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Rhesus monkeys have an interoceptive sense of their beating hearts

Joey A. Charbonneau[a,b], Lara Maister[c], Manos Tsakiris[d,e,f], and Eliza Bliss-Moreau[b,g,1]

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The sensation of internal bodily signals, such as when your stomach is contracting or your heart is beating, plays a critical role in broad biological and psychological functions ranging from homeostasis to emotional experience and self-awareness. The evolutionary origins of this capacity and, thus, the extent to which it is present in nonhuman animals remain unclear. Here, we show that rhesus monkeys (*Macaca mulatta*) spend significantly more time viewing stimuli presented asynchronously, as compared to synchronously, with their heartbeats. This is consistent with evidence previously shown in human infants using a nearly identical experimental paradigm, suggesting that rhesus monkeys have a human-like capacity to integrate interoceptive signals from the heart with exteroceptive audiovisual information. As no prior work has demonstrated behavioral evidence of innate cardiac interoceptive ability in nonhuman animals, these results have important implications for our understanding of the evolution of this ability and for establishing rhesus monkeys as an animal model for human interoceptive function and dysfunction. We anticipate that this work may also provide an important model for future psychiatric research, as disordered interoceptive processing is implicated in a wide variety of psychiatric conditions.

interoception | awareness | viscerception | heartbeat | rhesus monkey

Significance

The capacity to sense interoceptive signals is thought to be fundamental to broad functions including, but not limited to, homeostasis and the experience of the self. While neuroanatomical evidence suggests that nonhuman animals—namely, nonhuman primates—may possess features necessary for interoceptive processing in a way that is similar to humans, behavioral evidence of this capacity is slim. We presented macaques with audiovisual stimuli that were either synchronous or asynchronous with their heartbeat and demonstrated that they view asynchronous stimuli, whether faster or slower, for a significantly longer period than they do synchronous stimuli.

Signals from the body form a rich landscape that grounds the complex mental lives of humans and nonhuman animals. The capacity to sense* these signals and the physiological state of the body more generally, referred to as "interoception" (1, 2), are understood to underlie human processes as diverse as, but not limited to, energy regulation (3), subjective emotional experience (4, 5), decision-making (6, 7), and self-awareness (8). In humans, interoceptive capacities have long been characterized with measures that index people's ability to sense when their own hearts are beating, typically by counting the number of heartbeats that occur over a span of time (9) or discriminating between auditory, visual, or audiovisual stimuli presented synchronously or asynchronously with heartbeats (10, 11). Performance on these tasks is then quantified in terms of accuracy or sensitivity and, together with interoceptive sensibility (i.e., metacognitive self-assessment of interoceptive ability) and interoceptive awareness (i.e., coherence of accuracy and self-assessment), constitute the core of the multidimensional construct of interoception (12). Individual differences in cardiac interoception have trait-like stability which has been correlated with interoceptive capacity in other physiological domains, like gastric interoception (13, 14), as well as with a variety of psychological functions [e.g., emotional experience (4), metacognition (15), memory (16)] and dysfunctions [e.g., psychiatric disorders, broadly (17), anxiety (18) depression (19)].

Alterations and deficits in interoceptive processing are increasingly recognized to impact both physical and mental health (20–22). Animal models—and nonhuman primate models, specifically—of interoceptive function and dysfunction are therefore likely to be important for advancing our understanding of the etiology of such disorders and supporting the development of treatments and interventions for them, just as nonhuman primate models have proven critical for the advancement of other subfields of biomedical research (23–25). Evaluating interoceptive capacity in nonhuman primates also allows testing hypotheses about its evolution. Decades of neuroanatomical research demonstrates that, unlike rodents, primates have a phylogenetically new anatomical system for processing interoceptive information, which includes the lamina I spinothalamic tract, ventromedial nucleus of the thalamus, and insula, allowing for the direct projection of signals representing the physiological condition of the body onto

*Significant lack of theoretical and empirical clarity exists around what is meant by interoception relative to whether it is a sensory process, a perceptual process, or both. Here, we define sensing as basic information processing absent interpretation or awareness like other sensory information such as, for example, vision, smell, and touch. We define perception as the interpretation (inferences made about) and/or awareness of sensory information. A thorough discussion of this point is well beyond the scope of this manuscript and so we use sense here throughout for simplicity. See 1, 8, 12, 26, 38, 57 for related discussions.

Author affiliations: [a]Neuroscience Graduate Program, University of California, Davis, CA 95616; [b]Neuroscience and Behavior Unit, California National Primate Research Center, Davis, CA 95616; [c]School of Human and Behavioural Sciences, College of Human Sciences, Prifysgol Bangor University, Gwynedd, Wales, LL57 2AS, United Kingdom; [d]Department of Psychology, Royal Holloway University of London, Egham, Surrey, TW20 0EX, United Kingdom; [e]Centre for the Politics of Feelings, School of Advanced Study, University of London, London, WC1E 7HU, United Kingdom; [f]Department of Behavioural and Cognitive Sciences, Faculty of Humanities, Education and Social Sciences, University of Luxembourg, Luxembourg, L-4365, Luxembourg; and [g]Department of Psychology, University of California, Davis, CA 95616

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[1]To whom correspondence may be addressed. Email: eblissmoreau@ucdavis.edu.

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thalamocortical circuits (9, 26). The rodent interoceptive pathway also includes direct projections from the parabrachial nucleus to the insula and ventromedial prefrontal cortex (27), a pathway that is notably absent in nonhuman primates (28), and a difference which likely means that interoceptive processing in primates (including humans and monkeys) is radically different from that in rodents (29). Additionally, the nonhuman primate insula, like the human insula, has baroreceptor-sensitive neurons, providing evidence for the direct representation of cardiac cycle-related information in cortex (30, 31), is far more complex than rodent insula (32) and has different brain-wide connections than the rodent insula (33). The limited behavioral evidence that exists from monkeys suggests that, at the very least, monkeys can learn to alter their cardiac function. For example, rhesus monkeys (*Macaca mulatta*) have been classically conditioned to alter both their heart rate and blood pressure in response to the presentation of a light after pairing it with an electric shock (34, 35) as well as to raise and lower their heart rate to avoid an electric shock (36).

Despite this evidence from the early learning studies related to cardiac control (34–36) and decades of neuroanatomical studies (8, 26, 30–32), summarized above, it remains unclear whether nonhuman primates share an innate capacity to integrate interoceptive and exteroceptive sensory information in order to influence behavioral measures of psychological functions, as has long been established in humans (9, 10). To test this hypothesis, we capitalized upon the recent development of an implicit behavioral measure for assessing cardiac interoceptive capacity in human infants [*Infant Heartbeat Task* or *iBEAT* (37)] to assess the impact of spontaneous sensation and integration of cardiac interoceptive signals on visual attention in the rhesus monkey.

Results

Like Human Infants, Monkeys Look Longer at Stimuli Presented Asynchronously as Compared with Synchronously with Their Heartbeats. Four monkeys (monkeys A, D, M, and T) performed a sequential looking time paradigm to assess whether they were able to differentiate stimuli that were synchronous or asynchronous with their cardiac rhythms (Fig. 1*A*). On each trial, an eye tracker displayed stimuli which bounced and generated a sound either synchronously or asynchronously (faster and slower) with the monkey's heartbeats. As hypothesized, trial type (i.e., whether the stimulus was synchronous, asynchronous but faster than their heart rates [async-fast], or asynchronous but slower than their heart rates [async-slow]) was a significant predictor of looking time (χ^2 (2) = 13.39, $P = 0.001$), providing evidence that they are able to sense their heartbeats. Evaluation of the estimated marginal means revealed that monkeys looked longer at asynchronous stimuli regardless of whether they were faster (mean = 1.84 s; 95% CI: [1., 2.56]) or slower (mean = 1.69 s; 95% CI: [1.15, 2.48]), as compared with synchronous stimuli (mean = 1.01 s; 95% CI: [0.82, 1.25]). There was no significant difference in looking times between async-fast and async-slow trials ($P = 0.85$) suggesting that monkeys discriminated between trial types based on synchronicity with their heartbeats rather than based on stimulus presentation speed (i.e., it was not the case that they were simply more attentive when stimuli were relatively fast or relatively slow). Looking times across trial types are shown in Fig. 1*B* (*SI Appendix*, Fig. S2).

Given that looking times varied across the trial types, we were interested to know how many stimuli bounces were presented to monkeys during the different trial types in order to ensure that it was the case that even on trials where the monkeys looked at the stimuli for short durations of time, they experienced multiple presentations of the stimuli (i.e., multiple cardiac cycles). During async-fast and async-slow trials, monkeys looked at the stimuli for long enough to experience an average of 5.11 and 3.79 bounces/tones, respectively. During sync trials they experienced an average of 2.51 bounces/tones. These values were variable across monkeys and do not reflect time looking at the screen covertly (during which they could have extracted information about the speed of the stimulus presentation), but they do suggest that they saw multiple presentations reflecting multiple heart cycles within their focal attention.

All four monkeys looked for longer, on average, at asynchronous compared with synchronous stimuli (Fig. 2*A*). Consistent with our hypothesis, there was variation in the difference in looking times across monkeys (*SI Appendix*, Fig. S2). To quantify these differences, we computed a cardiac discrimination score for each monkey as was done in ref. 37. The cardiac discrimination score is the difference between async and sync looking times divided by the total looking time (i.e., [(mean looking time at async) − (mean looking time at sync)]/(mean async + mean sync)) and represents differential looking to async stimuli relative to total looking time, thus adjusting for total looking time variation across animals. The mean cardiac discrimination score in our sample was 0.26 (SD = 0.12) (compared with the mean discrimination score in ref. 37 which was 0.20). The two female monkeys we tested had lower discrimination scores (monkey A: 0.18; monkey M: 0.13) than the two male monkeys (monkey D: 0.39; monkey T: 0.33). However, we found that the main effect of sex on looking time was not significant (χ^2 (1) = 0.99, $P = 0.32$) and the interaction between sex and trial type was also not significant (χ^2 (2) = 0.39, $P = 0.82$).

Differences in General Interest or Attention Do Not Explain Differences in Cardiac Discrimination. Relatively lower cardiac discrimination scores did not appear to be associated with a general lack of attention to the stimuli. We computed the mean looking times for each monkey, collapsing across all three trial types. Three of the monkeys in our sample looked for nearly identical lengths of time on average (monkey A: 1.57 s; monkey D: 1.55 s; monkey M: 1.55 s). Monkey T looked, on average, for a shorter duration than the other monkeys (1.15 s), although he had a relatively high cardiac discrimination score.

We also indexed the monkeys' attention during the testing procedure to assess whether their general attention to the task (that is, attending to the screen but not necessarily attending to the experimental stimuli) appeared to drive interindividual differences in cardiac discrimination because our attentional measure discussed above captured overt visual attention to the experimental stimuli, potentially missing covert visual attention and/or auditory attention to the stimuli. There was no clear relationship between the duration of fixation on the entire eye tracker screen and cardiac discrimination scores in our sample. Monkey A spent an average of 2.95 s fixating within the bounds of the screen, monkey D spent 2.79 s, monkey M spent 2.43 s, and monkey T spent 2.10 s (*SI Appendix*, Fig. S3) per trial. While our relatively small sample prevents us from carrying out formal statistical analyses on these data, the rank orders suggest that visual attention to the screen—as gauged by mean fixation duration—is unlikely to be driving enhanced discrimination.

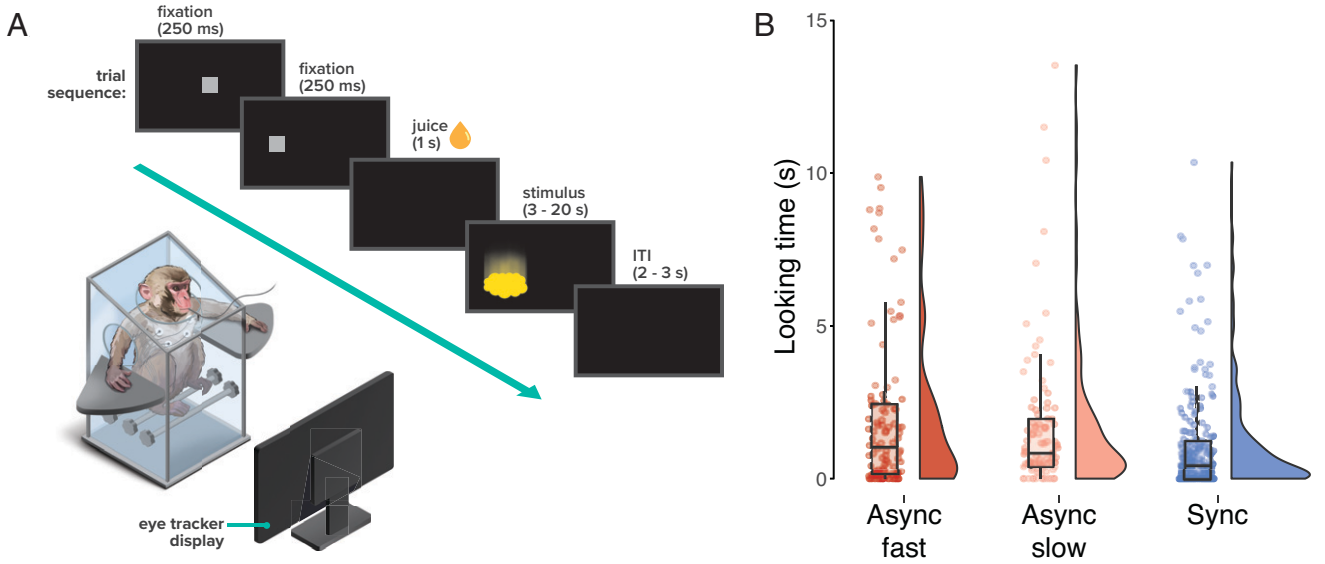

Fig. 1. Looking times in the mBEAT task. (*A*) Schematic of the modified iBEAT paradigm, which we refer to as monkeyBEAT (mBEAT). Monkeys were restrained in a nonhuman primate box chair in front of an infrared eye tracker while viewing alternating trials either synchronous or asynchronous with their heartbeat (as detected by a four-lead ECG on their chest). Stimuli were presented either on the left or the right side of the screen following a dynamic intertrial interval consisting of a center fixation, side fixation, and juice reward. (*B*) Raincloud plots (74) including individual data points, boxplots, and density functions for each of the three types of trials (asynchronous fast, asynchronous slow, and synchronous). Combined data from all four monkeys are shown (100 trials/monkey, 400 trials total) for visualization of the group-level effect of significantly longer looking times for asynchronous versus synchronous stimuli. Image credit: Matthew Verdolivo/UC Davis IET Academic Technology Services.

Trial-by-Trial Novelty and Stimulus Speed Do Not Explain Looking Time Differences. In order to rule out the possibility that the observed effects were driven by trials where the monkeys' hearts were beating particularly fast or slow compared with their normal cardiac rhythm, we analyzed the effects of novelty of the stimulus presentation speed and variation in the interbeat-interval (IBI; i.e., the time between R-spikes on the electrocardiogram [ECG] which here is equivalent to the speed of the stimulus presentation) on looking time. Trial-by-trial novelty scores were calculated as the deviance of the IBI on a given trial from the cumulative average of all trials a monkey had previously experienced, capturing trial-by trial variation in an animals' heart rate but also novelty variation created by the asynchronicity procedure. There was no main effect of trial novelty on looking time (χ^2 (1) = 0.002, P = 0.96), and the interaction between novelty and trial type was not significant (χ^2 (2) = 3.26, P = 0.20). The relationship between novelty scores and looking times is shown in Fig. 2*B* (*SI Appendix*, Fig. S4). Similarly, there was no main effect of IBI on looking time (χ^2 (1) = 0.76, P = 0.38), and the interaction between IBI and trial type was also not significant (χ^2 (2) = 1.19, P = 0.55). That is, novelty or surprise associated with the speed of stimulus presentation was not driving our results. The relationship between IBI and looking times is shown in Fig. 2*C* (*SI Appendix*, Fig. S5).

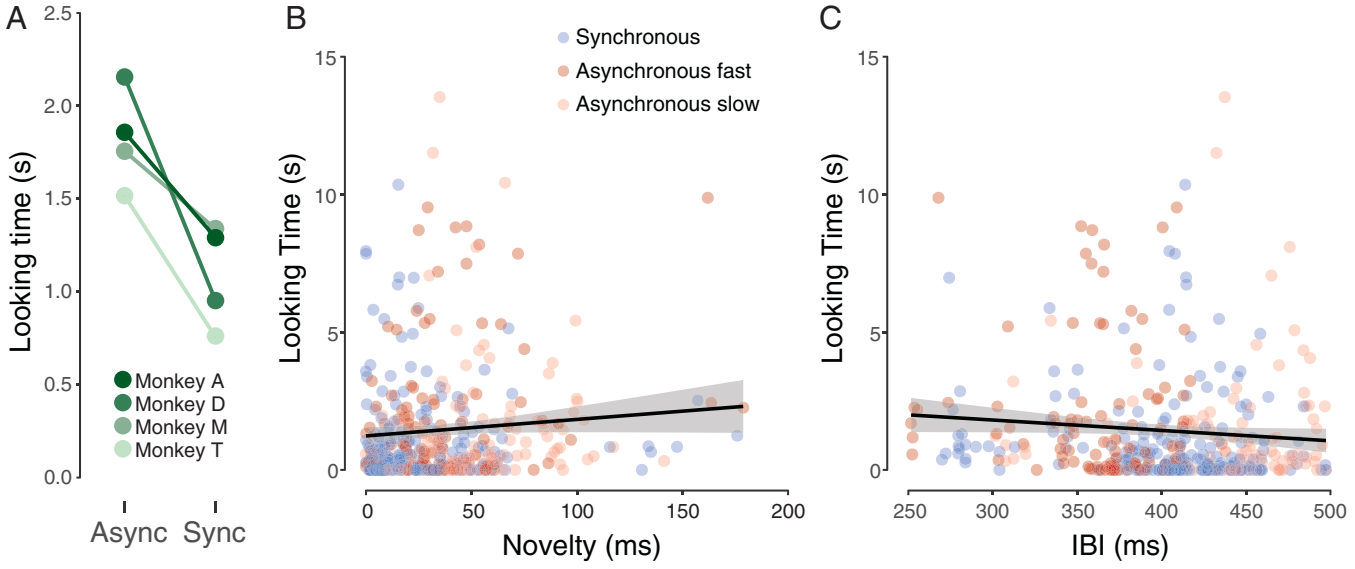

Fig. 2. Looking time differences cannot be explained by other means. (*A*) Paired individual mean looking times for each monkey across synchronous and asynchronous (fast and slow combined) trials, demonstrating greater mean looking times at asynchronous stimuli across all subjects. (*B*) Scatter plot showing the lack of relationship between trial novelty score (deviance of each stimulus presentation speed during each trial from the cumulative average experienced up to that trial) and looking time. (*C*) Scatter plot showing the lack of relationship between IBI (interbeat interval; i.e., stimulus presentation speed) and looking time.

Table 1. Summary of IBI features by monkey

			IBI (ms)				
Monkey	Sex	Cardiac discrim	Mean	SD	Minimum	Maximum	Range
A	F	0.18	412.01	41.21	246.13	509.54	263.41
D	M	0.39	425.34	62.06	251.61	532.45	280.84
M	F	0.13	344.97	46.37	246.76	438.71	191.95
T	M	0.33	428.37	33.20	360.19	505.53	145.34

Sex (F = female, M = male), cardiac discrimination (Cardiac Discrim) scores, and summary of IBI by monkey. IBI values are in milliseconds and reflect the time elapsed between R-spikes (synchronous trials) or between stimuli bounces (asynchronous trials). Mean IBI reflects each individual's resting heartrate, and the SD provides an index for the variability of their heart rate.

Because the stimulus presentation was based on the monkeys' heart rates, monkeys with more variable heart rates experienced a wider range of stimulus speeds and, likewise, monkeys with higher resting heart rates generally experienced faster stimuli (*SI Appendix*, Fig. S5). There was considerable variation in both heart rate variability and heart rate across the four monkeys we tested (*SI Appendix*, Fig. S6). A summary of heart rate data (presented as interbeat intervals, the timing between R-spikes on the ECG) is provided in Table 1 with the cardiac discrimination scores. The small sample size precluded the ability to carry out formal statistical analyses investigating the relationship between cardiac discrimination and aspects of the stimulus presentation speeds. However, inspection of the rank orders for heart rate variability and cardiac discrimination did not suggest any clear pattern. Monkey D, who had the highest discrimination score, had the highest variability, but monkey T, who had the second highest discrimination score, had the lowest heart rate variability. A potential pattern emerged when assessing the relationship between resting heart rate (mean IBI) and cardiac discrimination. Monkey M had the lowest cardiac discrimination score and lowest IBI, and monkey A had the second lowest values for both measures. The ranks for monkeys T and D were reversed across these two measures, but both of these monkeys had similar resting heart rates.

Finally, in order to ensure that changes in the monkeys' heart rates over the course of the task (both within and across test sessions) were not driving the observed effects, we evaluated the relationship between IBI, trial number, and test day. IBI was only recorded during synchronous trials (asynchronous presentation speed was based on the previous synchronous trial; *Materials and Methods*). Neither test day (χ^2 (3) = 7.26, P = 0.06) nor trial number (χ^2 (1) = 0.217, P = 0.64) were significant predictors of IBI. As such, it is unlikely that differences in looking times across trial types were driven by task-evoked changes in the monkeys' heart rates.

Discussion

Results of our study demonstrate that monkeys sense their heartbeats and direct more attention toward stimuli that are inconsistent with their beating hearts. All four of the monkeys we tested here looked for longer at stimuli that bounced and generated a sound asynchronously, as compared with synchronously, with their heartbeats, regardless of whether those asynchronous stimuli were faster or slower than their resting heartbeat rhythm (Fig. 1*A* and *SI Appendix*, Figs. S2 and S3). At the group level, this visual attentional bias for asynchronous stimuli was significant, and looking times across asynchronous stimuli did not differ significantly. These findings mirror the results obtained by Maister et al. (37), who used an essentially identical behavioral paradigm to evaluate interoceptive capacity in young human children. The mean cardiac discrimination score in our sample of 4 monkeys was 0.26, which was very similar to the mean discrimination score of the 29 infants tested by Maister et al. (0.20). Additional analyses that we carried out suggest that it is unlikely that the differences in looking times across stimuli observed in our sample can be explained by the novelty of the asynchronous stimuli or variation in resting heart rate. Our findings therefore provide evidence that, like humans, rhesus monkeys have the capacity to sense cardiac interoceptive signals and integrate these signals with exteroceptive sensory information (the bouncing stimuli and sounds) to drive differences in visual attention. That is, rhesus monkeys—at least the four animals in our sample—can detect their heartbeats.

While the human literature on heartbeat detection is rife with discussions of awareness of cardiac signals (12, 38, 39) and the relationship between heartbeat detection and other features of consciousness (40–42), the task we used here and the fact that our study animals are nonverbal precludes drawing conclusions about how our findings relate to awareness or consciousness per se. Thus, we operationalize what we are measuring in this task as "cardiac interoceptive sensing" to refer to the representation of cardiac information in a way that allows this information to guide behaviors outside of the cardiac domain (e.g., visual attention, as we show here). Here, "sensing" is contrasted with lower order "reflexes," including the beating and regulation of the heart itself, which can occur independently of any higher order function or cerebral representation (i.e., maintenance of homeostasis through adjustments to heart rate and blood pressure via brainstem mechanisms). In this framework, our study points to rhesus monkeys as having the capacity for cardiac interoceptive sensing, above and beyond the capacity for cardiac interoceptive reflexes (a basic capacity we would expect any mammal and many other nonmammal animals to have). Critically, while we could not ask monkeys to verbally report on their own heartbeats, the task we used has established validity with human adult tasks that ask people to report on their heartbeats. Human infants who demonstrated greater interoceptive capacity (i.e., higher discrimination) in the task we used here also have greater heartbeat-evoked potential amplitudes—a cortical index of interoceptive processing—to emotion-related stimuli (37), as is the case for adults who have greater interoceptive accuracy as tested using explicit interoceptive measures (see ref. 43 for a review and meta-analysis). The extent to which these different levels of cardiac interoceptive processing rely on different (either complementary or independent) neurobiological substrates and the means by which sensing and reflexes relate to high-order perception of interoceptive signals are important topics of further investigation.

One of the important outcomes of our experiment is that our four subjects varied in the extent to which they looked for

longer at the asynchronous, compared with synchronous, stimuli (*SI Appendix*, Fig. S2), resulting in variation in the cardiac discrimination score. That is, the variation across monkeys is a feature and not a bug of our paradigm. Interoception studies in humans document significant variation across people in the ability to report on their physiological states. For example, heartbeat detection studies in adult humans have shown anywhere from 17% (44) to 47% (45) of people tested demonstrating "good" performance, with many people performing extremely poorly. In the study on which our experiment is based (37), 17/29 or 59% of infants looked for longer at asynchronous stimuli, compared with the synchronous stimuli, resulting in an average cardiac discrimination score of 0.20. All of our monkeys looked for longer at the asynchronous stimuli than synchronous stimuli, but ultimately, our monkeys' average cardiac discrimination score was comparable to that reported by Maister et al. (37) at 0.26. Given the individual differences in our small sample, we would predict that there should be variability in interoceptive capacity in a larger sample which is comparable to that observed in human samples (44–46). In a sufficiently large sample, we anticipate that there might even be individual monkeys who display no preference between asynchronous and synchronous stimuli or the opposite preference of what we show here, recapitulating the patterns seen in human infants (37).

Individual differences in cardiac interoception are particularly important because they have been linked to a number of different disease states and pathological outcomes as well as variation in healthy emotional experience. For example, differences have been related to neuropsychiatric disorders like depression and anxiety (17–19), panic disorder (47), and eating disorders (48, 49) and the extent to which different therapies are effective for treating such mental health challenges (50). In one study, the efficacy of exposure therapy in arachnophobes was shown to be related to both the timing of stimulus presentation (in this case, images of spiders) relative to the cardiac cycle and interoceptive accuracy, such that treatment outcomes are actually worse for people who have better interoceptive accuracy (51). Accumulating evidence also suggests that individual differences in interoception—including differences across dimensions, including both accuracy and sensibility—may be core features of autism spectrum disorders (52–54). Deficits in interoception are not limited to the domain of neuropsychiatric disorders and have also been linked to neurodegenerative diseases like Alzheimer's disease (55); there is evidence to suggest that differences in interoceptive capacities may have great value in differentiating between neurological diseases and identifying whether sources of disease are neurological or cardiac in nature (56). Finally, even in healthy people, variation in interoceptive sensitivity is related to variation in reports of emotional experience—namely, reliance on arousal-based information (4), suggesting that meaningful variation in interoceptive processing spans a continuum of both health and disease. Such variation in cardiac interoception appears to be related to neuroanatomical features of the central nervous system including both the structure (57) and function (58) of the insula. The extent to which nonhuman primates exhibit cardiac cycle timing-dependent effects on phenomena like memory (59), threat processing (60), and other sensory experiences (61) in a manner that is related to their cardiac discrimination scores should be the subject of future research in order to further establish the validity and translational potential of this model.

Several decades of research on the neurobiology of interoception support the idea that monkeys have the capacity for interoception which is likely subserved by the same key central nervous system hubs as human interoception is—namely, the insula. Macaques and humans share homologous interoceptive pathways from the periphery to cortex (1, 26), which are likely to subserve the shared ability to detect cardiac function and integrate this information in such a way that these signals can then be used to guide behavior. Features in these interoceptive pathways, including the direct projections from lamina I and the nucleus of the solitary tract to the thalamus, appear to be phylogenetically new and thus present in primates but absent, or present in only a very rudimentary form, in other species (26). Further support comes from recent evidence that the macaque brain contains specialized cell types once thought to be unique to humans and apes, namely, von Economo and fork neurons (62). These atypical projection neurons have been proposed as a potential neural correlate of consciousness for their long-range corticocortical connections that make information globally available to multiple brain systems (63) and are present in both the macaque and human insula—the primary interoceptive cortex (8).

The interoceptive projections and specialized cell types present in primates, as well as anatomical structures like the posterior portion of the ventromedial nucleus of the thalamus, are notably absent in organisms phylogenetically distant from primates, including rodents (1, 26, 62). Despite this, rodent models continue to be used heavily in the service of psychiatric neuroscience, with an increasing use of mice—which are even more phylogenetically distant—instead of rats (64). Given the fact that disrupted interoceptive processes are one of the most important components of many psychiatric disorders (for reviews see refs. 17 and 46), identifying appropriate animal models for studying the bases of these disorders is critically important. The profound differences in interoceptive neurobiology between primates and rodents suggest that the primate model is likely better suited for psychiatric research—at least research into disorders for which altered interoceptive processing is a hallmark feature. While the older heartbeat conditioning literature (34–36) in monkeys suggested they could use their heartbeats to guide behavior, our data demonstrate that rhesus macaques are innately able to integrate interoceptive (physiological) and exteroceptive (sensory) information in a manner that is identical to human children, providing a clear demonstration of their interoceptive capacity, and, importantly, using a completely noninvasive task. As interest in interoception grows, establishing paradigms with direct translational potential allowing cross-species comparisons will be critical to garnering causal mechanistic insights into the relevant neural basis of human interoceptive processes. Studies of cardiac interoception dominate the human interoception literature (39), but human studies of the neurobiology of interoception are largely correlative. Establishing a nonhuman primate model of cardiac interoceptive processing is therefore critical to advancing the study of causal neurobiological mechanisms of interoception. Future research should, however, also evaluate the extent to which nonhuman primates share human-like interoceptive processing across other domains and whether accuracy or sensitivity measures (like our cardiac discrimination score) across domains are related to each other and to individual differences in neurobiology (e.g., connectivity or structure of the insula), opening up the mechanistic study of those domains as well.

Conclusions. In concert with the previously established clear neurobiological homologies between monkeys and humans, our data provide unique insights into the ways in which the rhesus

macaque model shares important behavioral homologies that can be harnessed to further our understanding of both healthy and disordered interoceptive processing. Our data suggest that rhesus monkeys integrate cardiac interoceptive information in a way that is very similar to how humans do it, including exhibiting evidence of interindividual differences in discriminatory capacity. Future studies can leverage these insights to perform causal manipulations of the nervous system—both peripherally and centrally—in order to improve our general knowledge of interoception as it relates to broad psychological function and specific translational applications to human psychiatric disorders.

Materials and Methods

Subjects and Living Arrangements. All protocols were approved by the University of California Davis Institutional Animal Care and Use Committee and carried out in accordance with the US National Institutes of Health guidelines. All procedures were performed at the California National Primate Research Center (CNPRC).

Subjects in the present study were four adult rhesus monkeys (*Macaca mulatta*) aged 15 to 16 y (mean ± SD = 15.96 ± 0.69) and weighing, on average, 13.73 kg (SD = 5.62). All monkeys were born at the CNPRC and were raised in outdoor field cages (0.2 hA; 30.5 m × 61.0 m × 2.4 m) with ∼60 to 120 monkeys per cage through adulthood (i.e., at minimum, 4 y of age). Monkeys were then relocated to standard indoor cages (85.5 cm × 68 cm × 82 cm or 113 cm × 69 cm × 93 cm, dependent on weight) in temperature-controlled rooms with automatically regulated lighting (12 h light/dark cycle with lights on at 6:00 AM and off at 6:00 PM). Throughout the present experiments, all monkeys were housed in full contact with an opposite-sex cage mate for at least 12 h/day (based on social compatibility and food aggression). Monkeys D and M were housed together; monkeys A and T were housed with other opposite-sex social partners of a similar age not tested in the present study. They were fed monkey chow (LabDiet High Protein Monkey Diet; Ralston Purina) twice daily, supplemented with fresh fruit and vegetables twice weekly, and had ad libitum access to water. Monkeys received standard CNRPC enrichment, including rubber Kong toys and daily rice/oat/pea forage mixture. None of the monkeys tested here had any history of cardiovascular illness or any type of autonomic nervous system dysfunction.

mBEAT Data Collection. All monkeys involved in the present study served as subjects for previous eye tracking experiments and had extensive experience testing in this environment. For the present experiment, they were transported individually from their home cages to the testing laboratory and sat in a nonhuman primate box chair. Monkeys were previously trained to voluntarily present their head and limbs for restraint as described in refs. 65 and 66. Each monkey experienced 3 d of habituation prior to beginning data collection for the present study in order to reacclimatize them to the chairing and restraint process. On the first day of habituation, the monkeys' arms and legs were gently restrained with leather straps (1.3 cm × 3 mm × 1 m); their chests were shaved with a battery-operated clipper, cleaned with gauze soaked in 70% ethanol, and allowed to air dry prior to the application of ECG electrodes. Silver/silver chloride foam electrodes with conductive adhesive hydrogel (Covidien) were applied in a modified lead II configuration and attached to a Shimmer3 Consensys ECG unit (Shimmer Sensing). After verification of a clean ECG trace using Consensys software (Shimmer Sensing) and a custom MatLab (R2015a; MathWorks) script, monkeys were maintained in the chair for at least 20 min and periodically given food rewards (grapes or peanuts) for sitting calmly. On the second and third days of habituation, the same procedures were followed with the exception of shaving the chest. All four monkeys' heart rates stabilized by the end of the third habituation session.

Following habituation, monkeys began experimental test sessions. Each monkey completed 4 test sessions, each with 25 trials, for a total of 100 trials. Test sessions occurred ∼5 h after their morning feeding and at the same time each day for the 4 d of testing. As before, monkeys were restrained in the box chair and electrodes were applied to the chest for the collection of ECG. After verification of a clean ECG trace, the chaired monkey was wheeled into a sound-attenuating testing chamber (Acoustic Systems; 2.1 m × 2.4 m × 1.1 m) at ∼60 cm in front of the Tobii TX300 infrared eye tracker. Test sessions began with calibration of the eye tracker (Tobii). A standard five-point calibration was conducted each day prior to testing to ensure accuracy of eye position data collection. Calibration stimuli were displayed on the eye tracker's integrated display (58.4 cm diagonal; 1,920- × 1,080-pixel resolution). Following calibration, live R spike detection was verified using a custom MatLab (R2015a; MathWorks) script. R spike detection parameters (i.e., minimum R-R interval and minimum prominence) were adjusted when necessary to ensure the detection of every R spike, and these parameters were updated in the stimulus presentation script.

The trial structure was very similar to that described by Maister et al. (37) with modifications for nonhuman primates. Stimulus presentation was controlled using a custom MatLab script adapted from ref. 37. ECG data and eye tracking data were captured directly into MatLab using the Shimmer MatLab Instrument Driver (Shimmer Sensing) and Tobii Analytics SDK, respectively. ECG data were sampled at 1,024 Hz, and eye position data were sampled at 250 Hz.

Each trial began with a dynamic intertrial interval (ITI). All monkeys tested were familiar with the dynamic ITI as other eye tracking tasks used in our laboratory follow a very similar structure (as in refs. 67 and 68), so no training was required. The dynamic ITI consisted of a fixation of 250 ms on a gray rectangle (4.5-cm height [H] × 7-cm width [W]) presented at the center of the screen (22 cm from the left screen edge, 12 cm from the bottom screen edge) followed by an additional 250-ms fixation on an identical gray rectangle presented on either the left or right side of the screen (the same side as the stimulus would be presented on during that trial, alternating; 6 cm from the left or right screen edge, 12 cm from the bottom screen edge). Following the side fixation, monkeys received a juice reward (∼0.25 mL of apple or white grape juice) dispensed using an automated juice dispenser (Crist Instrument Co., Inc.; model # 5-RLD-E3) through a metal straw affixed to the chair immediately in front of their mouth, followed by a 1-s delay. The stimulus was either a yellow or pink shape (8-cm H × 16.5-cm W at rest, 9.5-cm H × 16.5-cm W during bounce; 0.5 cm from the left or right screen edge, 10 cm from bottom screen edge), modified from ref. 37 to remove facial features due to the potentially aversive nature of direct eye contact to monkeys (*SI Appendix*, Fig. S1). The stimulus moved rhythmically up and down either synchronously or asynchronously with the monkey's heartbeat. During synchronous trials, the stimulus moved up and down and a tone was played each time an R spike was detected. During asynchronous trials, the script generated a cardiac-like rhythm, with identical variability to a monkeys' natural cardiac rhythm, that was either 10% faster or 10% slower than the speed of the monkey's average heart rate recorded during the previous trial (if the first trial was asynchronous, this rhythm was based on a brief collection period prior to the trial onset). That is, synchronous and asynchronous trials only differed on the basis of their speed relative to the monkeys' beating heart; all other perceptual features were the same across conditions. Trials alternated between synchronous and asynchronous presentation. The nature of each asynchronous trial (fast vs. slow) was pseudorandomized. The stimulus associated with each trial type (i.e., pink for synchronous trials and yellow for asynchronous trials or pink for asynchronous and yellow for synchronous) was counterbalanced across test sessions and monkeys, as were the starting trial type (i.e., synchronous or asynchronous), and the side of the screen that each stimulus type appeared on.

For each trial, the stimulus appeared on the screen for a minimum of 3 s, after which the continued presentation of the stimulus was contingent on the monkey continuing to fixate on it. If the monkey continued to look at the stimulus, it remained on the screen for a maximum of 20 s. If the monkey looked away from the stimulus for longer than 3 s consecutively, the trial was automatically terminated. Each trial was followed by a 2- or 3-s delay (pseudorandomized) prior to the onset of the next trial. Each session included 25 trials and typically lasted 20 to 45 min. All monkeys completed the requisite 25 trials in each planned test session, and no testing sessions had to be terminated early (i.e., the reported data are the only data that were collected, and monkeys had no other experience with the stimuli used in this task). At the end of each test session, monkeys were returned back to their home cages. Only one monkey was tested on a given day such that all testing sessions could occur within the same time frame for each monkey.

Data Processing. All collected data were included in the analyses. Looking time data were processed offline. Fixations were detected using GraFIX (69),

which includes initial parsing of the eye tracking data using velocity-based algorithms followed by hand coding to resolve discrepancies in the automatically generated fixations. All fixation coding was completed blind to trial type. Looking times for each trial were computed as the summed duration of all fixations that fell within the circumscribed rectangle encompassing the animated stimulus during that trial. Whole screen looking times were also computed to evaluate general attention to the screen. This was done by calculating the summed duration of all fixations that fell within the bounds of the display. As in ref. 37, we obtained a cardiac discrimination score by calculating the difference between asynchronous and synchronous looking times divided by the total looking time:

$$Cardiac\ Discrimination = \frac{(mean_{async} - mean_{sync})}{(mean_{async} + mean_{sync})}.$$

Statistical Analysis. Statistical analyses were performed in R version 4.0.4 (70). Looking time data were modeled using a generalized linear mixed model with a negative binomial distribution in the package lme4 (71). A generalized linear mixed model was used to maximize the power of our design, allowing variance at the trial and subject level to vary independently. A simulation study of infant eye tracking data collected using different preferential looking paradigms showed that including more trials per subject (i.e., 100 trials/subject here compared with a mean of ∼12 trials/subject in ref. 37) can render experimental designs more powerful and their results more robust and replicable (72); nonhuman primate research suffers from similar constraints in subject selection to infant research, and so, here, we take advantage of the additional power conferred by collecting data through more trials rather than more subjects. Trial type (synchronous, asynchronous fast, asynchronous slow), interbeat interval, novelty score, and sex were used as fixed effects and subject identity was used as a random effect. IBI was the rate of stimulus presentation on each trial. Novelty scores were calculated on a trial-by-trial basis as the absolute value of the difference between the IBI on a given trial (n) and the cumulative average IBI the monkey experienced prior to that trial:

$$Novelty_n = \mid IBI_n - \frac{1}{n-1}\sum_{i=1}^{n-1} IBI_i \mid.$$

Post hoc comparisons to determine differences in looking times across trial types were carried out using the package emmeans (73). All individual trial data collected are presented in Fig. 1*B* in the main text alongside boxplots and density functions.

Data Availability. All data are included in the article and/or *SI Appendix* and are available on the Open Science Framework at https://osf.io/3vmfs/ (75).

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