Conscious processing of narrative stimuli synchronizes heart rate between individuals

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Abstract

Heart rate has natural fluctuations that are typically ascribed to autonomic function. Recent evidence suggests that conscious processing can affect the timing of the heartbeat. We hypothesized that heart rate is modulated by conscious processing and therefore dependent on attentional focus. To test this we leverage the observation that neural processes can be synchronized between subjects by presenting an identical narrative stimulus. As predicted, we find significant inter-subject correlation of the heartbeat (ISC-HR) when subjects are presented with an auditory or audiovisual narrative. Consistent with the conscious processing hypothesis, we find that ISC-HR is reduced when subjects are distracted from the narrative, and that higher heart rate synchronization predicts better recall of the narrative. Finally, patients with disorders of consciousness who are listening to a story have lower ISC, as compared to healthy individuals, and that individual ISC-HR might predict a patients' prognosis. We conclude that heart rate fluctuations are partially driven by conscious processing, depend on attentional state, and may represent a simple metric to assess conscious state in unresponsive patients.

Introduction

In healthy individuals, heart rate fluctuates with breathing and changes in parasympathetic and sympathetic tone [1–3]. Physical activity naturally increases heart rate, but also just thinking about physical activity may increase heart rate[4]. Similarly, mental exercises such as meditation can reduce heart rate[5]. The effect of cognition on heart rate is perhaps even more direct than these traditional accounts [6,7]. We also know that suspense and surprise can transiently increase heart rate[8]. Most likely these immediate effects of the mind on the heart subserved the purpose of preparing the body for imminent action[9]. Despite this evidence, the role of conscious perception[10] on heart rate is less clear. It is well established that the brain can unconsciously detect novelty in the stimulus, as demonstrated with event-related potential studies (e.g. MMN[11–13], and N400[14,15]). Recent evidence shows that the timing of an individual heartbeat may be affected by the perception of an unexpected sound, but only when consciously perceived[16]. We hypothesize that conscious processing of perceptual information will affect heart rate. Therefore, we predict that fluctuations in heart rate will depend on top-down attention to the stimulus and predict memory performance, a known factor[17] and a correlate of conscious perception.[18]

To test these predictions we will leverage the observation that natural narrative stimuli guide cognitive processes resulting in reliable neural responses. This was first observed by measuring hemodynamic brain activity during movies: when humans watch the same movie, they have similar fluctuations in brain blood oxygenation[19]. Specifically, the temporal fluctuations of the signal measured with functional magnetic resonance (fMRI) are correlated between subjects. Significant inter-subject correlation of brain activity has now been observed with other neuroimaging modalities, including EEG, MEG and fNIRS[10–13]. Thus, neurophysiological fluctuations appear to synchronize on a wide range of time scales, from milliseconds to several minutes. This phenomenon is also not constrained to movies but has been observed for speech, music, or during driving [20–22]. There are even significant correlations in the spatial patterns of fMRI activity between speakers and listeners[23] or the time-courses of EEG signals of two individuals engaged in a conversation[24]. This similarity of neural activity in response to narrative stimuli suggests that these stimuli elicit similar perceptual and cognitive processes in different subjects.

Consistent with this, inter-subject correlation crucially depends on the cognitive state of the participant. Subjects that are not attentive or do not follow the narrative show significantly reduced inter-subject correlation, both in EEG and fMRI [25–27]. A drop in inter-subject correlation is also observed in patients with disorders of consciousness relative to healthy controls [28–30]. Indeed, a cohesive narrative is crucially important to elicit synchronized brain activity in fMRI, in particular at long time scales.[31] It comes as no surprise then that inter-subject correlation has been found to be predictive of a variety of behavioral outcomes, such as audience retention, memory of content, efficacy of advertising, efficacy of communication and political speeches, and more [23,25,32–35].

There are many studies reporting a correlation of physiological signals across subjects.[36] Generally this has been linked to physical or social interaction,[37–40] or at the very least a co-presence at the same place and time.[41] However, consistent with our hypothesis, the simultaneous experience is not crucial for synchronization. A few recent studies report a correlation of heart rate fluctuations across subjects watching the same movie at different times, and ascribe this to shared emotions elicited by the film.[42,43]

Our conscious processing hypothesis predicts that this synchronization phenomenon will occur not just for the film, but more generally for narrative stimuli, that inter-subject correlation of heart rate will be modulated by attention, that it will correlate with cognitive performance, and more dramatically, that it will be reduced in patients with disorders of consciousness. We confirm these predictions in a series of four experiments and conclude that heart rate synchronization has the potential to become a marker of cognitive state in a clinical setting.

Results

In all four experiments we presented narrative stimuli to each subject while recording their electrocardiogram (EKG, Figure 1A). Recordings were aligned in time between subjects and instantaneous HR was estimated as the inverse of the RR intervals (Figure 1B). Mean and standard deviation of these instantaneous measures provide HR and HR variability (HRV) for each subject. The instantaneous HR signals are upsampled to a common sampling rate and correlated between all pairs of subjects (Figure 1C). Inter-subject correlation of HR (ISC-HR) is then defined for each subject as the average Pearson's correlation with all other subjects (Figure 1D).

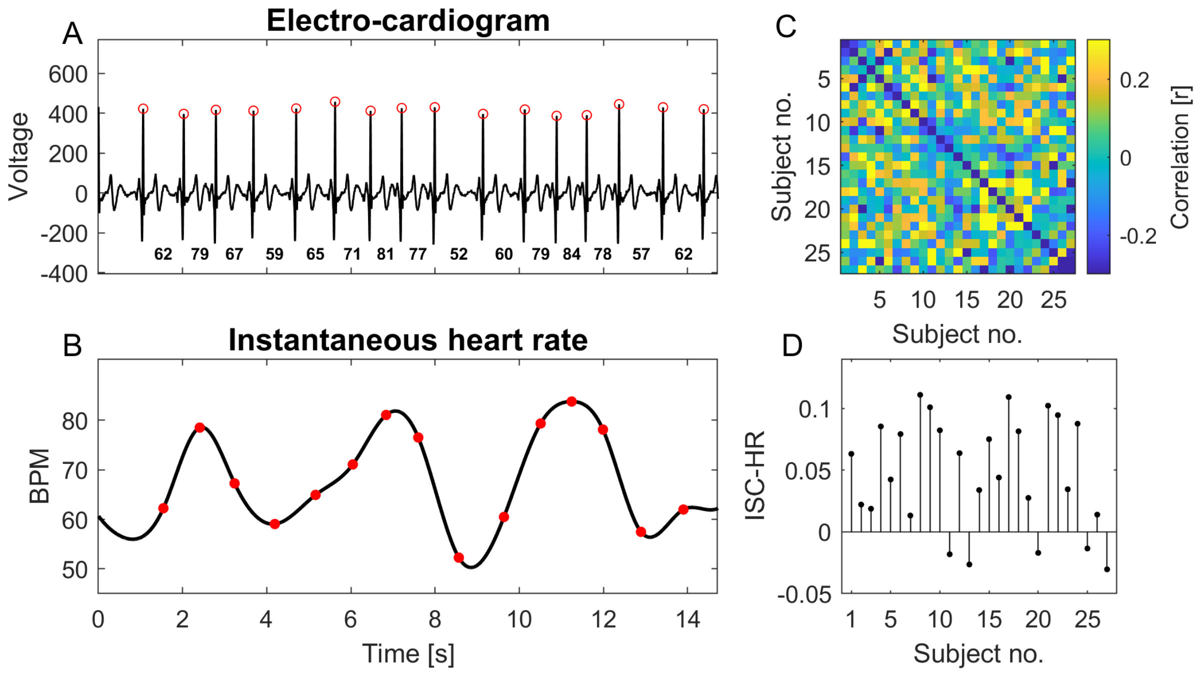

Figure 1: Inter subject correlation of heart rate (ISC-HR), **A:** Electro-cardiogram with peak of the R-wave detected (red o). **B:** The inverse of the interval between two R-waves defines the instantaneous heart rate (red o). This is interpolated (black) to convert heart rate into a signal with a uniform sampling rate across subjects. **C:** Pearson's correlation coefficient of this instantaneous heart rate between pairs of subjects. **D:** Inter-subject correlation of heart rate (ISC-HR) is computed for each individual as the mean across a row of this correlation matrix. Example in this figure is taken from history segment #1, dataset #1.

Auditory narratives synchronize listeners' heart rate fluctuations

The objective of the first experiment was to determine whether a common auditory narrative elicits similar heart rate fluctuations in healthy volunteers (Experiment 1). Subjects were presented with one-minute segments of an audiobook of Jules Verne's "20,000 leagues under the sea". First we tested whether there was significant inter-subject correlation of the instantaneous HR. To this end we compared the ISC-HR values to values computed on signals randomly shifted in time within-subjects (see methods). When this analysis is performed on individual one-minute segments, only a few subjects show significant non-zero ISC-HR (Fig. 2A, red dots, FDR at 0.05). When averaging ISC-HR values over the 16 minutes, 17 of the 27 subjects show statistically significant HR correlation (Fig. 2B; FDR at 0.05). No significant negative correlations were found. As an additional control, we randomly shuffle the one-minute story segments between subjects breaking the narrative synchrony across subjects. As expected, we observed a drop in ISC with values no longer statistically significant (Fig. 2C). In total, we conclude that the narrative stimulus induces similar HR fluctuations across subjects. ISC-HR therefore captures how strongly the stimulus drives the fluctuations of HR in each subject.

Results on average HR and HRV and their potential relation to ISC-HR are generally unremarkable for these data and are discussed in the Supplement (Fig. S1).

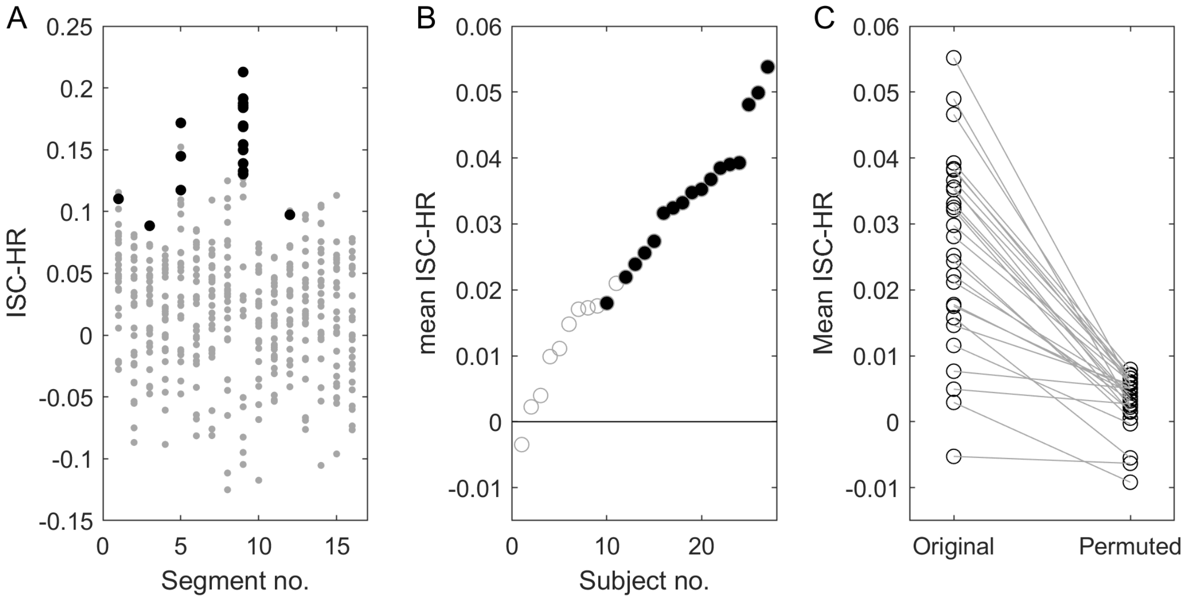

Figure 2: ISC-HR resolved in time and by subject. In Experiment 1, subjects listened to segments of audio narratives of 60 seconds each (N=16). **A**: ISC-HR is computed for each subject (N=27) and each segment. **B:** For each of the 27 subjects ISC is averaged over the 16 segments. Subjects are ordered by their ISC values. Black points (panel A and B) indicate statistically significant ISC values. Gray points are not statistically significant. Statistical significance is determined using circular shuffle statistics (10,000 shuffles and corrected for multiple comparisons with FDR of 0.01). Specifically, the heart rate signal of each subject is randomly shifted in time. **C:** As additional control here ISC is compared to the ISC obtained when story segments are swapped across subjects at random.

Attention modulates synchronization of HR fluctuations during audiovisual narratives

We demonstrated above that an auditory narrative can synchronize HR fluctuations across subjects. In the second experiment we aim to determine if this synchronization is modulated by attention to the stimulus (Experiment 2). Here we used short and engaging instructional videos of 3-5 minute duration, similar to our previous work[27]. Each subject viewed 5 videos in sequence normally. Then they view the same videos a second time, but now with the instruction to count backward silently in their mind in step 7 starting from a random number. This secondary task aims to distract subjects from viewing the video [26,27].

We find that ISC-HR drops in the distracted condition relative to the normal attentive state (Fig. 3A). A repeated-measures ANOVA shows a strong effect of attention ($F(1,238)=73.45$, $p=1.32e-15$) and an effect of the video ($F(4,238)=14.59$, $p=1.14e-10$) as well as a subject effect ($F(26,238)=2.86$, $p=1.34e-05$). The effect of attention is significant for each story individually (follow up pairwise t-test, all $p<0.05$) and when averaging over all 5 videos with a total duration of 22:33 minutes we see a numerical drop in ISC-HR with distraction in all but one of the 27 subjects (Fig. 3B).

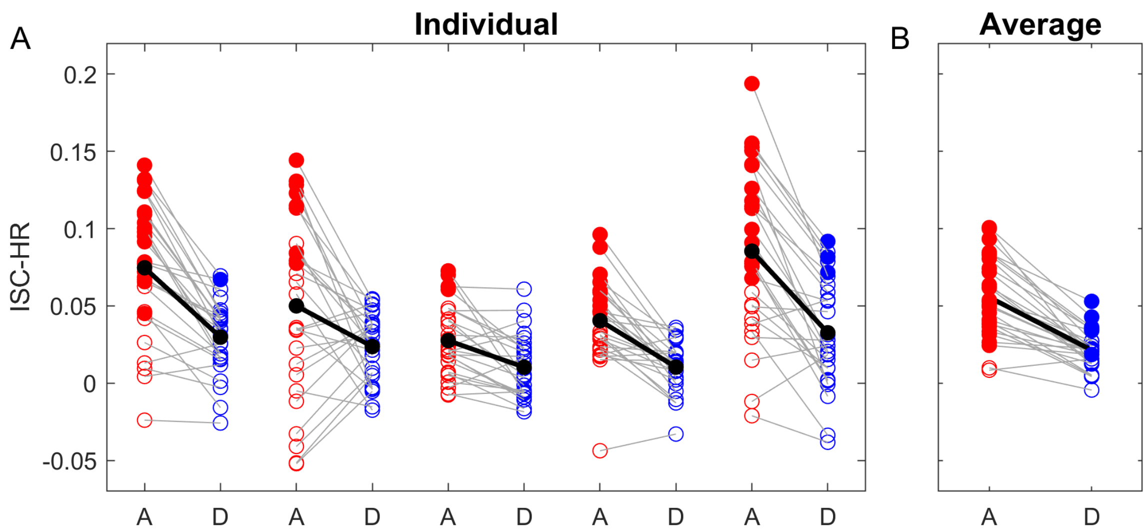

Figure 3: Intersubject correlation (ISC) of the instantaneous heart rate is modulated by attention. In Experiment 2, 27 subjects watched 5 educational videos of 3-5 minute duration each. Here ISC is measured against the attentive condition, i.e. both attentive and distracted subjects are correlated against the HR collected during the attentive condition. Filled points indicate individually statistically significant ISC-HR (FDR <0.01). **A:** Subjects watched the same videos twice, either in an attentive (A, red) or distracted (D, blue) condition. ISC was systematically higher in the attentive condition for the five videos. Gray lines indicate individual subjects and the black lines the group average. **B:** Same results when average across the five videos.

Attention modulates HRV, but this is not the driving factor in modulation of ISC

For this Experiment 2, in addition to ISC we also analyzed heart rate variability (HRV), defined here as the standard deviation of instantaneous HR (Fig. S2B). We see an increase in HRV when subjects are distracted. An ANOVA shows a fixed effect of attention ($F(1,211)=63.60$, $p=9.54e-14$), random effect of subject ($F(23,211)=29.56$, $p=1.57e-53$), but we see no significant video effect ($F(4,211)=0.77$, $p=5.44e-01$). Perhaps the increase in HRV in the distracted condition could explain the drop in ISC-HR. If this was the case, we would expect that HRV correlates negatively with ISC-HR as, by definition, the two are inversely related. However, the opposite seems to be the case: subjects with higher HRV have also higher ISC-HR (Fig. S2D). Therefore, it appears that the modulation of HRV and ISC-HR are independent phenomena. The effects on mean HR were generally unremarkable (Fig. S2A & S2C).

Synchronization of HR fluctuations is modulated in the time scale of 5-10 seconds

It is well established that HR fluctuates at different timescales [44]. This is confirmed on the present data (of Experiment 2) by computing HRV after band-pass filtering the instantaneous HR in different frequency bands (Fig. 4A). To determine which time scale dominates ISC and its modulation with attention we computed ISC similarly resolved by frequency band (Fig. 4B). We find that ISC and its modulation with attention are dominant in the mid-frequency range -- from 0.1 Hz to 0.2 Hz in this study -- a range of HR fluctuations that are known to disappear during slow-wave sleep [45].

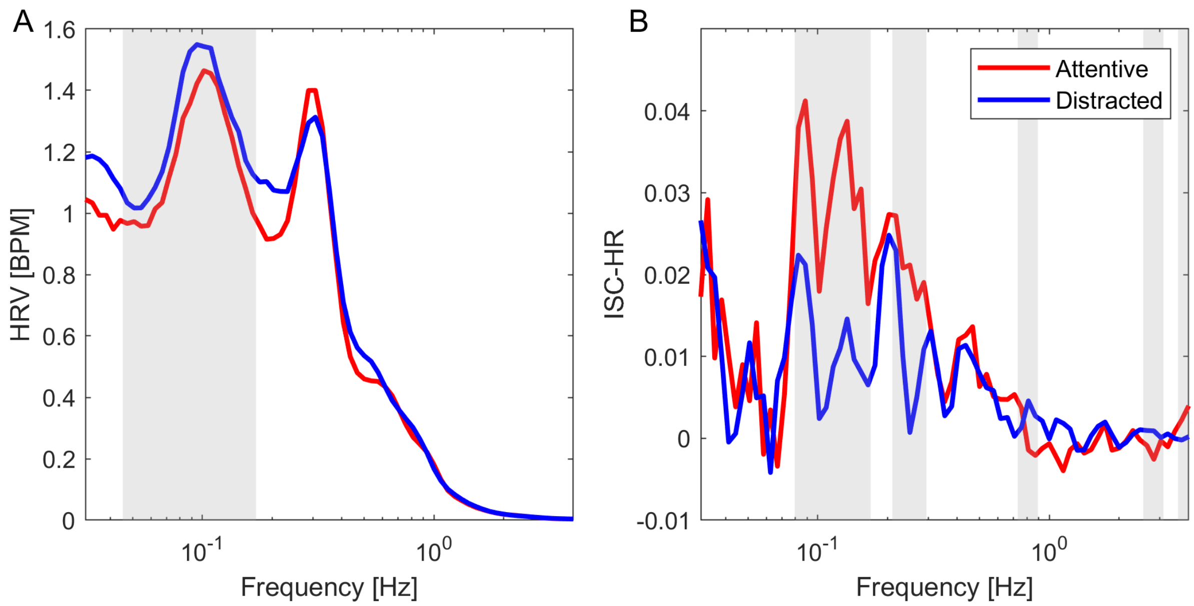

Figure 4. Spectrum of instantaneous HR and ISC-HR and its modulation with attention. For Experiment 2, instantaneous HR was band-pass filtered with center frequency on a logarithmic scale and a bandwidth of 0.2 of the center frequency. **A:** HRV is computed here as the root mean square of the band-passed instantaneous HR averaged over the 5 videos (~15 min total). **B:** ISC-HR is computed as before, but now on the band-passed instantaneous HR and averaged over the 5 videos. In both panels significant differences between attending and distracted conditions are established in each band with a paired t-test over the 27 subjects (grey shaded area indicates p<0.05, uncorrected).

Attention modulates synchronization of HR fluctuations during audio-only narratives, but does not synchronize breathing

Given the dependence of HR fluctuations on attention, we expected that HR would be predictive of cognitive processing of the narrative. In the next experiment (Experiment 3) we, therefore, recorded HR during the presentation of auditory narratives, and afterward asked adult subjects to recall factual information presented in the story, e.g. "What was the name of the two main characters?". Subjects listened to four auditory narratives, in either an attentive or distracted condition. This time the narratives were children's stories of 8-11 minute duration, and the secondary task consisted of counting target tones that were inserted in the audio asynchronously across subjects. To rule out order effects we now divided the participants in two groups. In group 1 (N=9) subjects listened to stories 1 and 2 in the attentive condition and stories 3 and 4 in the distracted condition. In group 2 (n=12) subject listened to the same stories with the attention condition reversed.

We find again that ISC-HR drops significantly when subjects are distracted (Fig. 5A, paired t-test $t(21)=8.2$, $p< 10^{-7}$). Similarly to experiment 2 with video, here 15 out of the 21 subjects show a statistically significant correlation of HR in the attentive condition and none in the distracted condition. As expected, subjects performed significantly better in recalling elements of the story in the attentive condition as compared to the distracted condition (Supplementary Fig. S3, Wilcoxon Signed-Rank Test, z = 4.03, p = 5.7e-5).

Our hypothesis postulates that ISC-HR is the result of similar conscious processing of the narrative stimulus, thus, we predicted that subjects with higher ISC-HR will be better at remembering elements of the stories. Indeed, we find that ISC correlates with memory recall performance across conditions (Fig 5B, r(40)=0.767, p=3.1e-9, Spearman's correlation is used here due to the bounded nature of the percent measure). More importantly, even within the normally attentive condition with a normal fluctuation of HR we find that ISC-HR is predictive of memory performance (r(19)=0.57, p=7.3 e-3). In the distracted conditions there was no correlation with memory performance (r(19)=-0.1, p=0.67) possibly because ISC-HR was not statistically significant for any of the subjects. Overall we conclude that ISC-HR is indicative of conscious processing of the narrative.

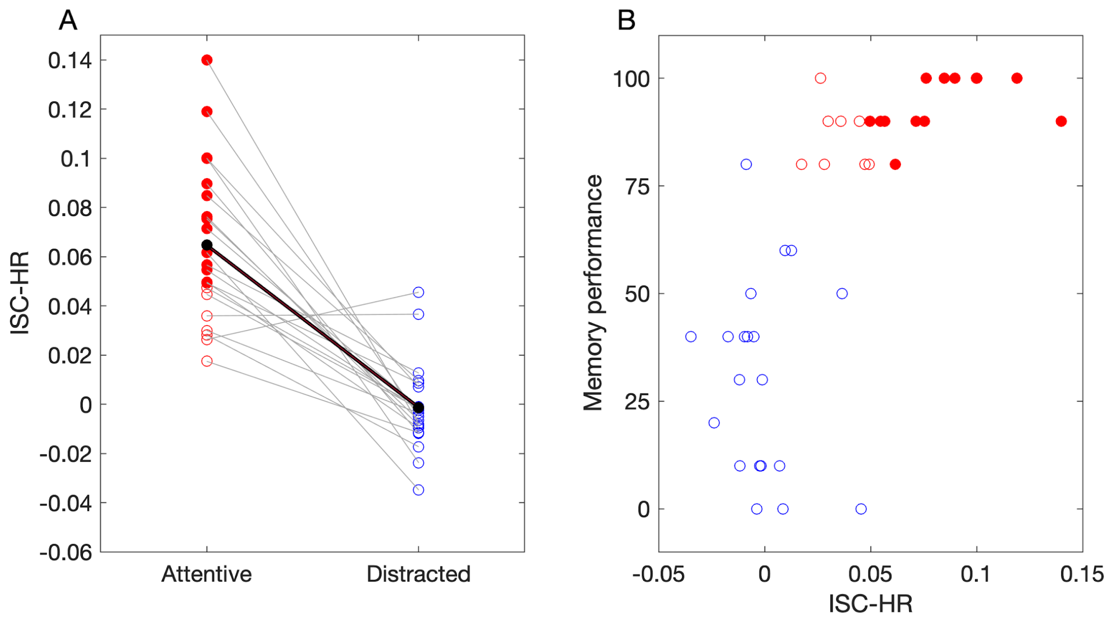

Figure 5: Intersubject correlation is higher when subjects were attentive to the auditory narrative and this correlation indexes the subjects' memory performance. In Experiment 3, Subjects listened to four recordings of children's stories 8-10 minutes in duration. Subjects were instructed to either attend to a story normally (attentive, red), or to count backward when they heard a target sound inserted in the audio (distracted, blue). Again ISC is measured against the attentive condition, i.e. both attentive and distracted subjects are correlated against the HR collected during the attentive condition. Filled points indicate individually statistically significant ISC-HR (FDR <0.01). **A:** ISC-HR for each subject (N=21) averaged over four stories. **B:** Memory performance measured as percent of correct answers to free recall questions about the content of the stories. Filled and empty circles indicate significant and non-significant ISC-HR respectively (p<0.05 shuffle statistics)

Intersubject correlation of heart rate is not driven by synchronous breathing

It is well established that HR fluctuations are driven in part by breathing. This phenomenon is known as respiratory sinus arrhythmia and is strongest in the frequency band around 0.1 Hz.[46] It is possible that the attentional modulation in this frequency band is caused by synchronization of breathing between subjects. We, therefore, collected in Experiment 3 also respiratory movement concurrently with the EKG and measured inter-subject correlation of breathing (Supplementary Fig. S5A). We did not find a significant ISC of breathing in any of the subjects, nor was there any effect of attention when comparing across all subjects (paired t-test, t(21)=0.5, p=0.6). In other words, the auditory narratives did not reliably entrain the subjects breathing nor was this modulated by attention. Interestingly, breathing does significantly correlate with HR (Supplementary Figure S5B, t(20)=4.49, p=2e-4) reflecting the well-established respiratory sinus arrhythmia. In addition, we found a reduction breathing-HR correlation in the distracted condition versus the attentive condition but it didn't reach statistical significance (t(20)=1.86, p=0.08), suggesting that this link does not depend on attention. In conclusion, these results suggest that the effect of cognition on instantaneous HR is not related to breathing.

Synchronization of heart rate fluctuations is disrupted in patients with disorder of consciousness

Given the dependence on attention and conscious processing of these synchronized HR fluctuations, we predicted that patients with disorders of consciousness (DOC) will have diminished HR synchronization when presented with an auditory narrative. We recorded EKG in 19 DOC patients, in addition to 24 healthy controls (Experiment 4). The patients were hospitalized to determine their state of consciousness and neurological prognosis. Patients were behaviorally assessed using the standard Coma Recovery Scale-revised[47]. State of consciousness was determined using the currently accepted categorization[48], patients were classified either in (1) Coma, (2) Vegetative state/Unresponsive wakefulness syndrome (UWS), (3) Minimally conscious state minus (MCS-), (4) Minimally conscious state plus (MCS+), and exit Minimally conscious state (EMCS). Patients and healthy subjects listened through headphones to a children's story of 10-minute duration. ISC-HR was calculated by correlating HR with that of healthy controls. As expected ISC-HR values were lower in patients (t-test: t(41) = 3.14, p = 0.003, Fig. 6A). Within patients no significant correlation was found between ISC-HR and state-of-consciousness (Fig. 6A, Spearman correlation, R(17) = -0.28, p = 0.24) nor between ISC-HR and the Coma Recovery Scale-Revised (CRS-R[47]; Fig 6B, Spearman correlation, R(17) = -0.3, p = 0.22). Reduced HRV is sometimes found in traumatic brain injury patients.[49] We therefore analyzed HRV to verify that the drop in ISC-HR is not a noise-floor effect, i.e. if HRV drops in patients it may be difficult to measure inter-subject correlation above random fluctuations (Fig. S6B). Contrary to what was expected we found higher HRV in the DOC patients compared to healthy controls (t(41) = 2.34, p = 0.02), ruling out a noise-floor effect. We also found higher mean HR in DOC patients compared to healthy controls (Fig S6A; t(41) = 4.7, p = 2.9e-05). However, given the previous lack of correlation between ISC and mean HR we do not believe this contributed to the decrease of ISC-HR in patients.

When measured individually, only two of 19 patients showed statistically significant ISC-HR (FDR corrected p<0.05, Fig. 6, purple filled circles). For these two patients outcomes at the six-month follow-up were mixed; one patient fully regained consciousness whereas for the other, life-sustaining therapies were withdrawn before the follow-up assessment. Among the remaining 17 patients only one additional patient recovered consciousness, although in a completely aphasic condition. These results suggest that the patients' ISC-HR might carry prognostic information with a specific emphasis on conscious verbal processing. To test this hypothesis we first correlated the patients' ISC-HR to the CRS-R improvement after six months of the initial assessment. We found a positive correlation between ISC-HR and CRS-R improvement, although not statistically significant (Fig 6C, Spearman correlation, R(14)=0.43,p=0.097, second assessment was available only for 16 patients). A limitation of behavioral assessment of patients is that it cannot detect covert awareness [50,51], a condition that can occur in up to 15% of the UWS patients[52]. Therefore, we also correlated the patients'

ISC-HR to an anatomical measure of brain integrity -- whole-brain white matter fractional anisotropy. This FA index has been linked to neurological recovery in DOC patients[53]. We found a significant correlation between ISC-HR and FA Index (Fig. 6D, Spearman correlation, R(9)=0.73,p=0.01, FA Index was available only for 11 patients).

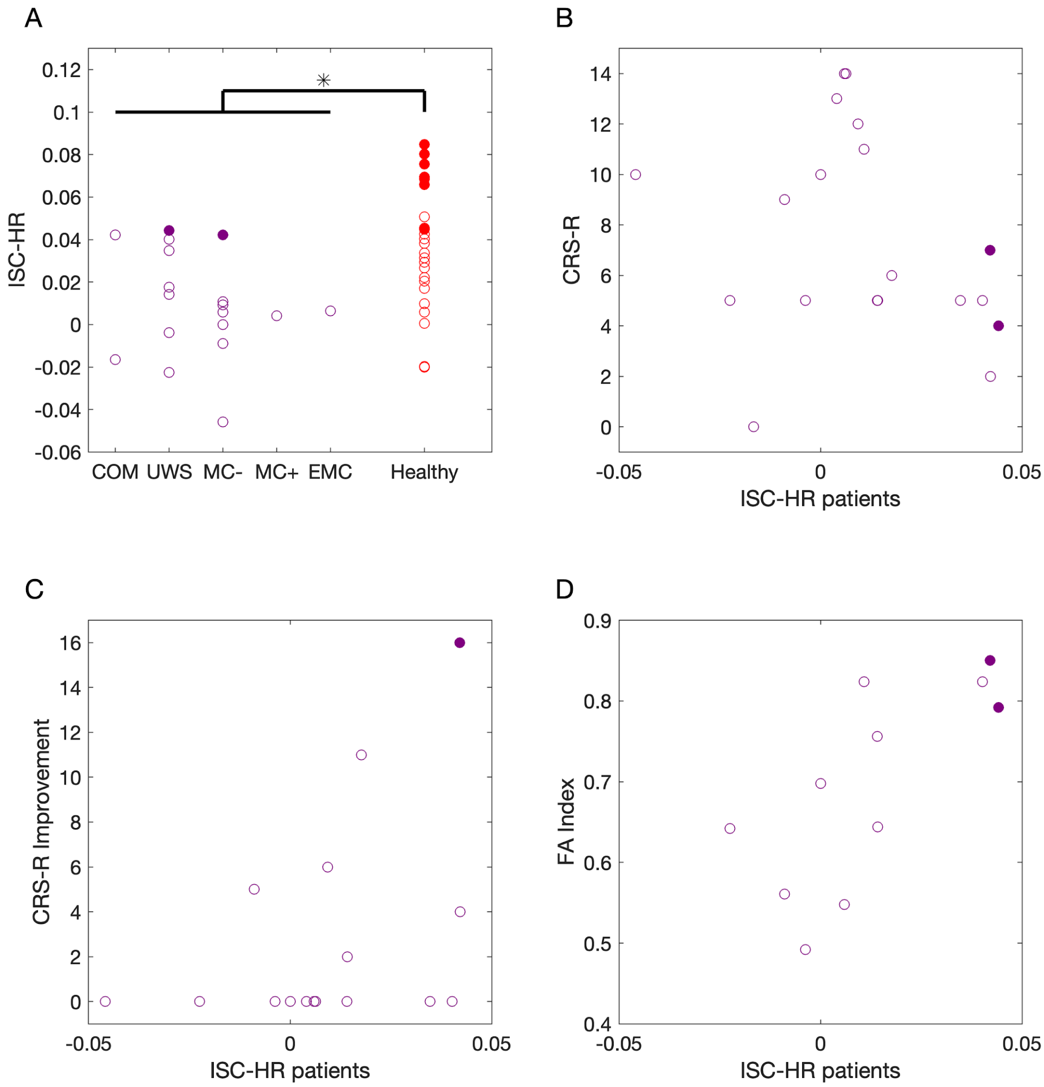

Figure 6: Audio narratives synchronize HR fluctuations in healthy controls but not in patients with disorder of consciousness. In Experiment 4, subjects listened to a children's story (La part des ancêtres from Leonora Miano; 10 minutes). **A:** ISC-HR is measured by correlating instantaneous HR with that of healthy subjects. Filled cycles indicated statistically significant ISC. **B:** Comparison of the ISC-HR with Coma Recovery Scale-Revised in patients (N=19). **C:** Comparison of the ISC-HR with improvement of Coma Recovery Scale-Revised six months after the first assessment (N=17) **D:** Comparison of ISC-HR and whole-brain white matter fractional anisotropy in patients, were available (N=11).

Discussion

The hypothesis that motivated this set of experiments was that conscious processing of information modulates instantaneous heart rate. This fluctuating heart rate will synchronize across subjects when presented with narrative stimuli that are processed similarly. We tested the predictions resulting from this hypothesis in a series of four experiments. In the first experiment with healthy volunteers we confirmed that heart rate fluctuations correlate between subjects for auditory narratives. In the second and third experiment we confirm that distracting the participants with a secondary task reduced this correlation, for video and audio narratives alike. Importantly, we confirm the prediction that synchronization of HR fluctuations is predictive of memory performance. We also determined that HR synchronization is not driven by synchronous breathing across subjects. Finally, in the fourth experiment we presented an auditory narrative to patients with disorders of consciousness and found that their heart rate fluctuations do not correlate with that of healthy subjects.

There is an extensive literature demonstrating that physiological signals such as heart rate, respiration, and skin conductivity can synchronize between individuals.[36] This literature emphasizes physical interaction and social relationships as the factors driving this synchronization. Even in the context of music, theater, or film, the emphasis is on the concurrent and shared experience of an audience that synchronizes heart rate to one-another.[37–39,54] Here we have emphasized instead that it is the stimulus that synchronizes HR, or more precisely, a similar processing of a common stimulus. There is no need for individuals to directly interact, be related to one another or perceive the stimulus together at the same time. Consistent with our hypothesis, previous reports already show that emotional movies can synchronize the HR of viewers, even when watching the movie individually.[42,43] The present findings go beyond this previous literature in that this HR synchronization phenomenon is not specific to live experiences or emotional movies. Rather, it occurs with many narrative stimuli, as we demonstrated here with audio recordings of children's stories or animated educational videos.

There is also an extensive literature on the inter-subject correlation of brain signals evoked by dynamic natural stimuli, starting with experiments in fMRI while subjects watched movies.[19] This work demonstrated that subjects process natural stimuli similarly, and that similarity of brain activity is predictive of memory performance.[55] Subsequent experiments replicated these findings with EEG.[56,57] Additionally, ISC of EEG is reduced when subjects are distracted[26] and is reduced in patients with disorder of consciousness,[58] similar to what we find here with the instantaneous heart rate. Given these parallels we expect that HR fluctuations will also synchronize across subjects listening to engaging music,[21] and that HR synchronization will be a good indication of how engaging a narrative is.[32,59]

We suggest that some previous work on physiological synchronization of autonomic signals can be reinterpreted in the context of the present conscious processing hypothesis. For example, the same performance is judged differently depending on the social relationship of performer and audience member, suggesting that it is a different way of processing information in the audience member.[37] In our view, it is the processing of the common stimulus, and not the co-presence in the same physical space that causes the synchronization of the heart rate fluctuations. We predict that many results obtained with live performances [37–39] or in-person interactions[26] could be recovered with asynchronous playback of the same experience recorded with video. Evidently the experience may be less powerful than live in-person experiences,[41] but the modulating factors of relationships, emotions, or empathy may still prevail in this virtual context.

We postulate that factors intrinsic to the story, such as semantics and emotions, driving a synchronized heart rate. This may include semantics of single-word to syntactic and multi-sentence level of representation as well as prosody, valence of single words, and more complex semantically mediated emotions. Capturing semantics and emotions require attention to the stimulus and some level of language comprehension. In this view, it is the narrative content that drives attention, engagement, interest and emotions. It is possible, indeed likely that the variations in ISC are due to this differing narrative content. Indeed we find a strong difference in ISC between stimuli, even within the same type of animated educational videos. Dependence of ISC on the stimulus has been found in previous EEG studies [32,35,60] and for heart rate in studies involving live performance for different pieces of classical music. [39] In contrast to EEG, we may expect that ISC-HR is less sensitive to low-level features of a stimulus. Neural evoked responses can be driven by low-level features such as luminance or sound fluctuations, which can elicit strong responses that would be trivially synchronized across subjects.[19,61] To us it is less clear how such low-level stimulus fluctuations could drive HR fluctuations.

We have shown here that the effect on HR synchronization is dominant in the frequency band around 0.1Hz, which falls in the frequency range of respiratory sinus arrhythmia.[46] However, we show here that breathing does not synchronize between subjects, nor is the link between breathing and instantaneous heart rate dependent on attention. Given the link between respiratory sinus arrhythmia and parasympathetic cardiac control,[62] this result suggests that attention does not affect parasympathetic activity.

Finally, we made a proof-of-concept that the ISC-HR could be used as a simple marker for cognitive state in unresponsive patients. Note that this is in line with previous work on ISC of EEG[28], fMRI[30], and similar findings with galvanic skin response[63]. While we were able to distinguish patients from healthy controls, we were not able to resolve conscious states among patients. However, the results do suggest that the ISC-HR might carry information related to the patients' recovery. Note that the proposed method requires the patients to be conscious, but also to be able to process language. This double requirement may explain the positive test in one patient who recovered with preserved language processing, and a negative test in a patient who recovered in an aphasic condition. In addition, we believe that the 10 minutes story we used may have been too short for a reliable measure of ISC-HR. In the present experiments we required at least 15 minutes of instantaneous heart rate to detect significant ISC, and a link to memory. We suggest that future studies on clinical utility use one or several narratives totaling at least 30 minutes of concurrent heart rate recordings. In addition, our results also indicate that the actual content of the story, and how engaging it is for the subject, plays a role in the individual ISC. Given the limited cognitive status of the patients it is critical to maximize this factor. We also suggest that the narratives should be adapted for every single patient, for instance by changing the name of the leading character using the patients' own name. By doing so we will amplify the patients' attention while keeping the overall structure of the story comparable across subjects.

Bibliography

1. Levy, M. N. & Martin, P. J. Autonomic Neural Control of Cardiac Function. in *Physiology and Pathophysiology of the Heart* (ed. Sperelakis, N.) 361–379 (Springer US, 1989). doi:10.1007/978-1-4613-0873-7_17.
2. Palma, J.-A. & Benarroch, E. E. Neural control of the heart: recent concepts and clinical correlations. *Neurology* **83**, 261–271 (2014).
3. Cooke, W. H. *et al.* Controlled breathing protocols probe human autonomic cardiovascular rhythms. *Am. J. Physiol.* **274**, H709-718 (1998).
4. Bernardi, L., Valle, F., Coco, M., Calciati, A. & Sleight, P. Physical activity influences heart rate variability and very-low-frequency components in Holter electrocardiograms. *Cardiovasc. Res.* **32**, 234–237 (1996).
5. Kyeong, S., Kim, J., Kim, D. J., Kim, H. E. & Kim, J.-J. Effects of gratitude meditation on neural network functional connectivity and brain-heart coupling. *Sci. Rep.* **7**, 5058 (2017).
6. Park, H.-D., Correia, S., Ducorps, A. & Tallon-Baudry, C. Spontaneous fluctuations in neural responses to heartbeats predict visual detection. *Nat. Neurosci.* **17**, 612–8 (2014).
7. Park, H.-D. & Tallon-Baudry, C. The neural subjective frame: from bodily signals to perceptual consciousness. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* **369**, 20130208 (2014).
8. Ekman, P., Levenson, R. W. & Friesen, W. V. Autonomic nervous system activity distinguishes among emotions. *Science* **221**, 1208–1210 (1983).
9. McCorry, L. K. Physiology of the Autonomic Nervous System. *Am. J. Pharm. Educ.* **71**, (2007).
10. Dehaene, S. & Changeux, J.-P. J. P. Experimental and theoretical approaches to conscious processing. *Neuron* **70**, 200–227 (2011).
11. Morlet, D. & Fischer, C. MMN and Novelty P3 in Coma and Other Altered States of

Consciousness: A Review. *Brain Topogr.* (2013) doi:10.1007/s10548-013-0335-5.

12. Bekinschtein, T. A. *et al.* Neural signature of the conscious processing of auditory regularities. *Proc. Natl. Acad. Sci. U. S. A.* **106**, 1672–7 (2009).
13. Schlossmacher, I., Dellert, T., Pitts, M., Bruchmann, M. & Straube, T. Differential Effects of Awareness and Task Relevance on Early and Late ERPs in a No-Report Visual Oddball Paradigm. *J. Neurosci.* **40**, 2906–2913 (2020).
14. Cruse, D. *et al.* The reliability of the N400 in single subjects: Implications for patients with disorders of consciousness. *NeuroImage Clin.* **4**, 788–799 (2014).
15. Rohaut, B. *et al.* Probing ERP correlates of verbal semantic processing in patients with impaired consciousness. *Neuropsychologia* **66**, 279–292 (2015).
16. Raimondo, F. *et al.* Brain-heart interactions reveal consciousness in noncommunicating patients. *Ann. Neurol.* **82**, 578–591 (2017).
17. Mack, A. & Rock, I. *Inattentional blindness*. xiv, 273 (The MIT Press, 1998).
18. Trübutschek, D., Marti, S., Ueberschär, H. & Dehaene, S. Probing the limits of activity-silent non-conscious working memory. *Proc. Natl. Acad. Sci.* **116**, 14358–14367 (2019).
19. Hasson, U., Nir, Y., Levy, I., Fuhrmann, G. & Malach, R. Intersubject synchronization of cortical activity during natural vision. *Science* **303**, 1634–1640 (2004).
20. Pérez, A., Carreiras, M. & Duñabeitia, J. A. Brain-to-brain entrainment: EEG interbrain synchronization while speaking and listening. *Sci. Rep.* **7**, 4190 (2017).
21. Madsen, J., Margulis, E. H., Simchy-Gross, R. & Parra, L. C. Music synchronizes brainwaves across listeners with strong effects of repetition, familiarity and training. *Sci. Rep.* **9**, 3576 (2019).
22. Bernardi, G. *et al.* It's not all in your car: functional and structural correlates of exceptional driving skills in professional racers. *Front. Hum. Neurosci.* **8**, (2014).
23. Chen, J. *et al.* Shared memories reveal shared structure in neural activity across individuals. *Nat. Neurosci.* **20**, 115–125 (2017).
24. Zhang, J. R., Sherwin, J., Dmochowski, J., Sajda, P. & Kender, J. R. Correlating Speaker Gestures in Political Debates with Audience Engagement Measured via EEG.

in *Proceedings of the 22nd ACM international conference on Multimedia* 387–396 (Association for Computing Machinery, 2014). doi:10.1145/2647868.2654909.

25. Hasson, U., Chen, J. & Honey, C. J. Hierarchical process memory: memory as an integral component of information processing. *Trends Cogn. Sci.* **19**, 304–313 (2015).
26. Ki, J. J., Kelly, S. P. & Parra, L. C. Attention Strongly Modulates Reliability of Neural Responses to Naturalistic Narrative Stimuli. *J. Neurosci.* **36**, 3092–3101 (2016).
27. Cohen, S. S. *et al.* Neural engagement with online educational videos predicts learning performance for individual students. *Neurobiol. Learn. Mem.* **155**, 60–64 (2018).
28. Iotzov, I. *et al.* Divergent neural responses to narrative speech in disorders of consciousness. *Ann. Clin. Transl. Neurol.* **4**, 784–792 (2017).
29. Naci, L., Graham, M., Owen, A. M. & Weijer, C. Covert narrative capacity: Mental life in patients thought to lack consciousness. *Ann. Clin. Transl. Neurol.* **4**, 61–70 (2017).
30. Naci, L., Cusack, R., Anello, M. & Owen, A. M. A common neural code for similar conscious experiences in different individuals. *Proc. Natl. Acad. Sci.* 1407007111- (2014) doi:10.1073/pnas.1407007111.
31. Honey, C. J. *et al.* Slow Cortical Dynamics and the Accumulation of Information over Long Timescales. *Neuron* **76**, 423–434 (2012).
32. Dmochowski, J. P. *et al.* Audience preferences are predicted by temporal reliability of neural processing. *Nat. Commun.* **5**, 4567 (2014).
33. Schmälzle, R., Häcker, F., Renner, B., Honey, C. J. & Schupp, H. T. Neural Correlates of Risk Perception during Real-Life Risk Communication. *J. Neurosci.* **33**, 10340–10347 (2013).
34. Schmälzle, R., Häcker, F. E. K., Honey, C. J. & Hasson, U. Engaged listeners: shared neural processing of powerful political speeches. *Soc. Cogn. Affect. Neurosci.* **10**, 1137–1143 (2015).
35. Cohen, S. S. *et al.* Neural engagement with online educational videos predicts learning performance for individual students. *Neurobiol. Learn. Mem.* **155**, 60–64 (2018).
36. Palumbo, R. V. *et al.* Interpersonal Autonomic Physiology: A Systematic Review of the

Literature. *Personal. Soc. Psychol. Rev.* **21**, 99–141 (2017).

37. Konvalinka, I. *et al.* Synchronized arousal between performers and related spectators in a fire-walking ritual. *Proc. Natl. Acad. Sci.* **108**, 8514–8519 (2011).
38. Ardizzi, M., Calbi, M., Tavaglione, S., Umiltà, M. A. & Gallese, V. Audience spontaneous entrainment during the collective enjoyment of live performances: physiological and behavioral measurements. *Sci. Rep.* **10**, 1–12 (2020).
39. Bernardi, N. F. *et al.* Increase in Synchronization of Autonomic Rhythms between Individuals When Listening to Music. *Front. Physiol.* **8**, (2017).
40. Gordon, I. *et al.* Physiological and Behavioral Synchrony Predict Group Cohesion and Performance. *Sci. Rep.* **10**, 8484 (2020).
41. Golland, Y., Arzouan, Y. & Levit-Binnun, N. The Mere Co-Presence: Synchronization of Autonomic Signals and Emotional Responses across Co-Present Individuals Not Engaged in Direct Interaction. *PLoS ONE* **10**, (2015).
42. Golland, Y., Keissar, K. & Levit-Binnun, N. Studying the dynamics of autonomic activity during emotional experience. *Psychophysiology* **51**, 1101–1111 (2014).
43. Steiger, B. K., Kegel, L. C., Spirig, E. & Jokeit, H. Dynamics and diversity of heart rate responses to a disaster motion picture. *Int. J. Psychophysiol.* **143**, 64–79 (2019).
44. Akselrod, S. *et al.* Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control. *Science* **213**, 220–222 (1981).
45. Baharav, A. *et al.* Fluctuations in autonomic nervous activity during sleep displayed by power spectrum analysis of heart rate variability. *Neurology* **45**, 1183–1187 (1995).
46. Angelone, A. & Coulter, N. A. Respiratory sinus arrhythmia: a frequency dependent phenomenon. *J. Appl. Physiol.* **19**, 479–482 (1964).
47. Giacino, J. T., Kalmar, K. & Whyte, J. The JFK Coma Recovery Scale-Revised: measurement characteristics and diagnostic utility. *Arch. Phys. Med. Rehabil.* **85**, 2020–2029 (2004).
48. Bruno, M.-A., Vanhaudenhuyse, A., Thibaut, A., Moonen, G. & Laureys, S. From unresponsive wakefulness to minimally conscious PLUS and functional locked-in

syndromes: recent advances in our understanding of disorders of consciousness. *J. Neurol.* **258**, 1373–1384 (2011).

49. Riganello, F., Dolce, G. & Sannita, W. G. Heart rate variability and the central autonomic network in the severe disorder of consciousness. *J. Rehabil. Med.* **44**, 495–501 (2012).
50. Owen, A. M. *et al.* Detecting awareness in the vegetative state. *Science* **313**, 1402 (2006).
51. Schiff, N. D. Cognitive Motor Dissociation Following Severe Brain Injuries. *JAMA Neurol.* **72**, 1413–1415 (2015).
52. Kondziella, D., Friberg, C. K., Frokjaer, V. G., Fabricius, M. & Møller, K. Preserved consciousness in vegetative and minimal conscious states: systematic review and meta-analysis. *J. Neurol. Neurosurg. Psychiatry* **87**, 485–92 (2016).
53. Velly, L. *et al.* Use of brain diffusion tensor imaging for the prediction of long-term neurological outcomes in patients after cardiac arrest: a multicentre, international, prospective, observational, cohort study. *Lancet Neurol.* **17**, 317–326 (2018).
54. Kaltwasser, L. *et al.* Sharing the filmic experience - The physiology of socio-emotional processes in the cinema. *PLoS ONE* **14**, (2019).
55. Hasson, U., Furman, O., Clark, D., Dudai, Y. & Davachi, L. Enhanced Intersubject Correlations during Movie Viewing Correlate with Successful Episodic Encoding. *Neuron* **57**, 452–462 (2008).
56. Dmochowski, J. P. *et al.* Audience preferences are predicted by temporal reliability of neural processing. *Nat. Commun.* **5**, 4567 (2014).
57. Cohen, S. S. & Parra, L. C. Memorable Audiovisual Narratives Synchronize Sensory and Supramodal Neural Responses. *eNeuro* **3**, ENEURO.0203-16.2016 (2016).
58. Iotzov, I. *et al.* Divergent neural responses to narrative speech in disorders of consciousness. *Ann. Clin. Transl. Neurol.* **4**, 784–792 (2017).
59. Cohen, S. S., Henin, S. & Parra, L. C. Engaging narratives evoke similar neural activity and lead to similar time perception. *Sci. Rep.* **7**, 4578 (2017).
60. Madsen, J., Margulis, E. H., Simchy-Gross, R. & Parra, L. C. Music synchronizes

brainwaves across listeners with strong effects of repetition, familiarity and training. *Sci. Rep.* **9**, 1–8 (2019).

61. Poulsen, A. T., Kamronn, S., Dmochowski, J., Parra, L. C. & Hansen, L. K. EEG in the classroom: Synchronised neural recordings during video presentation. *Sci. Rep.* **7**, 43916 (2017).
62. Katona, P. G. & Jih, F. Respiratory sinus arrhythmia: noninvasive measure of parasympathetic cardiac control. *J. Appl. Physiol.* **39**, 801–805 (1975).
63. Sinai, L. Naturalistic paradigms for neuroimaging and bedside measures of conscious awareness. *Electron. Thesis Diss. Repos.* (2015).
64. Jenkinson, M., Beckmann, C. F., Behrens, T. E. J., Woolrich, M. W. & Smith, S. M. FSL. *NeuroImage* **62**, 782–790 (2012).
65. Mori, S. *et al.* Stereotaxic white matter atlas based on diffusion tensor imaging in an ICBM template. *NeuroImage* **40**, 570–582 (2008).

Methods

Datasets

Experiment 1 : auditory narratives with healthy participants

Twenty-seven native English speakers and healthy participants (22 females, age range 18-26, median 21 years old) listened to a 16-minute extract of an audiobook read by a male British English voice (20,000 leagues under the sea. Author: Jules Verne. Read by: David Linski. Public Domain (P) 2017 Blackstone Audio, Inc.) while their EKG was recorded. The audiobook extract was taken from the first chapter and half of the second chapter. The text is relatively suspenseful as it describes reports of an unknown monster that destroys ships. We divided the story into essays of approximately 1 minute each so that participants could take breaks between segments if they wished.
The instructions given to the subject were 'to listen to the story and look at a fixation cross'. The stimuli were delivered by headphones - ER·1 Insert Earphones (Etymotic Research), using Psychopy v3.1.2. The EKG was recorded with two electrodes on the chest using SenseBox of ANT Neuro, sampled at 500Hz.
EKG data was cut into the 16 epochs of approximately 1-minute corresponding to each audio-segment.
This study was approved by the STEM ethics committee of the University of Birmingham, England.

Experiment 2: instructional videos with healthy participants

Thirty-one students watched 5 instructional videos while their EKG were recorded (19 females, age range 18-46, median 28 years old) in an attentive condition (A), where they were instructed to simply watch videos as they would regularly watch a video. Each educational video was 3-5 minutes long, chosen from popular YouTube channels covering biology, physics, and computer science. These are new recordings on videos we had tested previously.[35] After the students had watched all 5 videos, they were asked to answer 10-12 questions about factual information about material conveyed in each video. Lastly, students were instructed to watch the video again in a distracted condition (D). In this condition participants were asked to silently count in their mind backwards from a random prime number above 800 and below 1000, in steps of 7.

The experiment was carried out at the City College of New York in a sound-attenuated booth. Subject wore headphones and watched the videos on a 19" monitor. The EKG was recorded with a BioSemi Active Two system at a sampling frequency of 2048Hz. 2 EKG electrodes were placed below the left collar bone and one on the left lumbar region. For segmentation of the EKG signal onset and offset triggers were used, in addition a flash and beep sound was embedded right before and after each video which were recorded using a StimTracker (Cedrus) to ensure precise alignment across all subjects. Of the thirty-one participants 4 were removed from analysis due to bad signal quality resulting in usable data for N=27 participants. The experimental protocol was approved by the Institutional Review Boards of the City University of New York. Documented informed consent was obtained from all subjects for laboratory experiments.

Experiment 3: auditory narratives with healthy participants and respiration

The EKG of 25 french native healthy participants (15 females; age range 22-28, median age 25 years old) listened to four stories while their EKG and respiration was recorded using a Polygraph Input Box (PIB of EGI-Geodesic's physiological measurement system). This includes a chest belt to measure respiratory movement (Respiration Belt MR - Brain Products) and 2 EKG electrodes placed on the left subclavicular area and below the left axillary area. Of the twenty-five participants four were removed because of missing respiratory and/or cardiac data. The four audio stimuli come from https://www.franceinter.fr/emissions/une-histoire-et-oli : (1) Nadine et Robert les poissons rouges- Delphine de Vigan (8 min) (2) les villages du versant – Alice Zeniter (8 min) (3) Opaque et Opaline - Alex Vizorek (11 min) (4) le renard et le poulailler – Guillaume Meurice (10 min).

To test whether the ISC-HR is modulated by attention we divided the subjects into 2 groups: Group 1 (9 subjects) was recorded with stories (1) and (2) in a distracted condition, and (3) and (4) in an attentional condition. In group 2 (12 subjects) the stories were counterbalanced, stories (1) and (2) in the attentional condition, and (3) and (4) in the distracted condition. In the attentional condition (A), the subject's task was to pay attention to the story while disregarding tones (320/360/400/440/482 Hz, 400ms long) that were played in random intervals (between 800ms and 1100ms) in the background of the story. After each story the subjects received a control debriefing questionnaire including 5 questions testing the memory performance of the story content. In the distracted condition (D), the subject's task was to count backwards starting from 100 indexing the occurrence of 'counting' tones (same tones as in the attentional condition) in-between 2 'reset' tones (Audacity- the type of tones is a linear decay between 1300 and 400 Hz during 400ms). The reset tones were added uniformly and randomly every 14 seconds on average. After each 'reset' tone, subjects had to reset the counting back to 100. At the end of the block the subjects had to report the smallest number obtained between 2 'reset' tones. Subjects were instructed not to pay attention to the story and also receive the same debriefing questionnaire. The present research was promoted by the Inserm (CPP C13-41) and approved by the Comité de Protection des Personnes Ile-de-France 6. All subjects provided written informed consent.

Experiment 4: Auditory narratives with disorder of consciousness patients and healthy controls

Nineteen patients (8 females, age range 18 to 77, median age 50 years old) with disorders of consciousness (mostly resulting from brain lesions) and 24 healthy control subjects (14 females; age range 23-27, median 25 years old) listened to an auditory narrative (La part des ancêtres - Leonora Miano - 10 minutes, from: https://www.franceinter.fr/emissions/une-histoire-et-oli) through headphones while their EKG was recorded with a Polygraph Input Box (PIB of EGI-Geodesic's physiological measurement system). The only instruction given to all subjects (healthy controls and patients) was to listen to the story. These patients were hospitalized in neurointensive care at Pitié Salpetrière (medical center with expertise in disorder of consciousness) to determine their state of consciousness, to adapt treatment, and to evaluate their neurological prognosis. During this evaluation, we performed several exams: clinical assessment, MRI, EEG, evoked response potential, and positron emission tomography. The state of consciousness is determined with some[61] behavioral assessments, using the Coma Recovery Scale-revised[43] - a score which allows differentiating between consciousness states: Coma (the patient does not open their eyes), Vegetative State (VS - Eye-opening, and alternance between wakefulness and sleep), Minimally Conscious State (MCS - the patient is able to follow their own face in the mirror or to follow a simple instruction) and Exit Minimally Conscious State (EMCS - patient can communicate with code). Among the 19 patients, we diagnosed 2 patients in coma, 8 VS patients, 8 MCS patients (7 MCS- and 1 MCS+) and 1 EMCS (see supplementary data for more details). The Ethical Committee of the Pitie-Salpetriere approved this research under the French label of 'routine care research'.

Computation of intersubject correlation of heart rate (ISC-HR)

Previous studies have relied on the quantification of synchrony of neuroimaging based time series (i.e. BOLD in fMRI [25] or signals from EEG electrodes [27]). We follow a similar logic for the electrocardiographic (EKG) signal. We focus on the modulation of heart rate, by doing so we can determine if subjects increase or decrease their heart rate simultaneously, independently of their absolute level of heart rate. Step 1: We measure the EKG signal and detrend it using a high-pass filter (0.5 Hz cutoff) and subsequently notch filtered at either 50Hz (Experiment 1, 3 and 4) or 60 Hz (Experiment 2). We compute the instantaneous HR by detecting RR intervals from the EKG (Figure 1A). Peaks of the R-wave were found using *findpeaks* (built-in matlab function). Step 2: The instantaneous HR signal is then interpolated to keep the same sampling frequency for all subjects (Figure 1B). Step 3: This interpolated instantaneous HR signal is used to compute an inter-subject correlation matrix by calculating the Pearson's correlation between each subjects' instantaneous HR signal (Figure 1C). Step 4: Finally, the intersubject subject correlation of heart rate (ISC-HR) for each subject is obtained by computing the mean of correlations of that given subject to the rest of the group (Figure 1D).

For Experiment 2 (Fig 3. and 4) in step 3 we computed the inter-subject correlation matrix between the instantaneous HR signals in the attentive and distracted conditions with the instantaneous HR in the attentive conditions rather than within condition. In Experiment 3 (Fig. 5) we again used the instantaneous HR signals obtained when the groups were attentively listening to the stories as reference when computing the inter-subject correlation matrix for step 3 (Fig. 6.). For Experiment 4 we used the healthy participants as reference in the computation of the inter-subject correlation matrix in step 3. All other steps were as explained above.

Statistical significance of ISC-HR

The instantaneous HR signals for a given epoch are first aligned across subjects. Then ISC-HR was calculated for all subjects in all epochs and the ISC across epochs. To test whether the ISC-HR value for each epoch was statistically significant (for Fig. 2A), circular shuffle statistic was used: Each subject's instantaneous HR is circularly shifted by a random amount within the 60 second segments and the ISC-HR is re-computed. This procedure is repeated 10.000 times and the ISC-HR of the epoch is compared to this distribution of ISC-HR values for the circular shifted instantaneous HR signals. The p-value is obtained by counting how many circular shifted ISC-HR values were below the actual ISC-HR value. For Fig. 2B we repeat the circular shift to compute ISC-HR values and then average across epochs; p-values are then computed on these averaged ISC-HR values. For Figure 2C, instead of circular shifts within 60 s story segments, we instead randomly swapped segments between participants.

Frequency analysis of heart rate fluctuations

To investigate which time scale the inter-subject correlation and HRV is modulated by attention we do a frequency analysis of the instantaneous HR signal (Figure 4). The instantaneous HR signal was band-pass filtered using 5th order butterworth filters with logarithmic spaced center frequencies with a bandwidth of 0.2 of the center frequency. The ISC was computed in each frequency band referenced to the attentive group (Fig. 4A). The HRV was computed as the standard deviation of the instantaneous HR normalized with the average HR (Fig. 4B).

Computation of Fractional Anisotropy index (FA index)

Diffusion Tensor Images (DTI) were acquired on a 3T Siemens Skyra scanner (64 diffusion gradient directions, b value = 1000 s/mm^2, TR/TE = 3000/80 ms, voxel size = 2x2x2 mm^3). DTI data were pre-processed using the FDT package from the Functional MRI of the Brain (FMRIB) software library (FSL) package 5.01[64]. This consisted of: 1) correcting for motion and distortions caused by eddy currents; 2) brain segmentation using the brain extraction tool algorithm; 3) computing the fractional anisotropy (FA) maps using the diffusion-tensor model; 4) registration of the FA and MD maps on the FA template in the standard Montreal Neurological Institute (MNI) space using linear as well as nonlinear spatial transformations. FA values were averaged within a deep white-matter mask defined in the MNI space as the outline of the ICBM-DTI-81 white-matter labels atlas[65]. For each subject, this FA value was normalised with the mean of FA values measured from 10 healthy volunteers acquired with the same imaging protocol, such that an average FA index of 1.0 can be considered normal.

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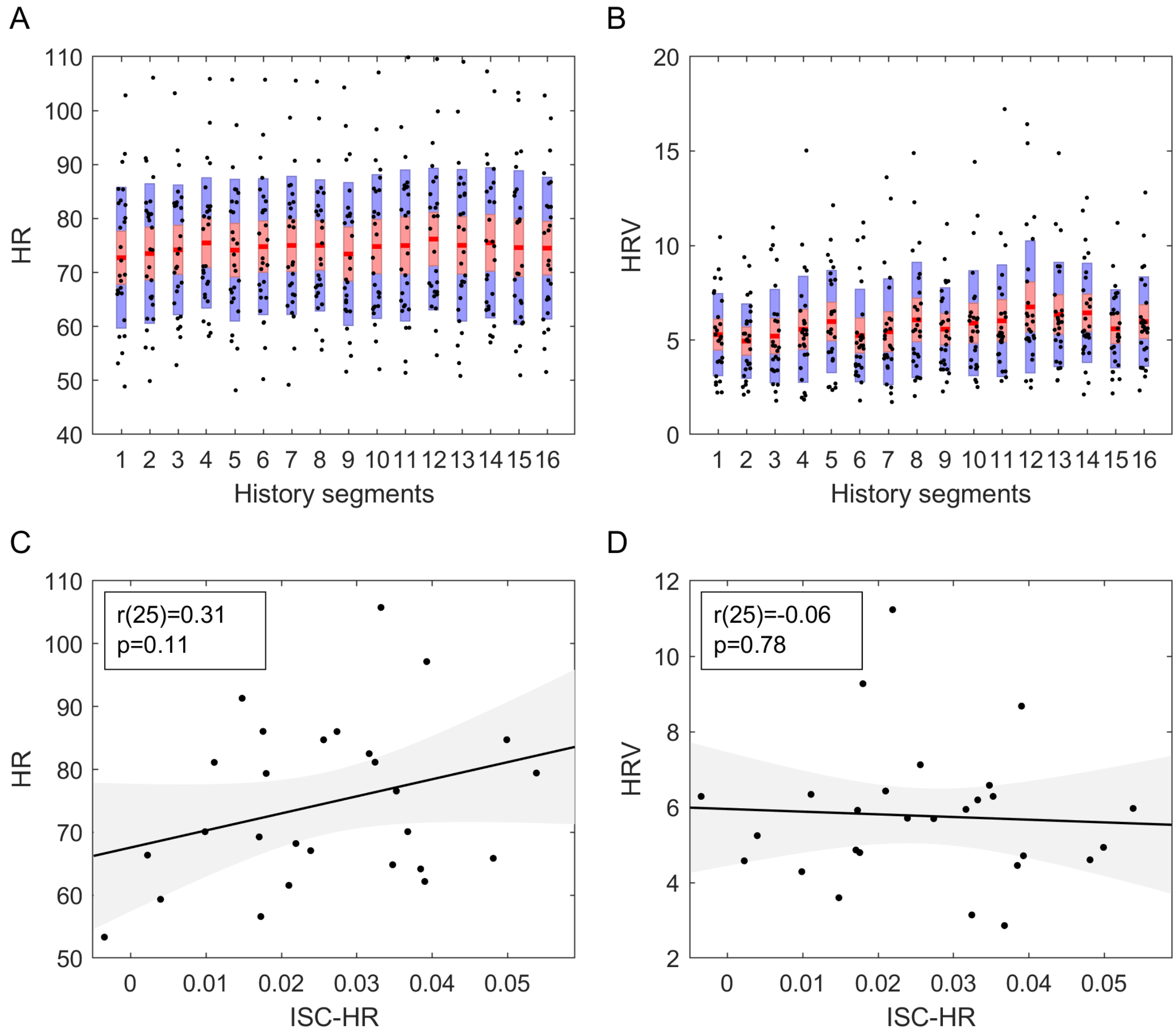
Supplementary materials

Analysis of mean HR and HRV for experiment 1

For experiment 1 we also checked whether mean HR or HR variability (HRV) differed between story segments or between subjects (Fig. S1A and S1B). ANOVA with segment as fixed effect and subject as random effects shows that mean and standard deviation of HR differed between segments (HR: F(15,390)=2.46, p=1.89e-03, HRV: F(15,390)=1.73, p=4.26e-02), and between subjects (HR: F(26,390)=316.92, p=2.93e-244, HRV: F(26,390)=13.52, p=4.92e-40). We did not see a relationship between HR-ISC and mean HR (Fig. S1C, r(25)=0.31, p=0.11,) or between HR-ISC and HRV (Fig. S1D, r(25)=-0.06, p=0.78).

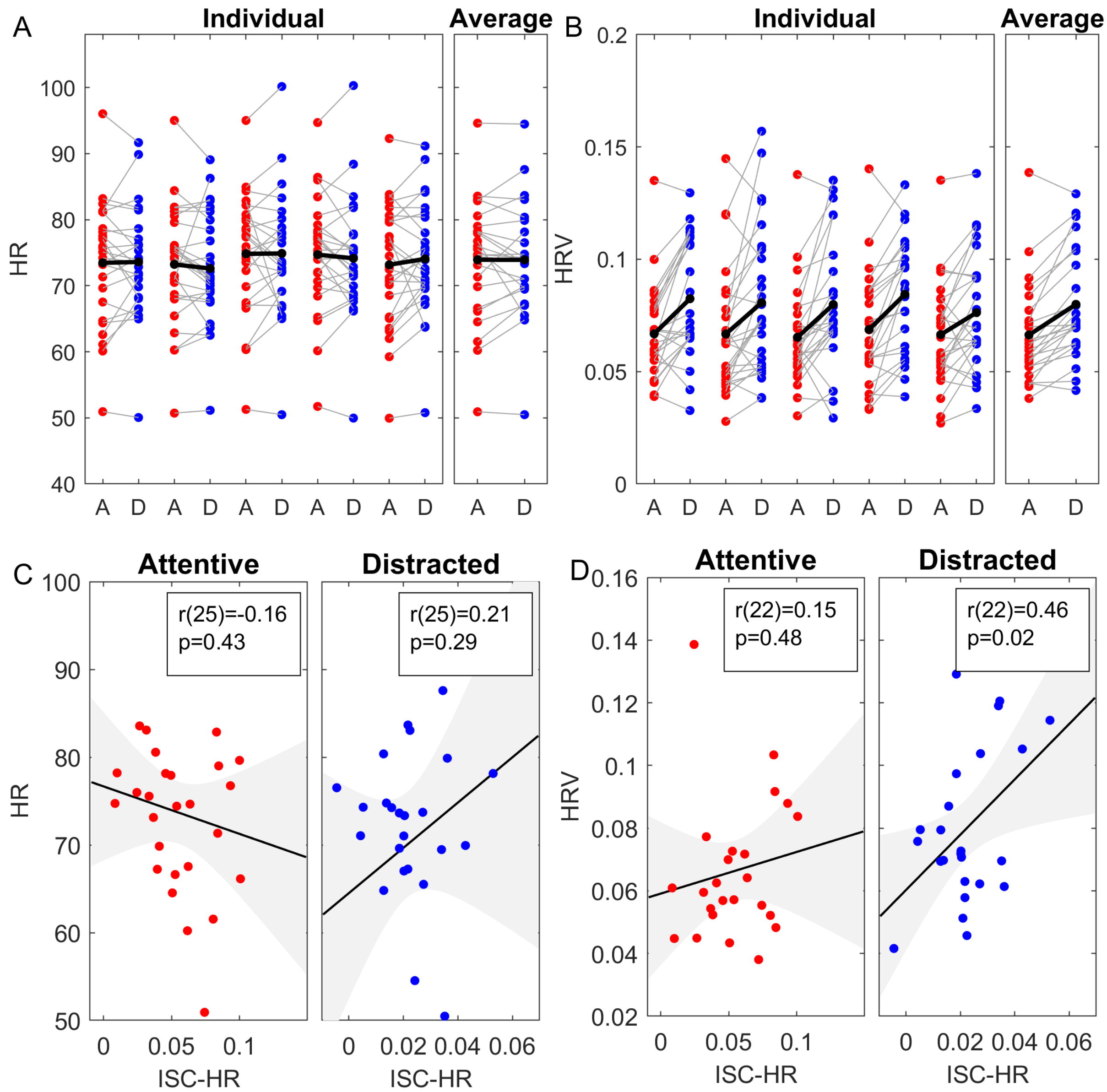


Supplementary Figure 1: A: The instantaneous heart rate shows no modulation across epochs (Anova F(15,390) = 1.04, p = 0.41), but differences across subjects (Anova F(26,390)=173.88, p=0). **B:** Heart rate variability measured as the standard deviation across the instantaneous heart rate for each segment.
C: ISC-HR for each subject averaged across segments versus corresponding mean HR (each subject is a dot). We found no linear relationship between these two variables.

D: ISC-HR for each subject averaged across segments versus corresponding HR variability (each subject is a dot). We found no linear relationship between these two variables.

Analysis of mean HR and HRV for experiment 2

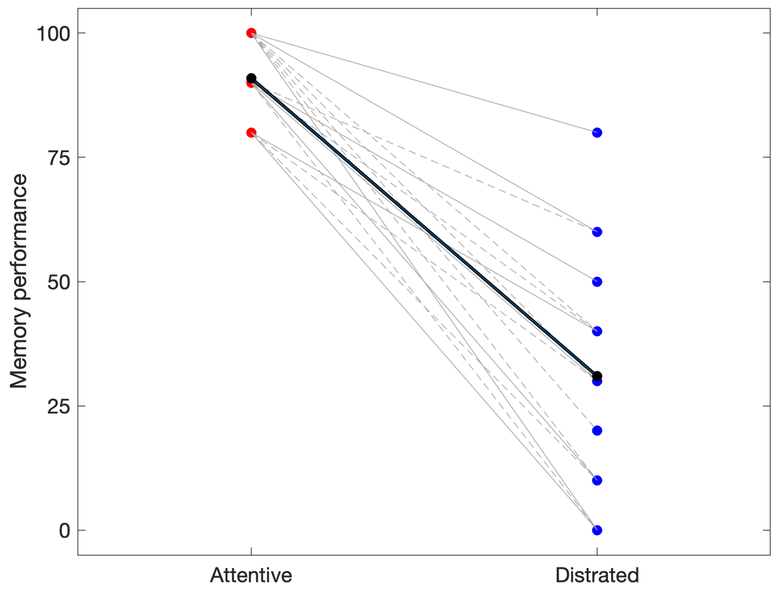
For experiment 2, in addition to the attentional effects reported in the main results section, we also checked whether mean HR or HR variability differed between each educational video and between subjects (Fig. S2A and S2B). ANOVA with video as fixed effect and subject as random effects shows that mean HR differed across videos (HR: $F(4,211)=3.05$, $p=1.81e-02$), but not standard deviation ($F(4,211)=0.77$, $p=5.44e-01$), and both differed significantly between subjects (HR: $F(23,211)=89.19$, $p=1.87e-95$, HRV: $F(23,211)=29.56$, $p=1.57e-53$). We did not see a relationship between ISC-HR and mean HR (Fig. S2C, Attentive: $r(25)=-0.16$, $p=0.43$, Distracted: $r(25)=0.21$, $p=0.29$) or between ISC-HR and HRV (Fig. S2D, Attentive: $r(22)=0.15$, $p=0.48$, Distracted: $r(22)=0.21$, $p=0.46$).



Supplementary figure 2: A: mean HR, **B:** HRV, **C**: correlation of ISC with HR. **D:** correlation of ISC with HRV

Behavioral results of experiment 3

For experiment 3, we checked the modulation of memory performance in the attentive and distracted condition like a proof that the task was correctly completed. After each story, subjects answered 5 short questions about the story content testing their memory performance (i.e name of protagonist?, place?...). Memory performance was significantly higher in the attentive condition than in the distracted condition (Figure S3, Wilcoxon signed-rank test: z = 4.03, p = 5.6789e-05). In none of the conditions we found a difference between group 1 and 2 in terms of memory performance. In both groups the performance was always similar, in the attentive condition (Median group 1 = 90; Median group 2 = 90; Mann-Whitney U test, U = 93, p = 0.67), in the distracted condition (Median group 1 = 40; Median group 2 = 30; Mann-Whitney U test, U = 106, p = 0.66), or in the contrast between the attentive and distracted conditions (Median group 1 = 40; Median group 2 = 65; Mann-Whitney U test, U = 86.5, p = 0.39)

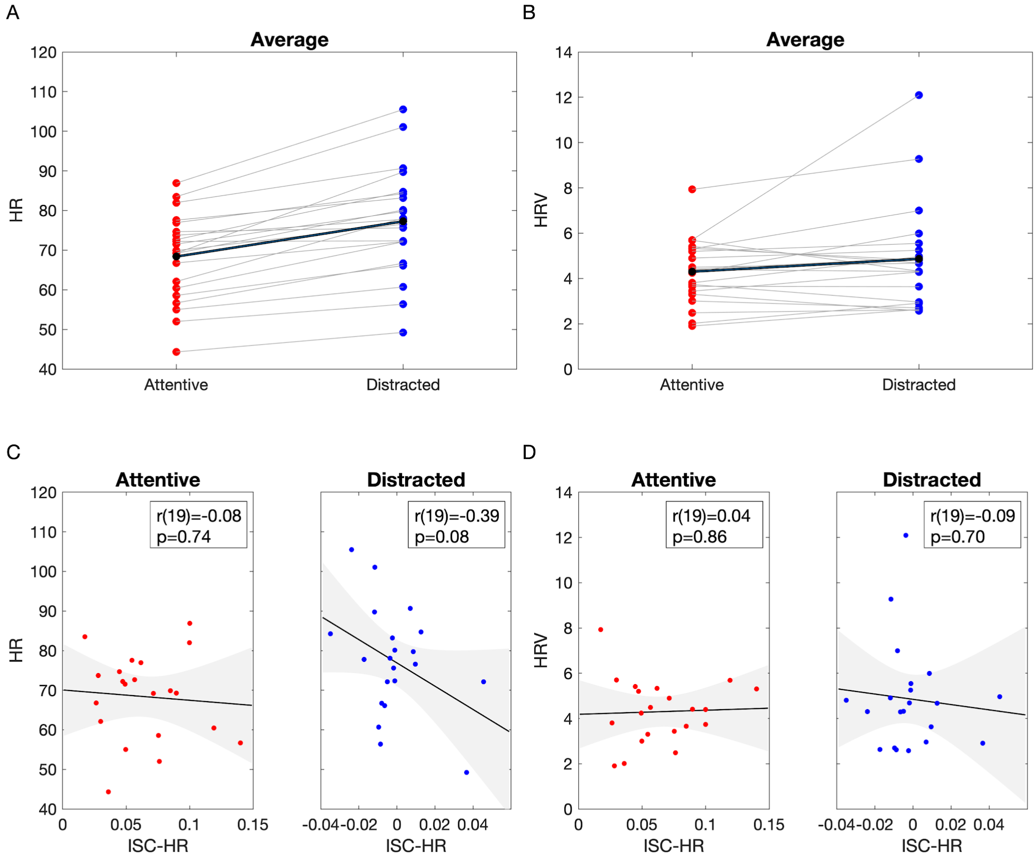


Supplementary figure 3: Behavioral responses attentive and distracted conditions (n=21). Solid lines correspond to subjects in group 1 and dashed lines to subjects in group 2. Each group listened to 2 two stories in the attentive condition and two in the distracted condition.
Subjects answered 5 short questions about each story content. The memory performance (rate of good response) was systematically higher in the attentive condition compared to the distracted conditions. We observed no differences in memory performance between groups.

Analysis of mean HR and HRV for experiment 3

For experiment 3 we also checked whether mean HR or HR variability differed between each condition and between subjects. We found that the mean HR was significantly higher in the distracted condition compared to the attentive condition (Fig S4A, paired t-test, t(21) = 7.32, p = 4.5e-7). We found no differences in HRV between the attentive and distracted conditions (Fig S4B, paired t-test, t(21) = 1.64, p = 0.12).

We also did not see a relationship between ISC-HR and mean HR (Fig. S4C, Attentive: r(19)=-0.08, p=0.74, Distracted: r(19)=-0.39, p=0.08) or between ISC-HR and HRV (Fig. S3D, Attentive: r(19)=0.04, p=0.86, Distracted: r(19)=-0.09, p=0.70).

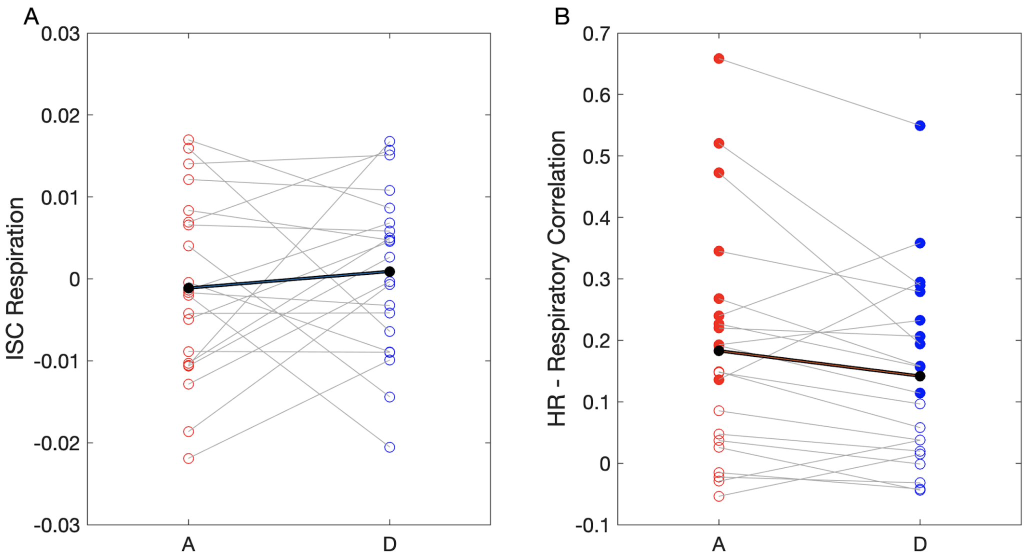


Supplementary figure 4: A: mean HR, **B:** HRV, **C**: correlation of ISC with HR in the attentive condition (left), and distracted condition (right), **D:** correlation of ISC with HRV in the attentive condition (left), and distracted condition (right)

Respiration and HR and for experiment 3

Breathing is known to be a determinant of the heart rate. We checked whether the synchronization of respiration between subjects was modulated by the attentional/distracted conditions. We showed no difference of ISC respiration between both conditions (Fig S5A, paired t-test, t(21)=0.5, p=0.6), in addition none of the subjects had significant individual ISC value in either condition.

However, we tested if breathing cycle correlates with HR for each subject (Individual Pearson correlation between displacement of the chest sensor and instantaneous HR), and if this correlation is modulated by the attentional condition (Fig. S5B). The phase of breathing cycle and HR were significantly correlated (one-sample t-test averaging the coupling of each individual in the attentive and distracted conditions, t(20)=4.49, p=2e-4). However, the difference in coupling between the attentive and distracted conditions did not reach significance (paired t-test between attentive and distracted conditions: t(20)=1.86, p=0.08). Permutation tests, shuffling the temporal relationship between HR and respiration time-series of each individual indicated that 11 out of the 21 subjects (both in the attentive and distracted conditions) showed individually significant HR-Respiratory correlation (FDR corrected, p <0.01).

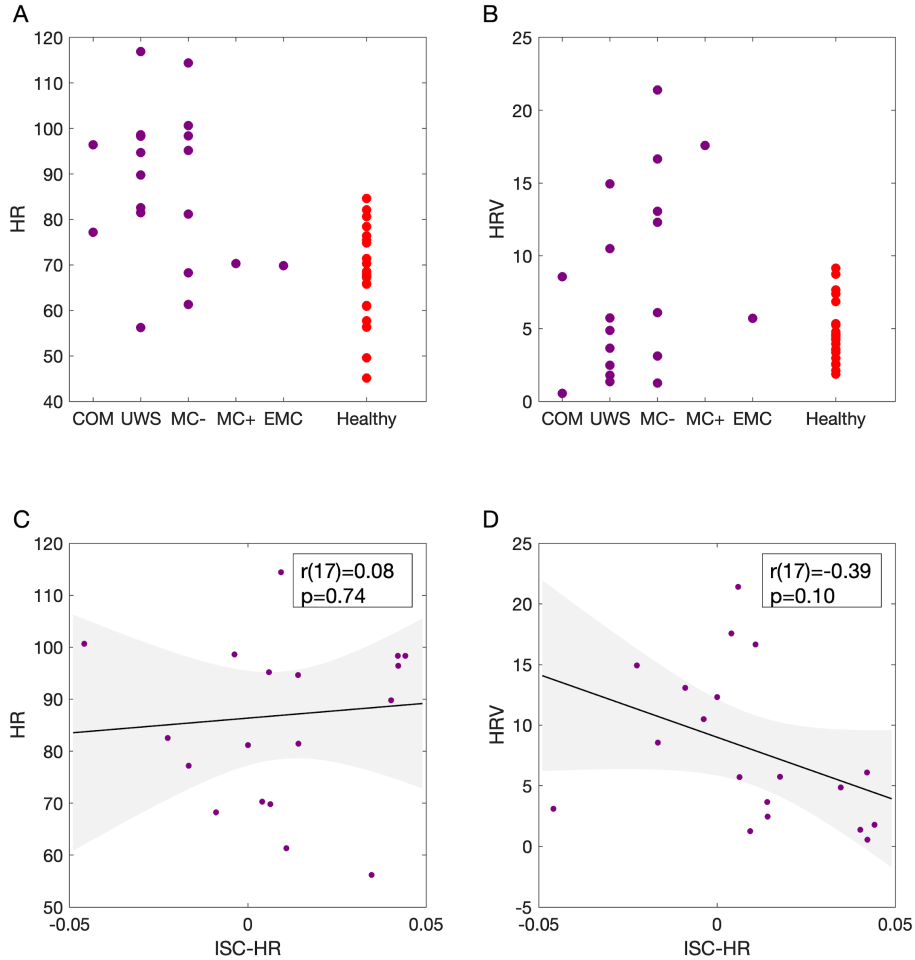


Supplementary figure 5: (A) ISC of respiration shows no significant changes of ISC between attentive and distractive conditions. (B) HR-Respiratory cycle coupling was significant for each subject represented by the filled circles (p<0.005), attention and distractive conditions did not modulate the HR-Respiratory cycle coupling (paired t-test: t(20)=1.86, p=0.08).
Filled and empty circles indicate subject-level significant and non-significant respectively (FDR p<0.01 permutation statistics, shuffling the temporal relationship between HR and respiration time-series)

Analysis of mean HR and HRV for experiment 4

For experiment 4 we also checked whether mean HR or HR variability differed between the different states of consciousness (Fig. S6). The mean HR of DoC patients was significantly higher than healthy participants (Fig S6A, t(41) = 4.7, p = 2.9e-05). To test if HR changed with the state-of-consciousness among the DoC patients we performed a Spearman correlation between state-of-consciousness (Coma = 1, VS = 2, MCS- = 2, MCS+ = 3, EMCS = 4) and HR and found no significant correlation ($R(17) = -0.18$, $p = 0.45$). Similar for the HR variability, HRV was significantly higher in DoC patients compared to healthy controls (Fig S6B, $t(41) = 2.34$, $p = 0.02$). We found no significant relationship between the patients' state-of-consciousness and HRV (Spearman correlation, $R(17) = 0.41$, $p = 0.08$).

We also controlled the relationships between HR and ISC, and HRV and ISC for patients. In none of the cases the relationship was significant (Fig. S6C, HR versus ISC, $r(17)=0.08$, $p=0.74$; Fig. S6D, $r(17)=-0.4$, $p=0.09$).



Supplementary figure 6: A: mean HR for DoC patients and healthy participants (Note that DoC patients are ordered in individual columns corresponding to their clinical state-of-consciousness (1=Coma, 2=VS/UWS, 3=MCS-, 4=MCS+, and 5=EMCS) **B:** HRV, idem to A **C**: correlation of ISC with HR for DoC patients. **D:** correlation of ISC with HRV for DOC patients.

Subject	Sex	Age (years)	Etiology	Delay (days)	State	CRS-R	FA	Outcome
1	M	71	Acute Polyradiculoneuritis	12	Coma	0	no exam	VS/Death*
2	F	77	Meningitis	86	Coma	2	no exam	VS
3	M	18	TBI+Anoxia	170	VS	5	0.756	VS
4	M	29	TBI+Anoxia	510	VS	5	artefacted	VS
5	M	29	Anoxia	556	VS	5	0.492	VS
6	M	55	TBI	27	VS	6	artefacted	MCS+
7	F	53	Anoxia	328	VS	5	0.824	VS
8	F	24	TBI	68	VS	5	0.644	MCS-
9	F	63	Anoxia	41	VS	5	0.642	VS
10	M	18	Anoxia	59	VS	4	0.792	VS/Death*
11	F	50	Anoxia	5852	MCS-	10	0.698	MCS-
12	M	26	Status Epilepticus	209	MCS-	9	0.561	MCS+
13	M	50	Anoxia	60	MCS-	7	0.85	EMCS
14	F	61	Status Epilepticus	90	MCS-	10	noDTI	MCS-
15	M	58	Anoxia	302	MCS-	14	0.548	MCS-
16	M	56	TBI	478	MCS-	11	0.824	MCS-*
17	F	36	Left hematoma	121	MCS-	12	noDTI	EMCS
18	F	49	TBI	980	MCS+	13	noDTI	MCS+
19	M	28	Status Epilepticus	313	EMCS	14	no exam	EMCS

Description of patient cohort: summary table including patients with sex, age, etiology of brain lesion, delay between brain lesion and the evaluation, state of consciousness, CRS-R (Coma Recovery Scale-Revised), Fractional anisotropy (FA) from MRI and outcome. *Outcome collected before 6 months.