fetal brain?** MEG Center/Internal Medicine IV/Institute for Diabetes Research and Metabolic Diseases of the Hemholtz Center Munich, University of Tübingen & German Center for Diabetes Research, Tübingen, Germany, <u>http://preissl-lab.net/</u>; <u>hubert.preissl@uni-tuebingen.de</u>



#### Keynote Speaker: Morten Kringlebach - Awakening: predicting perturbation to force transitions between different brain states Associate Professor, Hedonia Group, University of Oxford, UK

Professor of Neuroscience, Aarhus University, Denmark;

2:40 - 3:20



morten.kringelbach@queens.ox.ac.uk Silvia Casarotto - Assessing consciousness through cortical perturbations Department of Biomedical and Clinical Sciences "L. Sacco", University of Milan, Italy; silvia.casarotto@unimi.it

### 3:40 - 4:10 Refreshments



Katie Warnaby - Slow waves and anaesthesia-induced unconsciousness Wellcome Centre for Integrative Neuroimaging, Nuffield Department of Clinical Neurosciences, University of Oxford; <u>katie.warnaby@ndcn.ox.ac.uk</u>



#### Michael Nitsche - Transcranial electrical stimulation to modulate sleepdependent processes

Department of Psychology and Neurosciences, Leibniz Research Centre for Working Environment and Human Factors (IFADO), Dortmund, Germany; <u>nitsche@ifado.de</u>



Aurore Thibaut - Non-invasive brain stimulation to promote consciousness in the injured brain GIGA Institute | GIGA Consciousness | Physiology of Cognition Research Lab, University of Liège, Belgium ; <u>athibaut@uliege.be</u>



Niels Birbaumer - Brain Computer Interfaces in complete paralysis: rebirth of the grandmother cell Institute of Medical Psychology and Behavioral Neurobiology, University of Tubingen, Germany; <u>birbaumer@uni-tuebingen.de</u>



Marcello Massimini - Concluding Remarks Department of Clinical and Biomedical Sciences, University of Milan, Italy; marcello.massimini@gmail.com

Please let us have your feedback on the event online at: <u>bit.ly/workshop-luminous</u>.





### Studying, Measuring and Altering Consciousness: Abstracts

### Perturbing whole-brain dynamics of the psychedelic state with music

Ahrends C  $^{1,2}$  , Stevner ABA  $^{1,2}$  , Vidaurre D  $^3$  , Carhart-Harris RL  $^4$  , Nutt D  $^4$  , Deco G  $^{5,6,7,8}$  , Vuust P  $^1$  , & Kringelbach ML  $^{1,2}$ 

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<sup>8</sup> School of Neuropsychology, Max-Planck-Institute for Human Cognitive and Brain Sciences, Leipzig,

of Psychological Sciences, Monash University, Melbourne, Victoria, Australia

This study investigated how music guides whole-brain dynamics during the psychedelic state. Across cultures and throughout history, music has been intimately linked with psychedelics, suggesting that music serves a fundamental function. This observation has led to efforts to make music an integral part of psychedelic therapy approaches for neuropsychiatric disorders. However, there is a lack of understanding of the brain in the psychedelic state as an altered state of consciousness and the mechanisms through which music interacts. Here we hypothesised that psychedelics can cause a fundamental reorganisation in the evolving dynamical system of the brain and that music perturbs brain dynamics within this altered state of consciousness.

In order to estimate brain dynamics of psychedelics and music through timeresolved whole-brain connectivity patterns, we applied a Hidden Markov Model (HMM) (Vidaurre et al., 2016; Vidaurre et al., 2017) to the fMRI-data of a previously reported multimodal neuroimaging study with LSD (Carhart-Harris et al., 2016). In this single-blind study, healthy, non-drug naïve participants (N=15) were given either LSD or placebo. In both drug conditions, participants first underwent one EPI-scan without music (pre-music resting state condition),followed by a scan during which they listened to music (music condition), and finally a second scan during which no music was played (postmusic resting state condition), each lasting seven minutes. The HMM allows estimating a temporal sequence of hidden brain states, i.e. brain networks that reoccur over time, from the fMRI time courses as well as transition probabilities between these states.

The HMM revealed changes in dynamic whole-brain patterns between placebo and LSD, as well as between music and no music within the LSD condition. These changes manifested as significant differences in fractional occupancy, i.e. the time spent in a given state as a proportion of all states, of several brain states as obtained through permutation testing, as well as distinct transition "paths" between these states (see Fig. 1A). Compared to placebo, the brain reorganises into fundamentally different patterns under LSD, which are then shaped into a unique structure by music. This reorganisation of brain dynamics has previously been suggested to be marked by increased entropy, moving the brain closer towards criticality (Carhart-Harris, 2018; Carhart-Harris and Friston, 2019; Carhart-Harris et al., 2014). Using model entropy and switching rates as measures of uncertainty and stabilityin these conditions, we could describe the brain in the psychedelic state as a dynamical

system and how music serves as a perturbation in this state. These results can shed new light on the debate of consciousness as a reorganisation of brain dynamics in relation to criticality and associated energy landscapes (see Fig. 1B), as well as the way in which these dynamics can be perturbed.

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Vidaurre, D., Smith, S.M., Woolrich, M.W., 2017. Brain network dynamics are hierarchically organized in time. Proc Natl Acad Sci U S A 114, 12827-12832.

# Electrophysiological markers of interoceptive and exteroceptive integration

Leah Banellis, Damian Cruse

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Previous research has found that the brain uses temporal cues from interoceptive (cardiac) signals to predict exteroceptive (auditory) stimuli. This is reflected as a larger heartbeat-evoked potential (HEP) during omission periods from a stream of auditory stimuli presented in cardio-audio synchrony, relative to asynchrony (Pfeiffer & De Lucia, 2017). This 'surprise' response may reflect increased prediction error from expecting a sound on the basis of the heartbeat, supporting interoceptive predictive coding accounts (Seth, 2013; Barrett & Simmons, 2015).

We investigated if attention modulates the cortical processing of interoceptive predictive mechanisms, by integrating a heartbeat discrimination task with an omission detection task. Comparing HEP responses during omission periods is advantageous because it allows for the observation of pure interoceptive predictive signals, without the contamination of auditory potentials. Analyses of HEPs during omission periods revealed an early main effect of cardio-audio delay (14-250ms), demonstrated as a frontocentral positive cluster (p = .001). This early effect may reflect differences in the expectation of upcoming sounds, guided by the individual's heartbeat during perceived synchronous (R+250ms) trials. Additionally, we observed an attention and cardio-audio delay interaction.

Specifically, we found a larger positivity to short-delay (R+250ms) omissions than long delay (R+550ms) omissions, possibly reflecting increased prediction error when cardio-audio stimuli are integrated (R+250ms), but only when attending internally (p = .002). In comparison, no significant differences was observed between the two cardio-audio delay conditions when attending externally. In conclusion, our results suggest that interoceptive signals can guide expectations of exteroceptive stimuli and that attention to internal signals modulates interoceptive predictive mechanisms.

### A touch of grounding

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### **Objectives**: Rationale for measuring infant consciousness

For Dennett "the way to take consciousness, as a phenomenon, seriously" is by investigating other's User Illusions/consciousness <sup>1</sup>. Assessing the extent of any User Illusion (UI) in infants is nevertheless confounded by the opaqueness of reporting in such others: signalling opportunity for investigation via electromagnetic signs <sup>2</sup>. Such signs are expected to emerge in parallel with the neuro-physiological development <sup>3</sup> of substrates associated with the UI – in algorithmic terms: the virtual machines (VMs) performing nested layers <sup>1</sup> of predictive coding <sup>4</sup> (PC).

For Dennett the 'practice of sharing information in communicative actions with others, giving and demanding reasons, is what creates our personal user-illusions' <sup>1</sup>. This can be interpreted both from evolutionary and developmental perspectives: (a) Our adult brain's VM substrate arose as evolutionary consequence of memetic selection by such actions; (b) an infant's UI develops in parallel with its competence to perform such actions. Taking the former as given we consider the latter.

### Material / methods: theoretical discourse

It's hard to conceive of newborns trading reasons with carers/parents: Yet this implies they experience negligible UI before they are able to do so, and thus no signs would manifest until an infant enters the pre-operational development stage <sup>5</sup> and demonstrates an explicit grasp of before-and-after with the concomitant attribution of appreciation of apparent cause-and-effect. Yet, if we identify infants harbouring 'proto-reasons' might we attribute 'proto-user-illusions' to them and look to measure their signs during early development? Below weoutline the case for a particular basic 'proto-reason' that grounds evidence for a material reality comprising macroscopic solids while eliciting a 'proto-user-illusion'.

Although the form and function of the PC substrate (delivering competence without comprehension) is grounded in survival <sup>1</sup>, when hypotheses formed within that substrate begin to be externally expressed then an ulterior grounding arises: Evidence gets shared and we ask it to be grounded <sup>6</sup> in reality – tending towards that ontological grounding valued by UIs of philosophers and scientists. A developmental ontological impetus may occur when an infant can no longer occupy the same physical space as their mother – on first encountering empty space and returning into contact with (external) surfaces: mother's arms etc.

### Three factors may coalesce:

1) instantiation of the Bayesian hyper-prior, in the PC substrate, to stipulate no two solids occupy the same physical space  $^7$  .

2) 'proto-reason': grounding of explicit spatial comprehension <sup>8</sup> – anchoring subsequent empirical learning from evidential chains.

3) 'proto-user-illusion': onset of contact-/tactile- sentience in the circuits that mediate the "resonant loop between body states and brain states" <sup>9</sup> – e.g. those serving fingers, lips and body surfaces – providing an 'ontologically underwriting/grounding', at least while those loops are not inhibited by sleep or adaptation.

### Results / conclusions: contingent reflections

Conditional on the above, electromagnetic signs would correlate with brain areas associated with newborns learning spatial relationships between surfaces of their own body <sup>10</sup>; learning the visual appearance of objects within arms-length; and subsequently – extrapolating their grounding – to distant objects. Furthermore, the insula <sup>11 12</sup> is a common nexus transited by somatosensory loops (for pressure, pain, and warmth) into which 'ontological grounding' and sentience might be further propagated.

### References:

1. Dennett D.C., From Bacteria To Bach and Back, Norton, New York NY, 2017. See Chapters. 6 &14 for the citations in main text. TABLE 1 presents Dennett's position, indicating how particular algorithmic/learning substrates map on to evolutionary mechanisms and thus "Dennett's Creatures". We append rows indicating how his scheme is paralleled by infant development/comprehension. Key to our discourse are the transitions from Skinnerian to Popperian creatures around birth, and then from Popperian to Gregorian later when reasons become expressed – Ontological grounding instilled around birth may be instrumental to that later expression.

2. Tononi G, Boly M, Massimini M, Koch C. "Integrated information theory: from consciousness to its physical substrate". Nat Rev Neurosci.;17(7):450-61, 2016.

3. Dehaene S. Consciousness and the brain deciphering how the brain codes our thoughts, Viking Penguin, New York NY, 2014. – See Chap. 7 for extensive discussion.

4. Huang, Y. & Rao, R.P., "Predictive coding". WIREs Cogn Sci, 2: 580-593, 2011.

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6. Leuenberger, S. 2013. "Grounding and Necessity" Inquiry: An Interdisciplinary Journal of Philosophy, 2013, p.157.

For a wide-ranging critical discussion see also: Sellar, W. Science, Perception and Reality, Routledge & Kegan Paul London. 1963, pp.127-196.

7. Clark, A., "Whatever next? Predictive brains, situated agents, and the future of cognitive science". Behavioral and Brain Sciences, 36(3), 181-204. 2013. – see p.196.

8. I.e. the onset of "Sensory-motor stage" (Piaget cited above) – see also T ABLE 1 which also indicates the "Pre-operational Stage" and "Hand-on-science" – see Gregory R.L., "Hands-on Science", Science in the Twenty First Century, Casino Pio IV, 19-21 Nov. 2001.

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11. Seth, A.K., Interoceptive inference, emotion, and the embodied self, Trends in Cognitive Sciences, Vol. 17, No. 11 565-573, 2013.

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Evolutionary mechanism	Trial & Error	Natural Selection / genetic replication					Memetic replication, Language, Thinking tools		
<b>Dennett's Creature</b>		Darwinian		Skinnerian		Popperian	Gregorian		
Algorithmic		Representational Learning							
substrates	Reinforcement Learning								
	Predictive Coding / Bayesian networks								
							Nested Virtual Machines		
Infant development			CONCEPTION	Reflexive agency	BIRTH	Sensor-motor stage	Preoperational stage	Hands-on- Science	
Comprehension	1 1			Implicit spatio-temporal		Explicit spatial Implicit temporal	Explicit spatio-tempora	Scientific l knowledge	
Aftermaths	∭ Big Bang }				阗C	ontact sentience	<b>阅</b> Reason		

**TABLE 1** indicating how particular algorithmic/learning substrates map on to evolutionary mechanisms and thus onto "Dennett's Creatures". We align these with Infant development and Comprehension. Key to our discourse are the transitions from Skinnerian to Popperian creatures around birth, and then from Popperian to Gregorian later when reasons become expressed – Ontological grounding instilled around birth may be instrumental to that subsequent expression.

### When the Window Cracks - Altered Self-Consciousness in Depersonalisation and Meditation: A Multisensory Approach

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<sup>2</sup> DPD experiencer

<sup>3</sup> University of Bath

Keywords: Depersonalisation; Self; Visual Remapping of Touch; Touch; Social Cognition

**Background:** The sense of self lies at the heart of conscious experience, anchoring our disparate perceptions, emotions, thoughts and actions into a unitary whole. There is a growing consensus that sensory information about the body plays a central role in structuring this basic sense of self. Depersonalisation (DP) is an intriguing form of altered subjective experience in which people report feelings of unreality and detachment from their sense of self and their bodily feelings.

**Aims:** Our project brings together interdisciplinary resources from philosophy, cognitive neuroscience and psychophysiology in order to explore the relationship between the experience of DP and sensorimotor processing of self and other.

**Method:** The current study used the Visual Remapping of Touch (VRT) paradigm to explore self-bias in visual tactile integration in non-clinical participants reporting high and low levels of depersonalisation experiences. In VRT, observing tactile stimuli being applied to a face on a screen led to participants becoming more accurate in detecting threshold level tactile stimulation being applied to their own face. Importantly this effect is strongest when participants are observing their own (self-bias) face suggesting that self-representation plays a key role in mediating this process. 63 participants (17 male) with a mean age of 24  $\pm$  4 participated in this study.

**Results:** Due to the alterations in self-experience that characterise DP, we predicted that participants in our high DP group would show a reduced overall VRT effect regardless of the observed face (H1) and fail to show the self-bias VRT effect previously reported in other studies (H2). Our results offered support for H2 by showing that amount of anomalous body experiences reported by participants was negatively correlated with the size of their VRT self-bias. However contrary to H1 we found evidence for increased overall VRT effect in the high DP group compared to the low DP group.

**Conclusions:** Our findings revealed that participants high in DP showed an increased overall VRT effect but a no self-face bias, instead showing a greater VRT effect when observing the face of another person. In addition, across all participants, self-bias was negatively predicted by score on the anomalous body experiences subscale suggesting that this effect was specifically linked to disruptions in the perception of the bodily self. These results provide evidence for

disrupted integration of tactile and visual representations of the bodily self in those experiencing DP.

In closing we contrast the experience of "losing" one's sense of self in depersonalisation and in meditative states. We argue that while meditative states enhance the underlying transparency of basic, embodied pre-reflective forms of self-consciousness. By contrast, depersonalisation enhances the use of mentalistic hyper-reflective forms of self-consciousness, which leads in turn to distressing feelings of being detached and "cut off" from one's self, body and world.

We suggest that the phenomenon of "losing" one's sense of self in meditation and depersonalisation seems to point towards the idea that the sense of self is a fundamental albeit "transparent" feature of self-conscious states that can be enhanced or disrupted but not "lost".

# Measuring graded changes in consciousness with perceptual filling-in challenges first-order theories of conscious perception

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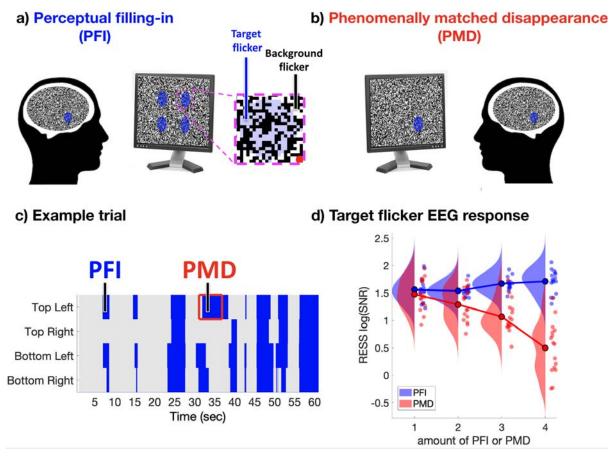
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\* Equal contribution

**Background and Objectives**: Perceptual filling-in (PFI) occurs when a physicallypresent visual target disappears from conscious perception, with its location filledin by the surrounding visual background. Although PFI occurs regularly in normal vision, it is relatively understudied compared to other forms of visual illusions used to investigate the neural correlates of consciousness (NCC). This is surprising, given that perceptual changes during PFI are relatively simple and crisp, and can occur for multiple spatially separate locations simultaneously. Here we set out to show that contrasting neural activity during the presence or absence of multi-target PFI can complement other bistable phenomena to reveal the neural correlates of consciousness (NCC), and shed light on present neurobiological theories of conscious perception.

**Materials and Methods:** In a series of experiments, we asked participants to report on PFI by pressing one of four buttons, which were spatially mapped to four simultaneously presented targets. While participants reported on target disappearances/reappearances via button press/release, we tracked neural activity entrained by both the target and background by flickering these stimuli at unique frequencies (Figure 1a). By flickering our stimuli, we were able to record

steady-state visually evoked potentials (SSVEPs) in the electroencephalogram, which serve as an index of target - or background - specific neural processing. Results and conclusions: We found that background SSVEPs closely correlated with subjective report, and increased with an increasing amount of PFI. These results demonstrate that PFI can be used to capture graded changes to the contents of consciousness when frequency-tagging the background of a visual display. Counterintuitively, frequency-tagged responses to disappearing target stimuli increased during PFI. This pattern was not obtained for phenomenally matched disappearances (PMD), during which the same flickering targets were physically removed from the display (Figure 1b). This activity scaled with the amount of invisibility reported (Figure 1d), and as such, directly challenges theories of perception which propose that an increase in stimulus-specific neural activity increases the vividness of conscious experience.



**Figure 1.** Experiment summary. a) Four peripheral targets, defined by their blue-colour, were superimposed over a dynamic texture to induce perceptual filling-in (PFI). b) Phenomenally-matched disappearances (PMD) were embedded within each trial, to mimic the subjective quality of PFI, during which one to four targets were physically removed from screen. c) Each trial lasted 60 seconds (48 trials), during which participants reported on the visibility of all four peripheral targets, using four unique buttons. d) The strength of target-specific EEG responses uniquely increased with an increase in invisibility during PFI.

### The ethical relevance of the unconscious

Michele Farisco

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**Background:** Contemporary cognitive science increasingly reveals that the traditional way of depicting the unconscious as a dimension deeply separated from and even opposed to consciousness is misleading and overly simplistic (Hassin, 2013). Also, consciousness is showed to be not disconnected from but highly related to and even shaped by the unconscious (Lau & Passingham, 2007; Monahan, Murphy, & Zajonc, 2000).

Ethical analyses of disorders of consciousness (DOCs) traditionally focus on residual awareness (Kahane & Savulescu, 2009; Wilkinson, Kahane, & Savulescu, 2008). Going one step further, I would like to explore the potential ethical relevance of the unawareness retained by patients with disorders of consciousness, focusing specifically on the ethical implications of the description of the unconscious provided by recent scientific research.

**Objective:** To check whether the actual focus of ethical analysis of DOCs only on residual awareness is somehow limited.

**Methods:** A conceptual methodology is used, based on the review and analysis of relevant scientific literature on the unconscious and the logical argumentation in favour of the ethical conclusions.

**Results:** Two conditions (experiential wellbeing and having interests) that are generally considered critical components in the ethical discussion of patients with DOCs (Sinnott-Armstrong, 2016) might arguably be both conscious and unconscious. If so, then also the unconscious is ethically relevant. Two arguments are provided in support of this inference. The first is qualified as strong because it is based on the assumption that unconscious abilities are comparable to conscious abilities: If consciousness is ethically relevant because of what it can enable, and the unconscious may enable comparable things, then the unconscious is also ethically relevant.

A weaker (less controversial) argument is the following: If consciousness is ethically relevant, and the unconscious is (at least in part) the result of consciousness, then the unconscious is also ethically relevant. Or conversely: if consciousness is ethically relevant, and the unconscious plays an important role in shaping consciousness, then the unconscious is also ethically relevant.

**Conclusions:** The retained unconscious abilities, as well as residual consciousness, should be taken into account in the ethical discussions of patients with DOCs.

References:

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Wilkinson, D., Kahane, G., & Savulescu, J. (2008). "Neglected personhood" and neglected questions: remarks on the moral significance of consciousness. Am J Bioeth, 8(9), 31-33. doi:10.1080/15265160802412486

# Computational modelling of posterior hot zone in anaesthesia-induced loss of consciousness

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How are the brain's large scale networks affected by unconsciousness induced by anaesthetic drugs? Despite recent empirical advances, the underlying changes in

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brain networks during anaesthesia-induced transitions between consciousness and unconsciousness still remain incompletely described.

Here, for the first time, we computationally evaluated evidence for the posterior hot zone of consciousness<sup>1,2,3</sup> by examining the specifics of the cortical networklevel mechanisms and the relative contributions of three resting state networks (RSN) to loss of consciousness - the default mode network (DMN), the salience network (SAL) and the central executive network (CEN). We used dynamic causal modeling (DCM) of ongoing brain dynamics observed in 10 minutes of highdensity EEG collected during wakefulness and propofol-induced loss of consciousness.

Using a dataset that has been previously investigated with different methods<sup>4,5,6,7</sup>, we ran a set of DCM analyses (DCM for cross spectral density) focusing on the three prominent RSNs that have been previously associated with consciousness<sup>8</sup> and which were found to overlap with the source level activations<sup>4</sup>. First, by inverting the RSNs separately and modelling the between-session effects at the first level (individual DCMs), followed by Bayesian model reduction to identify the most likely parsimonious model, we found that connections in the DMN were particularly modulated by the loss of consciousness. Using novel parametric empirical Bayes (PEB) analysis, we found that connections to/from the precuneus were especially strongly modulated; forward connections going into and originating from precuneus were largely decreased while backward connectivity was increased due to LOC.

In comparison, many connections in the SAL and CEN models were considered less important for explaining the change in brain dynamics associated with the change in the state of consciousness. Going further, one large scale DCM consisting of the 14 nodes of the 3 RSNs was inverted, again modelling the between-session differences at the first level and using PEB to estimate the grouplevel parameters. Extra connections were specified to investigate the possible between-resting state network connections (DMN-SAL and DMN-CEN) that we based on previously identified network of structurally highly connected central hubs on overlapping locations (precuneus, superior parietal cortex, and dACC).<sup>9</sup>

When focusing on between-resting state network connections, the results suggested relatively large modulations on bi-directional connections between the posterior nodes, while no modulations were found on the connections between precuneus and dACC. Taken together, these results highlight first, the importance of DMN in explaining the propofol-induced LOC, and second, the importance of particular connections relating to the posterior nodes within the DMN and between-RSN connections, roughly corresponding with the previously suggested posterior hot zone for consciousness.

## **Co-Evolution of Consciousness and Biases That Make Humans Behave Against Their Own Interest**

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**Introduction/Motivation:** A number of biases (such as hedonic adaptation, lack of self-control, and conspicuous consumption) have been studied by psychologists and behavioral economists. More recently, a theoretical literature has analyzed the evolutionary origins of these biases [1] and has found that they result in fitness-enhancing behaviors that are nonetheless detrimental for the individual, what results in a gene-individual conflict. But if these behaviors are detrimental for the individual, why are they performed? I provide a framework, consistent with the Attention Schema theory of consciousness [2] and other relevant theories of consciousness, that can explain how biases and consciousness co-evolved, in such a way that fitness-enhancing behaviors that are detrimental for the individual operate outside of consciousness.

**Methods:** I review the empirical evidence on biases as well as the theoretical literature on their evolution, and show that they share the property that decision utility (wanting) is not aligned with experienced utility (liking), what generates a gene-individual conflict. I provide a theoretical framework, which I call the Biased Conscioussness theory, based on the aforementioned literature and the Attention Schema theory, that suggests a mechanism for the co-evolution of consciousness and biases, which resulted in the resolution of the gene-individual conflict in an adaptive manner.

**Results and Discussion:** The Biased Consciousness theory can explain the (seemingly paradoxical) phenomenon by which humans perform actions which are adaptive (in terms of genetic fitness) but detrimental to the individual. In addition, the theory has several additional predictions. First, any other bias that also make people behave against their own interest, should not be conscious; and even when the individual's attention is called to focus on the bias, not easily correctable without a substantial amount of training. Second, any consciousness that is the result of evolution, will (to some degree) exhibit the property of excluding relevant biases that make the individual behave against their own interest. This also applies to the evolution of consciousness in non-human organisms, such as primates and other animals. Moreover, the Biased Consciousness theory has implications when it comes to the "engineering of consciousness" [3]: when attempting to engineer conscious systems (such as a conscious robot), designed to fulfill a particular task (in our interest), we might face a similar conflict: we want to design a robot that is intelligent and conscious. but we also want the robot to act in our interest, not in the robot's own interest. In this case, it will be optimal to endow the robot with some biases which are not included in its conscious experience, what raises pragmatic and ethical considerations.

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# Beyond integrated information: A taxonomy of information dynamics phenomena

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In a seminal series of papers in the 1990s, Tononi, Sporns, and Edelman (TSE) introduced the idea that the neural dynamics underlying conscious states are characterised by a balance of integration and differentiation between system components. This idea remains prevalent in consciousness research today, influencing both theoretical and experimental work.

Such work has faced a number of challenges. First, distinct measures designed to measure such a balance can behave very differently from each other in practice, making it hard to choose which is the "right one". Second, even in theory there is no canonical balance of integration and differentiation in a scenario in which these move in opposite directions under a parameter search. Third, dynamics of conscious and unconscious brains have been seen to defy some of the predictions of this framework. Here, we argue that these problems arise, at least in part, from the non-specific nature of the concepts of integration and differentiation when applied to neural dynamics.

To address this issue, we present a revised mathematical theory of neural complexity. In particular, we propose a more fine-grained description of the structural and dynamical properties of neural information dynamics. We

introduce a new measure, called O-information, that quantifies the balance between redundancy and synergy within a system, and is easily computable.

We show that this metric is more effective than TSE's original measure at describing phenomena where large-scale correlation and short-scale independence coexist. We further develop a formalism to decompose different "modes" of information dynamics, that provides an exhaustive taxonomy of redundant and synergistic effects in cause (forward in time) and effect (backward in time). Finally, our formalism allows us to place previous measures of integrated information and complexity within a common framework, which can mathematically explain their similarities and differences.

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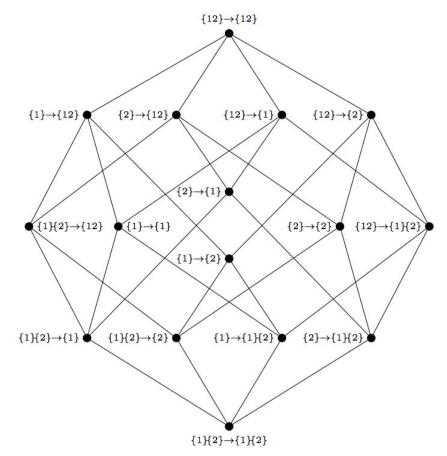
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### Classification and regression analysis of anesthetic states using Electroencephalography and deep learning

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**Objectives:** Neuroscience has shown a number of advances in the search for the neural correlates of consciousness, but our understanding of the neurophysiological markers remains incomplete [1]. Electroencephalography (EEG) under anesthesia provides a powerful experimental setup to identify electrophysiological signatures of altered states of consciousness, as well as a testbed for developing systems for automatic diagnosis and prognosis of patients with disorders of consciousness [2]. In the United States alone, over 100,000 people receive general anesthesia every day, from which up to 5% is affected by unintended intraoperative awareness [2, 3]. Despite this, brain-based monitoring of consciousness is not universal in the clinic, and has had mixed success [4, 5]. Given this context, our aim is to develop and explore an automated deep learning model that accurately predicts and interprets the depth and quality of anesthesia (DOA).

**Material and Methods:** In this study, we develop deep convolutional neural networks (cNN) with EEG measurements of brain activity during anaesthesia, in order to assess the model's ability to differentiate and classify various states and depths of unconsciousness. We use datasets from two propofol studies with different experimental designs [6, 7], where EEG states were determined based on either the behavioural responses of the participants (9 participants, Ramsay score 2-5), or based on target levels of the drug concentration (20 participants, target concentration:  $0.6-1.2 \mu g/ml$ ),

respectively. The cNN relies solely on 1 sec epochs of raw EEG, with minimal preprocessing, as described in [11].

**Results:** Our results with leave-one-participant-out-cross-validation show that the cNN is able to classify and predict with 86% accuracy the behaviourally distinct states of wakefulness/recovery, moderate sedation and loss of consciousness. However, it was unable to accurately predict target or blood concentrations of propofol. Further, when trained to predict behavioural (Ramsay) scores during anaesthesia, the cNN generalised smoothly to track the transitional periods between anaesthetic states, as well as to previously unseen behavioural responses.

**Discussion:** We investigated the ability of a cNN to provide meaningful predictions of anaesthetic states of consciousness. As neither behavioural nor drug concentration measures can provide us with an infallible ground truth for consciousness in the brain [8–10], we tested its consistency in both cases. Our results showed that states with different behavioural characteristics could be distinguished by the cNN. Further, it was able to generalise to previously unseen states and behavioural responses.

**Conclusions:** Our findings highlight the potential of the convolutional neural networks to identify and track generalised patterns of brain activity indexing anaesthetic loss of consciousness. These patterns represent signatures of altered states of consciousness, and could provide viable drivers of accurate depth of anesthesia monitoring [2].

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### On possible simple general principles of brain organization

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A framework to characterise the organization of nervous system dynamics in conscious and unconscious states is introduced derived from a perspective on the coordinated activity of brain cell ensembles. The scenario that emerges underscores the importance of the creation and dissipation of energy gradients in brain cell networks resulting in maximisation of the configurations in the functional connectivity among those networks that favour conscious awareness and healthy conditions. These considerations are then applied to indicate approaches that can be used to improve neuropathological syndromes.

**Methods:** The study is based on neurophysiological recordings analyzed from 27 subjects in conscious and unconscious conditions: wakefulness, seizures, sleep, and coma (details in Guevara Erra et al., 2016, Mateos et al., 2017).

**Results:** Initially the macroscopic entropy associated with the number of configurations of connected brain networks was computed derived from phase synchrony analysis of all pairwise combinations of the brain signals in each montage and each individual; as well, at the "microscopic" scale, the joint Lempel Ziv complexity (JLZC) was assessed to evaluate the fluctuations in short time windows of the connectivity patterns. Hence, entropy and complexity were set in the context of connections among brain networks to evaluate variability and global information content. Both the entropy and the JLZC were higher in conscious states (Guevara Erra et al., 2016, Mateos et al., 2017). Thus, during

normal cognition the brain macroscopic state derived from connectivity considerations is near equilibrium.

Then, using these observations, thermodynamic considerations regarding brain dynamics in conscious and unconscious states are evaluated. Inspection of trends in the evolution of free energy for brain macrostates associated with conscious and unconscious states —using the aforementioned entropy of the number of configurations of connected brain networks, plausible brain energy derived from metabolic considerations and a noise (temperature) term drawn from fluctuations in synchronization— revealed that brain free energy tends to decrease in the wakeful states as opposed to pathological unconscious conditions. As well, the neurophysiological tendency towards greater energy dissipation in healthy and conscious states emerged from basic thermodynamic considerations.

In conclusion, the creation and dissipation of energy gradients is associated with brain conscious awareness and healthy conditions, which may indicate approaches that can be used to improve neuropathological syndromes. To obtain an evolution equation describing the dynamical evolution of brain macrostates, we introduce the perspective of the probabilities of interactions among neuronal networks and the Shannon's formalism as thebasis to start developing an evolution equation, from where an expression for the change in dissipation over time was obtained.

Based on the observations that conscious awareness and healthy brain states are characterised by higher entropy, decreased free energy and increased dissipation, speculations to improve healthy brain dynamics in pathological states of low entropy are discussed.

**Conclusion:** Brain macrostates associated with conscious awareness possess more microstates (configurations of connections) whose emergence and dissolution determine cognitive states. These observations suggest that conscious awareness brings brain dynamics close to a "healthy" equilibrium with some dissipation needed to establish communication channels between cell networks.

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# The effects of anticipating nocturnal stimulation on healthy sleep and cognition: a placebo study

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**Background:** Previous research has attempted to enhance NREM sleep with various methods for greater physiological, psychological, and cognitive gain. The ability of individuals to self-enhance aspects of their sleep by anticipating such effects from outside intervention without actually receiving any has been demonstrated in insomniacs, but remains unexplored in healthy sleepers. While the extent to which such placebo effects are mediated by explicit awareness is under debate, it is thought that a general anticipatory, yet not fully conscious state may suffice to elicit the effect. In this study, we compare the impact of simulated auditory closed-loop stimulation (placebo) and an undisturbed baseline night on sleep and sleep-dependent cognition in healthy adults.

**Methods:** Twenty-two (15 female) healthy adults aged 18-28 (mean 23.32 years) were tested in a within-subject crossover design and underwent one night of placebo stimulation and one baseline night. Participants were assessed for overnight change in declarative and procedural memory performance, as well as alertness, and subjective perceptions of sleep quality and affect. We further analysed sleep architecture, spectral slow wave, and slow and fast spindle activity.

**Results:** Placebo stimulation had no differential impact on sleep architecture or cognitive performance when compared to baseline. However, frontal slow spindle power appeared to be transiently and inconsistently altered in stable NREM sleep stages across different time intervals of the night.

**Conclusions:** Our findings suggest that anticipating stimulation during sleep impacts on slow spindle activity. We conclude that induction of consistent placebo effects was not possible by simulating an auditory closed-loop protocol, which contrary to our intentions resulted in transient placebo as well as nocebo outcomes. Potential placebo and nocebo effects should thus be given adequate consideration when designing future (auditory) stimulation experiments.

## Investigating top-down conscious awareness using auditory speech entrainment

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The rhythmic sound of an alarm clock leads to "entrainment" of our brain over auditory areas following the same rhythm (Regan, 1982). Listening to speech also makes our brain follow the speaker's rhythm and if we understand the language, we know which words build a sentence, based on their semantic information. Previous studies showed that this semantic information can lead to entrainment of the brain without any acoustic cues (Ding et al., 2016, 2017).

In these studies, a stream of mono-syllabic 250ms long words, which either built meaningful sentences (e.g. adjective-noun-verb-noun) or scrambled sequences (e.g. noun-noun-adjective-verb) provoked acoustic entrainment at the word frequency. An additional peak at the "sentence level" could only be observed for meaningful sentences, reflecting top-down comprehension of the sentential structure.

Since here participants were informed about stimulus structure, we were interested in whether the sentential entrainment could also be observed in complete naive participants. Furthermore, we were wondering whether auditory attention had an influence on the strength of the entrainment. We used this paradigm in an EEG study on 72 healthy participants; two groups of participants (n=24 per group) were naïve to the stimulus structure, while a third group (n=24) was instructed about the sentential structure in the stimulus material. Group 1 was instructed to passively listen to the stimuli, group 2 was asked to identify individual words in the auditory stream and group 3 performed a task based on the sentential structure of the stimuli and identified grammatically incorrect word sequences.

We found that neither prior knowledge about stimulus structure nor an active task is necessary for significant entrainment at the sentence level, although both parameters led to an increase in entrainment at the sentence level, showing significantly stronger sentence-level entrainment for group 3 compared with groups 1 and 2. These findings are specifically important for future use of this paradigm in behaviourally unresponsive patients with prolonged disorders of consciousness (PDOC) as it is hard to tell to which degree those PDOC patients, who have remaining capacities of conscious awareness, are able to understand instructions and how long their attentional range is. Our results thus suggest that the paradigm is suitable to be tested in this patient population which we currently pursue. Ultimately, this could help to improve diagnosis in PDOC patients by investigating top-down conscious awareness.

## Large-scale brain networks and transition dynamics during fluctuations between wakefulness and sleep in humans

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Through sleep we are accustomed to regular and substantial modulations of consciousness. How does the brain support this modulation? Traditional models of sleep brain activity, using low-resolution scalp electroencephalography (EEG) to define a low number of homogenous sleep stages may be too simplistic to address this question <sup>1</sup>. In fact, the expression of traditional EEG signatures of sleep stages is much less predictive of conscious content (or lack hereof) than previously thought.

Modern neuroimaging techniques and analyses allow for the data-driven identification of dynamic large-scale network activity from on-going brain activity, as measured with e.g. functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG). The resolution of functional connectivity networks has thus far mainly been applied to neuroimaging recording of wakefulness, with the aim of mapping large-scale signatures with relevance for on-going cognition and behaviour. An equivalent data-driven discovery of dynamic whole-brain network states in recordings of sleep could reveal spatial and temporal features of brain activity with more relevance for consciousness than traditional sleep staging. I would like to present our recent advances in applying a data-driven strategy to fMRI recordings from a large group of healthy participants undergoing periods of wakefulness and NREM sleep in the MR scanner during concomitant EEG and BOLD (Blood Oxygenation Level-Dependent) acquisition 2. The resulting decomposition of the BOLD data into 19 dynamic whole-brain network states, defined in space and time by a Hidden Markov Model (HMM) <sup>3</sup>, revealed a complex transition map across the wake/NREM sleep cycle <sup>4</sup>.

Interestingly, several aspects of the dynamic system of whole-brain networks could not be accounted for by traditional sleep staging when this was performed on the simultaneously recorded EEG and compared to the independent HMM results. Specifically we found evidence in the fMRI data for a multitude of pathways that whole-brain networks can take through wakefulness and NREM sleep.

In line with behavioural evidence <sup>5</sup> we found the sleep onset period to be much more heterogeneous in terms of whole-brain activity compared to the classical EEG criteria. Unlike traditional sleep staging, our analysis showed clear wholebrain differences between periods of wakefulness before and after sleep. Finally the distributions of activity of the whole-brain networks, their dynamics, and the way in which they changed with depth of sleep provide important evidence for some of the leading theories on neural correlates of consciousness <sup>6,7</sup>.

In general we believe that similar data-driven approaches to data of related changes in consciousness, such as anaesthesia, or more subtle alterations during wakefulness represent a crucial exploratory task in the attempt to get closer to a mechanistic account of how the brain supports conscious experiences.

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### Non-strategic and strategic expectations in language comprehension

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Perception is facilitated by expectations about upcoming sensory information based on previous knowledge and perceptual context. If the expectancy model matches with the sensory information, perception and action are facilitated; otherwise, prediction error signals are generated and the model updated to accurately expect future sensory stimuli. Predictive mechanisms support successful language comprehension by generating models from previous semantic knowledge and current semantic context.

We investigated the neural basis of strategic expectations of meaning in a wordpair semantic-priming paradigm. By manipulating the overall proportion of semantically-related or unrelated word-pairs across the task, we created two global contexts that differentially encouraged strategic use of primes. Specifically, each trial included a visual target word 1240ms after a visual prime word presented in one of two colours that cued participants about the probability of the target being related –i.e. prime's validity (78%/22%).

Participants were required to read the target aloud while we recorded reaction times and high-density EEG. First, we replicated our previous finding of greater priming in the high validity context, reflecting strategic expectations of upcoming targets based on 'global' context. However, our pre-registered EEG analyses found no evidence that global expectations were reflected in the power of alpha/beta bands, contrary to several prediction error minimisation accounts. Furthermore, our pre-registered ERP analyses found no evidence of differential prediction error signals between contexts, as would be anticipated from the behavioural data. Nevertheless, we observed a prediction error ERP effect (i.e. priming effect) approximately 250ms prior to the mean reaction time that reliably differ across global contexts in exploratory follow-up analyses.

In conclusion, our behavioural data are consistent with strategic expectations of upcoming stimuli to facilitate processing, supported by an ERP effect (300mspost-target) modulated by the 'global' context indexing prediction error signals. However, our analyses suggest a less clear link between EEG oscillations and expectations. An auditory design may be beneficial for improving the accuracy of diagnosis of patients with disorders of consciousness in the clinically-relevant domain of residual language processing.

### Whole-brain network modelling of psilocybin treatment for depression

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**Introduction:** Major Depressive Disorder is a brain condition with vast health implications worldwide. Many subjects are non-responsive to a first-line of antidepressant treatment (Gaynes, 2009). In the last decade, a research on psychedelic medicine has shown a novel direction for treatment-resistant depression (Carhart-Harris et al., 2016). However, to understand how psychedelic drugs such as a psilocybin (a psychoactive component of 'magic' mushrooms) and LSD modulate the brain's dynamical repertoire, it is essential to look at the underlying mechanisms (Lord et al., 2019) (Deco et al., 2018). Here, we investigated patients with treatment-resistant depression pre- and post-treatment with psilocybin by analysing their brain dynamics using fMRI. Furthermore, we used a computational whole-brain model to simulate the underlying brain dynamics during the experiments and through perturbing the model we identified the outcome treatment activity.

**Method:** In this study, we investigated a cohort of treatment-resistant patients undergoing psilocybin intervention. 15 subjects underwent T1w and fMRI scans pre- and one-day post- the psilocybin intervention (Carhart-Harris et al., 2016). In brief, the BOLD time-series were obtained from 8 minutes fMRI scans with TR = 2000ms and were further registered and averaged to an AAL atlas. The patients were split into 6 responders and 9 non-responders according to their assessment scores 5 weeks post-treatment. Leading eigenvector dynamics analysis (LEiDA) was applied to the time-series data to detect recurrent brain state representations across all the subjects and for pre- and post- treatment conditions (Figure 1A and 1B) (Cabral et al., 2017). We implemented a Hopf-bifurcation model for each brain region connected through structural connectome and simulated the emerging brain activity (Deco et al., 2017). First, the model was adjusted to describe the

'depressive' brain pre- psilocybin treatment. Then, the model was systematically stimulated to determine the causal regions responsible for the treatment effects.

**Results:** The clustering of the leading eigenvectors to three-state solution was chosen by the best combination of the silhouette criterion and Davies-Bouldin score. We found the probabilistic metastable substates (PMS) of state three to be significantly different between the two conditions for treatment-respondent patients between the conditions (permutation paired t-test (5000 permutations), p-value = 0.026, fdr-corrected) (Figure 1B). We built and fitted the Hopf network model both to the PMS to obtain the most accurate spatio-temporal representation of the states from brain activity (Figure 1C). By systematically stimulating nodes in the whole-brain model, we were able to determine the regions that causally affect significant network changes resulting from the treatment in the responders.

**Conclusion:** Firstly, we demonstrated that the PMS for the third state changes between the conditions for responders potentially hinting at the importance of given state-specific dynamics for a successful treatment. Lastly, by deploying the computational model, we inferred the possible mechanisms that lead to the significant re-balancing of functional brain dynamics with successful treatment.

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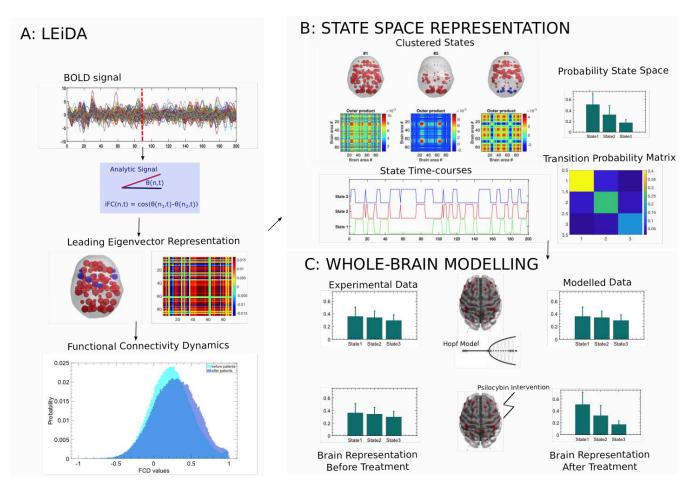
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**Figure 1:** Experimental Design Summary: **A** – Leading Eigenvector Dynamics (LEiDA) in the fMRI data registered to AAL atlas. **B** – State-space representation of the leading eigenvectors across time performed by k-means clustering. **C** – Supercritical Hopf network model fitted to the pre-experimental data and then stimulated with known psilocybin neuropharmacology.

### Bringing action into the picture. How action influences visual awareness

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Recent studies suggest that action may influence visual awareness. Here, we report two studies investigating the relation between action and awareness on behavioural and neuronal level. Both studies applied perceptual discrimination task. In E1, presentation of the stimulus was immediately followed by a cue requiring a motor response that was irrelevant to the task but could be the same, opposite, or neutral to the correct response to the stimulus. After responding to the cue, participants rated their stimulus awareness using the Perceptual Awareness Scale (PAS), and then carried out their discrimination response.

Participants reported a higher level of stimulus awareness after carrying out responses that were either congruent or incongruent with the response required by the stimulus, compared to the neutral condition. In E2, we used a single-pulse Transcranial Magnetic Stimulation (sp-TMS) to excite primary motor cortex (M1). Delivering sp-TMS to M1 resulted in higher average PAS ratings as compared to the control stimulation condition, but only in trials where stimulation was congruent with the following identification task response. We concurrently measured motor evoked potentials (MEPs) and showed that they can serve as an indirect measure of both perceptual and non-perceptual evidence accumulated for visual awareness ratings. Based on the results of both studies, we argue that activity in motor cortex influences visual awareness of the participants. We also discuss the possible mechanisms that underlie these influences on both the cognitive and the neural levels.

We propose that action may affect visual awareness because (1) it serves as additional information in the process of evidence accumulation; (2) it restricts the number of alternatives in the decisional process; (3) it enables error detection and performance monitoring; and/or (4) it triggers attentional mechanisms that modify stimulus perception. We also discuss the possible neuronal mechanisms of the aforementioned effects, including feedback-dependent prefrontal cortex modulation of the activity of visual areas, error-based modulation, interhemispheric inhibition of motor cortices, and attentional modulation of visual cortex activity triggered by motor processing. We also concluded that interactions between action and visibility judgments allows us to better understand the mechanisms of visual awareness.

#### Studying, Measuring and Altering Consciousness through information theory in the electrical brain

Our vision is that consciousness will someday be electromagnetically measured and altered. The associated needed insights will prove crucial to the development of cognitive sciences. The conceptual framework of the project rests on information theoretic developments that link consciousness to the amount of information that a physical system can represent and generate as an integrated whole, and from the related idea that consciousness can be quantified by metrics reflecting

### information processing and representation complexity.

Supported by computational neuroscience models, we aim to create non-invasive consciousness-probing technologies integrating electro- and magneto-encephalography, peripheral and non-invasive brain stimulation (NIBS) with advanced techniques to analyse brain activity – including functional and effective connectivity. Based on the derived brain activity metrics, we will explore intervention, i.e. the use of NIBS to alter consciousness.

To achieve these goals, we will pursue computational neuroscience models and human studies - in perception, sleep, anaesthesia, locked-in syndrome, disorders of consciousness, and in uterosupported by machine learning to disentangle the essential aspects of consciousness. The project will also explore the ethical implications of such technologies and the prospects for clinical translation. If successful, this paradigm-shifting work will have profound social and clinical impact and provide key insights in fundamental neuroscience, artificial cognition research, and science of consciousness.

### Studying Consciousness in the electrical brain

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