Active sampling during visual search is modulated by the cardiac cycle

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Abstract

Recent research has demonstrated that perception and reasoning vary according to the phase of internal bodily signals such as heartbeat. This has been shown by locking the presentation of sensory events to distinct phases of the cardiac cycle. However, task-relevant information is not usually encountered in such a phase-locked manner nor passively accessed, but rather actively sampled at one's own pace. Moreover, if the phase of the cardiac cycle is an important modulator of perception and cognition, as previously proposed, then the way in which we actively sample the world should be similarly modulated by the phase of the cardiac cycle. Here we tested this by coregistration of eye movements and heartbeat signals while participants freely compared differences between two visual arrays. Across two experimental samples and three different analyses, we found a significant coupling of saccades and subsequent fixations with the cardiac cycle. More eye movements were generated during the systolic phase of the cardiac cycle, which has been reported as the period of maximal effect of the baroreceptors upon cognition. Conversely, more fixations were found during the diastole phase (i.e., quiescent period of the baroreceptors). These results provide novel evidence and are congruent with the hypothesis of humans optimizing the processing of sensory inputs by sampling the external environment during quiescent internal periods of the organism.

Keywords: interoception, visual sampling, saccades, baroreceptor, motor

Significance statement

Numerous studies show how participants' responses to sensory events fluctuate according to the cardiac phase in which these are presented. However, it is unclear how this relates to everyday interactions where information is not presented according to our cardiac cycle. One possibility is that we optimize the sampling of the world according to our cardiac signals. Here we tested this hypothesis by coregistration of eye movements and heartbeat signals during the active sampling of visual information. We show that more saccades were generated during the systolic cardiac phase (maximal firing of interoceptive information) whereas more fixations were generated during the quiescent period. This suggests that we optimize the sampling of sensory inputs according to our moment-by-moment inner bodily state.

Introduction

Interoception refers to the set of physiological and cognitive processes that are involved in determining the physiological condition of the body (Craig, 2002). It can be distinguished from the better-known domains of exteroception (information about the external environment of the organism) and proprioception (the position of the body in space) as a distinct sensory domain. Recently, research studying interoception has markedly increased (Ludwick-Rosenthal et al., 1985; Khalsa and Lapidus, 2016; Khalsa et al., 2018). There have been broadly two motivations for this renewed interest. The first concerns establishing the extent to which interoception contributes to cognition and perception in the healthy, neurotypical brain. The second aims to assess the clinical impact of atypical interoception. The primary physiological focus of the vast majority of studies on interoception is the cardiovascular system. Since early evidence of a modulatory effect of the carotid sinus in both autonomous and central nervous system (Koch, 1932; Kreindler, 1946), research in humans have shown that participants' response to sensory events changes according to the phase of the heartbeat in which the information is presented (Craig, 2003; Garfinkel et al., 2014; Garfinkel and Critchley, 2016; Salomon et al., 2016; Azevedo et al., 2017a, 2017b; Critchley and Garfinkel, 2018).

Over the time course of a single heartbeat two main cardiac phases are observed. The systolic phase refers to the period of the heartbeat in which the heart contracts and ejects the blood whereas in the diastole phase the heart expands while being filled with blood. From heartbeat to heartbeat, both phases comprise a whole cardiac cycle, with the R-peak (i.e., peak in the electrocardiogram depicting the hearts' contraction at the start of the systole) indicating the phasic change within a cardiac cycle. Recent studies have highlighted the influence of the cardiac cycle upon perception and cognition. Presenting stimuli locked to the different phases (i.e., systole vs. diastole) elicits distinct effects depending on the type of stimuli and the type of computation associated with the stimuli. For instance, in memory, the recall of words encoded during the systolic phase is lower than that for words encoded during diastole (Garfinkel et al., 2013). In emotion and visual detection, the detection of fearful faces among a stream of visual masks is increased during systole (Garfinkel et al., 2014; Garfinkel and Critchley, 2016). In basic sensorimotor functions, processing information during systole has been

103 associated to the reduction of sensitivity towards pain, visual, and auditory stimuli (Edwards et al.,
104 2001, 2007; McIntyre et al., 2006; Pramme et al., 2014). The results of these studies are consistent with
105 the hypothesis that the afferent signals from the heart seem to play an important role in the interaction
106 of the heart-brain axis. These signals modulate cognitive processes, compete for the allocation of
107 attentional and representational resources, and dampen/enhance sensory processing (Critchley and
108 Harrison, 2013; Seth, 2013; Critchley and Garfinkel, 2018; Khalsa et al., 2018). The demonstrations
109 that perception and cognition are modulated as a function of the cardiac cycle have been achieved by
110 deliberately time-locking the presentation of task-relevant information to the distinct phases of the
111 cardiac cycle (i.e., stimuli presented to the participants during the diastole and/or systole phases).
112 However, in our everyday experiences sensory information is not presented phase-locked to the cardiac
113 cycle. Therefore, although of considerable interest, it is unclear how these findings impact on our
114 perception and cognition outside of the laboratory setting. If the phase of the cardiac cycle is an
115 important modulator of perception and cognition, as previously proposed, then the way in which we
116 actively sample the world should be similarly modulated by the phase of the cardiac cycle. The current
117 study was designed to test this hypothesis. Specifically, we tested the hypothesis that the timing of
118 saccades in a free visual search task would be modulated by the phases of the cardiac cycle. To this
119 end, we developed a paradigm in which human participants performed a visual search task comparable
120 to 'spot the difference' while their oculomotor behaviour and electrocardiogram (ECG) were recorded.
121 Specifically, we recorded saccades and fixations while participants compared differences in colouration
122 between two bilateral arrays (Figure 1a). The number of saccades and fixations generated in diastole
123 and systole were calculated. The prediction was that if the free visual search task was modulated by the
124 cardiac signal then the number of saccades and subsequent fixations would be different between the
125 different phases of the cardiac cycle.

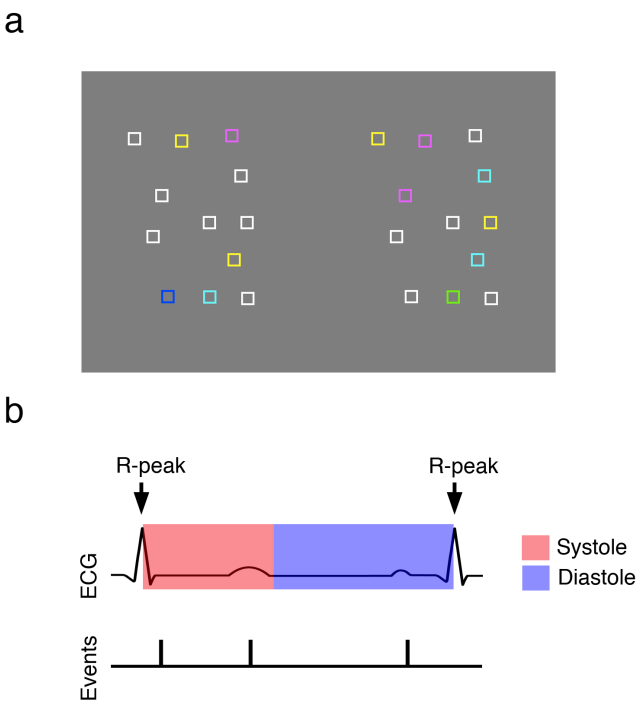

Figure 1. Task and schematic illustration of cardiac and oculomotor events. (a) Shows an example of a single trial. Participants were instructed to count the number of boxes that differed in colour between the two bilateral arrays. The arrays were identical in every other way other than the colour of some boxes. (b) A schematic of the analysis. The systolic (red) and diastolic (blue) phases of the cardiac cycle were defined for each cardiac cycle, from consecutive R-R peaks. The number of saccadic events were then summed and averaged for each phase of the cardiac cycle. The trial shown above depicts 9 differences.

Results

Descriptive results.

Thirty-two adults participated in two identical experiments (16 in each experiment). The second experiment was a direct replication of the first, performed to test the reproducibility of the results. All participants reported both normal or corrected-to-normal vision and normal cardiac condition. Three participants were excluded from the first experiment: two participants were excluded due to tachycardic heart rates (>100 bpm) and the third was excluded due to a technical issue that meant that oculomotor recording was missing.

The removal of noisy sections of the ECG (see *Methods - ECG recording and pre-processing*) comprised approximately 5.7% of the detected R-peaks; $M = 6.3\%$ and $M = 5.2\%$ in experiment 1 and

2, respectively. The number of detected R-peaks across both experiments was ~966 and no significant differences in detected R-peaks was found between groups ($t_{(1,12)} = -0.417$, $p = 0.684$, $d = -0.116$). Likewise, the heart rate was similar across both experimental samples ($t_{(1,12)} = -0.320$, $p = 0.755$, $d = -0.089$; $M = 73$ bmp in both cases, SEM = ±3.2 and ±2.4, respectively). After removal of noisy sections of the ECG, blinks, and erratic oculomotor events (see *Methods - eye tracker recording and pre-processing*) the average number of saccades across participants in both experiments was 3033. The mean length of the saccades across both experiments was similar and no differences between groups were found ($t_{(1,12)} = 0.024$, $p = 0.981$, $d = 0.007$; $M = 45$ms in both experimental samples, SEM = ±1.3 and ±1.1). On average participants generated 3.2 saccades per heartbeat.

Number of saccades and percentage of fixating time in windows bounded to the cardiac phases.

In an initial analysis we computed the total number of saccades and the length of the fixations in two time-windows of similar duration. The first window was bounded to the systolic phase at 200-400ms after the R-wave, which has been reported as the period of maximal effect of the baroreceptors upon cognition (Edwards et al., 2001; McIntyre et al., 2006; Garfinkel et al., 2014; Garfinkel and Critchley, 2016; Azevedo et al., 2017b) . The second was bounded to the diastole phase at 500-700ms after the R-wave, which has been reported as the quiescent period of the baroreceptors (Critchley and Harrison, 2013). The data were normalised by dividing the length of the time window by the resulting number of saccades per second in the systole or diastole windows. This approach emulates previous studies that examine the influence of cardiac cycle upon perception where stimuli are usually presented in time windows of equal length, concurring with the diastole or systole phases, and with a brief separation between them (Critchley and Garfinkel, 2015; Fiacconi et al., 2016; Azevedo et al., 2017b).

In *experiment 1* participants generated a greater number of saccades in the time window bounded to the systolic phase ($M = 3.891$; $SD = 0.454$) than in the diastole phase ($M = 3.768$; $SD = 0.398$). This difference was statistically significant ($t_{(1,12)} = -2.469$, $p = 0.030$, $d = -0.685$). This was replicated in *experiment* 2 with participants generating more saccades in systole ($M = 3.890$; $SD = 0.311$) than in diastole ($M = 3.816$; $SD = 0.259$). This difference was statistically significant ($t_{(1,15)} = -$

2.754, p = 0.015, d = -0.688). To test if there were any differences between the two experiments we computed a repeated-measures ANOVA including both experiments' datasets. The factors were the number of saccades generated in each cardiac phase and the experimental sample. This analysis revealed a main effect of cardiac phase ($F_{(1,27)}$ = -13.398, p = 0.001, η_p^2 = 0.332). Critically, there was no main effect of experimental sample and no significant interaction between the number of saccades per cardiac phase and the experimental samples ($F_{(1,27)}$ = 0.843, p = 0.367, η_p^2 = 0.030).

In *experiment 1* the percentage of fixating time in each cardiac phase revealed that participants fixated longer during diastole than systole, however, this difference was not significant (M = 0.825, SD = 0.028 *vs.* M = 0.828; SD = 0.023; $t_{(1,12)}$ = 1.009, p = 0.333, d = 0.280). Likewise, in *experiment 2* participants fixated longer during diastole and this difference was not significant (M = 0.827, SD = 0.021 *vs.* M = 0.828; SD = 0.020; $t_{(1,15)}$ = 0.910, p = 0.377, d = 0.228). A repeated-measures ANOVA with the percentage of fixating time in each cardiac phase and the experimental sample as factors produced a non-significant difference between fixations generated in the short time windows bounded to diastole and systole ($F_{(1,27)}$ = 1.923, p = 0.177, η_p^2 = 0.066). In addition, there was no significant main effect of experimental sample and no significant interaction between the cardiac phase ($F_{(1,27)}$ = 0.265, p = 0.611, η_p^2 = 0.010). Overall these results demonstrated that participants across both experimental samples generated saccades more frequently in the systolic phase than during diastole.

Number of saccades and percentage of fixating time over the whole cardiac phases.

Despite the broad use of brief time windows, the diastole and systole phases extend in time beyond these windows. Moreover, the systole and diastole phases vary as a function of heart rate. The length of the systolic phase varies inversely with heart rate; the relative length of the systole increases with faster heart rates. Conversely, the length of the diastole phase decreases with faster heart rate (Lombard and Cope, 1926; Weissler et al., 1968; Mao et al., 2003). This variability needs to be accounted with more refined procedures. In a second analysis we calculated the number of saccades and fixations while estimating the relative length of the diastole and systole in a heartbeat by heartbeat basis. To do this we used the parameters described in the study of Mao and colleagues (2003). The authors examined the

length of the diastole and systolic phases in more than 800 participants, noting the percentage of these phases relative to the whole cardiac cycle and according to the participants' heart rate. Similar to the above-mentioned analyses, we calculated the number of saccades generated in a given unit of time (seconds) and the percentage of time spent fixating, but this time in each entire cardiac phase.

In *experiment 1* participants generated significantly more saccades in the whole of the systolic phase than in the diastole (M = 3.910, SD = 0.462 *vs.* M = 3.8, SD = 0.404; $t_{(1,12)}$ = -2.348, p = 0.037, d = -0.651). This was replicated in *experiment 2* where participants generated significantly more saccades in the systole than in the diastole phase (M = 3.909, SD = 0.285 *vs.* M = 3.811, SD = 0.277; $t_{(1,15)}$ = -4.292, p = 0.0006, d = -1.073). As we did in the previous analysis, we computed a repeated-measures ANOVA with the number of saccades generated in each cardiac phase and the experimental sample as factors. This analysis revealed a main effect of cardiac phase ($F_{(1,27)}$ = -17.991, p = 0.0002, η_p^2 = 0.400) and a similar pattern of saccades across both experimental samples ($F_{(1,27)}$ = 0.050, p = 0.824, η_p^2 = 0.002) and not significant interaction between the two factors (Figure 2).

Regarding the percentage of time spent fixating on the stimuli, in *experiment 1* participants fixated longer during diastole than systole, however, this difference was not statistically significant (M = 0.821, SD = 0.029 *vs.* M = 0.824; SD = 0.025; $t_{(1,12)}$ = 1.707, p = 0.107, d = 0.483). Likewise, in *experiment 2* participants fixated longer during diastole than systole, in this cohort the difference was significant (M = 0.823, SD = 0.019 *vs.* M = 0.826; SD = 0.022; $t_{(1,15)}$ = 2.206, p = 0.043, d = 0.551). We also computed a repeated-measures ANOVA with the percentage of fixating time in each cardiac phase and the experimental sample as factors. The analysis revealed a main effect of fixations generated in each cardiac phase ($F_{(1,27)}$ = 7.690, p = 0.010, η_p^2 = 0.222). The main effect of experimental group and the interaction between cardiac phase and the experimental group did not reach significant ($F_{(1,27)}$ = 0.008, p = 0.928, η_p^2 = 0.0003). The post-hoc analysis revealed a significant difference between the percentage of fixating time spent in each cardiac phase ($t_{(1,28)}$ = 2.848, p = 0.008, d = 0.529).

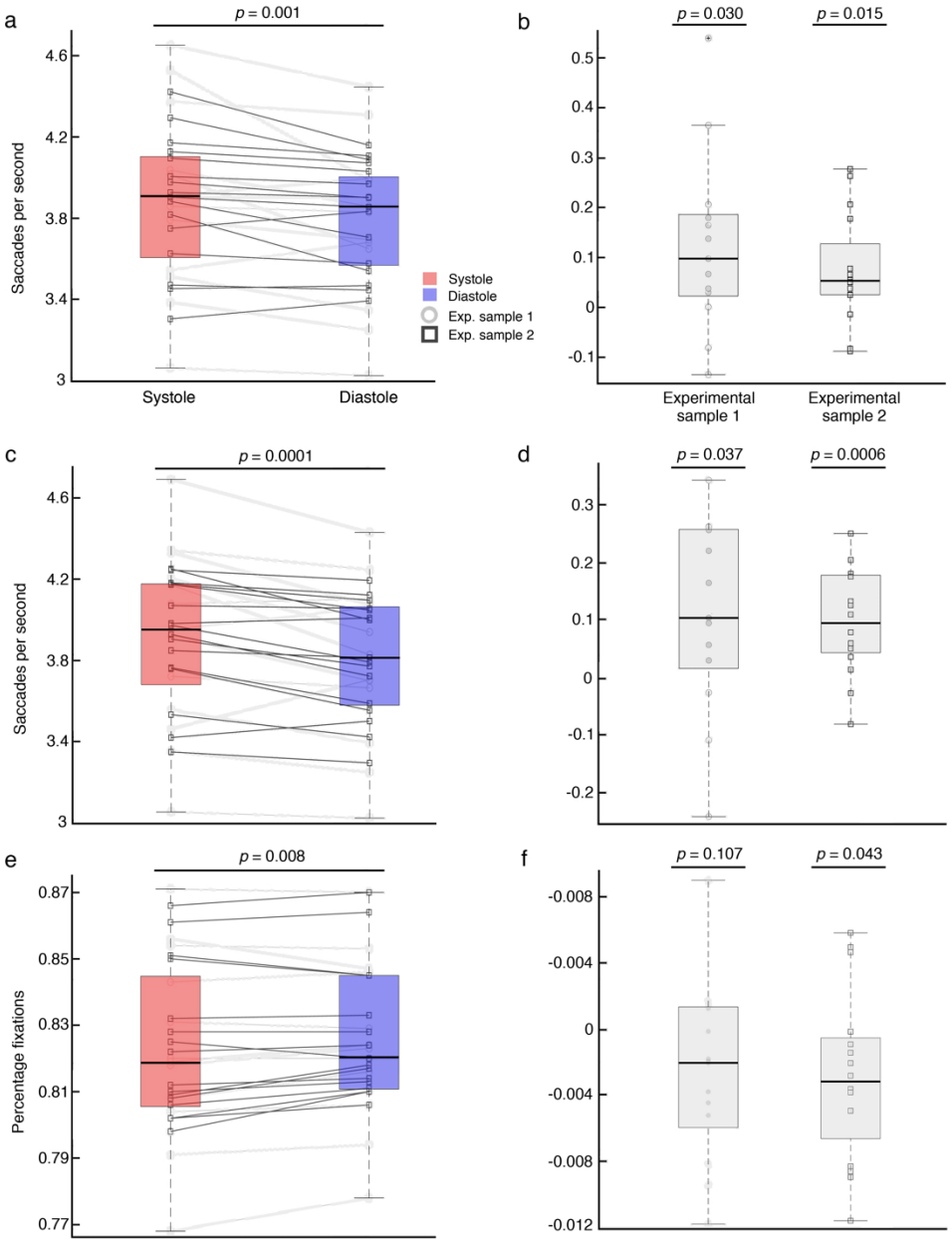

Figure 2. Number of generated saccades and percentage fixating time in each cardiac phase. Right plots are based on the left plots' data but depicted for each experimental sample and removing between subject's variability (i.e., oculomotor events in each cardiac phase minus the mean of both phases, then, computing the difference between the subsequent results). (a) Estimated number of saccades in units of time (i.e., saccades per second) generated in time windows bounded to the systole and diastole. A greater number of saccades were generated in systole (p= .001). (b) Estimated number of saccades in units of time from saccades generated in the entire cardiac phases. Similarly, a greater number of saccades were generated in systole (p= .0001). (c) Percentage of time spent fixating in each entire cardiac phase, longer fixations found in diastole (p= .008). Lines plotted in light grey: participants of sample 1 (n=13); dark grey: sample 2 (n=16). *P* values in left plots depict results from combining both experimental groups; *P* values in right plots depict results from each group. In each boxplot, the central line

indicates the median, the bottom and top indicate the 25th and 75th percentiles. Whiskers extend to the data points not considered outliers. Outliers are plotted with a '+' symbol.

Number of saccades over time.

The previous analyses did not allow examining the number of saccades generated over time, namely, a potential interaction between the number of saccades and time. To this aim, we computed histograms by calculating the number of saccades in consecutive time bins of 100ms. We normalised each individual's data by dividing the number of saccades generated in each bin by the total number of saccades in the whole task. Furthermore, we compared the normalised number of saccades in each bin against the expected uniform distribution (i.e., constant probability of generating saccades; each bin *vs.* 0.1).

We conducted a repeated-measures ANOVA with the factor bin (i.e., 10 windows containing saccades along time). In *experiment 1* this analysis yielded a significant effect of bin ($F_{(1,12)} = 3.385$, $p = 0.005$, $\eta_p^2 = 0.242$), indicating that the number of saccades generated along the cardiac cycle varies in a consistent manner. We followed-up this analysis by conducting post-hoc analyses comparing all bins, however, none of these bins survived Bonferri-correction (all *ps* > 0.134). In the next step we compared the generated saccades in each bin against 0.1 (i.e., uniform distribution). This yielded similar results, with none of the bins surviving the succeeding corrections (all *ps* > 0.170). In *experiment 2* similar analyses yielded a significant effect of bin ($F_{(1,15)} = 5.114$, $p = 0.0004$, $\eta_p^2 = 0.254$). Here the post-hoc analyses revealed a significant difference between the 1st and 8th bin, being these centred at -100 and 600ms (after the R-peak) in the histograms; $t_{(1,15)} = 4.667$, $p = 0.014$, $d = 1.167$. The post-hoc analyses also revealed a significant difference between the 2nd and 10th bin, which are centred at 0 and 800ms (after the R-peak) in the histograms; $t_{(1,15)} = 4.809$ $p = 0.010$, $d = 1.202$. These results revealed that indeed more saccades were generated during the early phase of the cardiac cycle compared to the later diastole phase. Thenceforward, when comparing the number of saccades per bin against the expected uniform distribution, only the 8th bin centred at 600ms after the R-peak survived the Bonferroni-correction ($t_{(1,15)} = -3.473$ $p = 0.030$, $d = -0.868$).

Lastly, we examined whether or not the modulation of saccades was coherent across experimental samples. We computed a repeated-measures ANOVA with the number of saccades per bin and the experimental sample as factors. The analysis yielded a significant effect of bin ($F_{(1,27)}$ = 8.190, p = 9.228e - 8, η_p^2 = 0.233) and no interaction by experimental sample ($F_{(1,27)}$ = 0.770, p = 0.595, η_p^2 = 0.028). Next, we conducted post-hoc analysis, since this revealed that several comparisons reached significance, the results are organised in a table (figure 3c) accompanying the histograms of figure 3a. As can be seen, there is a robust modulation in the number of saccades generated over time with more saccades in the early phase of the cardiac cycle (systole) than in the later diastole phase. Lastly, when comparing the number of saccades per bin against the expected uniform distribution, the 2nd, 3rd, 8th, and 9th bins (centred to 100, 200, 600, and 800ms after the R-peak) yielded significant results. Accordingly, the normalised number of saccades in the 2nd and 3rd bins (i.e., 0 and 100 ms after R-peak) are greater than 0.1 ($t_{(1,28)}$ = 4.003 p = 0.004, d = 0.743; $t_{(1,28)}$ = 3.232 p = 0.030, d = 0.600). Conversely, the opposite pattern is found for the 8th and 9th bins ($t_{(1,28)}$ = -4.258 p = 0.004, d = -0.791; $t_{(1,28)}$ = -3.542 p = 0.010, d = -0.658).

In summary, the results of the short-bounded time windows show that a greater number of saccades were generated in the systolic phase than in the diastole, being the latter concomitant to the quiescent period of the baroreceptors. These results were replicated in both experimental samples and extended in the analyses of saccades that were generated in the whole cardiac phases. Moreover, the further analysis of participants' fixations supported this finding; longer fixations were found during diastole. In the analyses of the histograms, our results show a main effect of time bin, suggesting that the number of saccades generated along the cardiac cycle varies over time in a consistent manner. Post-hoc analyses revealed that indeed more saccades were generated during the early phase of the cardiac cycle compared to the later diastole phase. Finally, the number of saccades generated in these phases deviated significantly from a uniform distribution. In conclusion, by coregistration of eye movements and heartbeats signals, we found statistical evidence for a significant coupling of saccades and subsequent fixations with the distinct phases of the heartbeat.

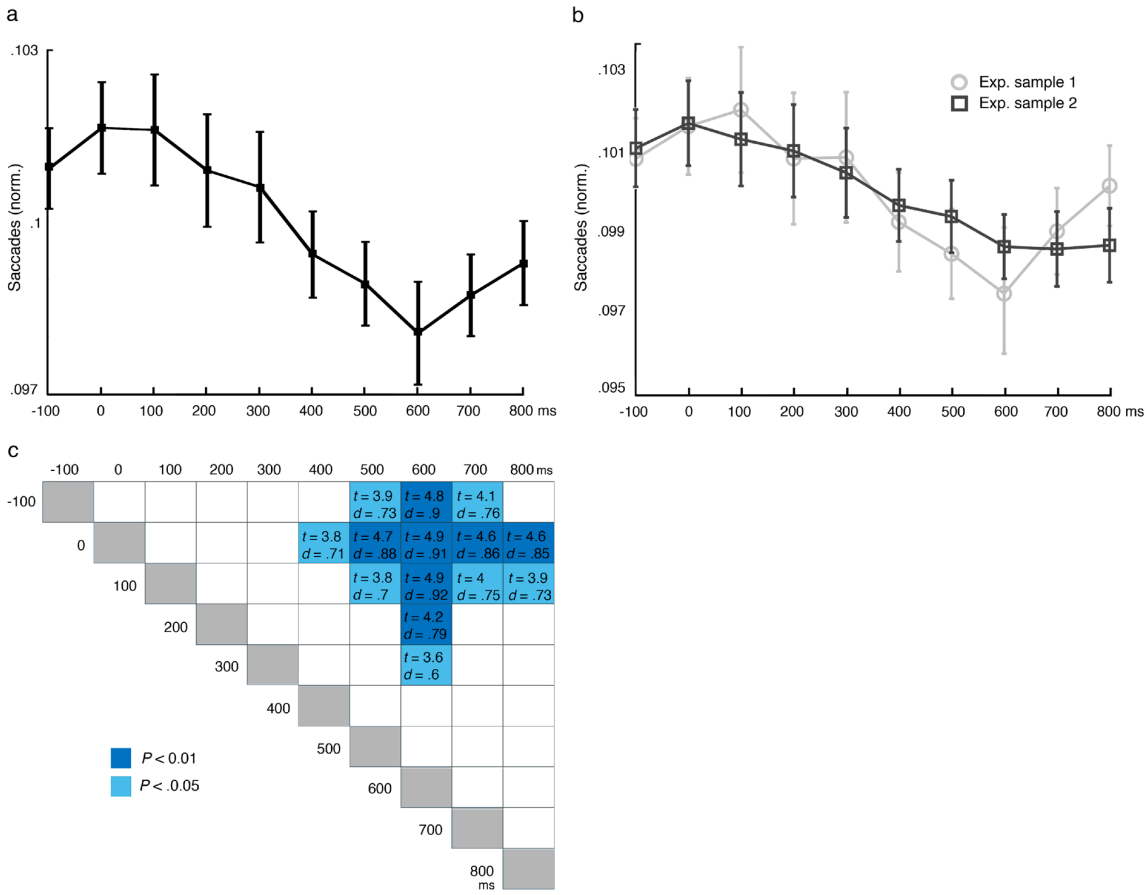

Figure 3. Number of saccades generated over time (-100 to 800ms after R-peak). (a) After normalising the data, histograms show an increase in the number of saccades generated in the early systolic phase of the cardiac cycle compared to the latter diastole phase. The number of significant comparisons is indicated in the table below (b) Histograms depicting the data of both experimental samples; similar pattern of generated saccades was found with an increase in the number of saccades generated in systole *vs.* diastole. (c) Results of the comparisons between histograms' bins. Each coloured square contains the *t* value and the effect size *d*. Significant *P* values are denoted by the colouration of the squares: dark squares, $P < 0.01$; lighter blue: $P < 0.05$; white: no significant. These statistical values result from combining both samples. In figure b, lines in light grey: experimental sample 1 (n=13), dark grey: sample 2 (n=16). Bars depict 95% CI.

Discussion

In the current study we examined the oculomotor behaviour of two experimental samples in a visual search where participants had to compare differences in colouration between two bilateral arrays. We developed a novel paradigm combining research in interoception and eye tracker methodology. Namely, research in interoception showing that biobehavioural responses differ when the information is presented in distinct phases of the cardiac cycle (Garfinkel et al., 2014; Azevedo et al., 2017a; Park et al., 2017), as well as research on the visual system examining saccadic eye movements and emphasising the importance of these in cognition (Zelinsky and Sheinberg, 1997; Liversedge and Findlay, 2000; Ibbotson and Krekelberg, 2011). While the effect of the cardiac cycle on cognition has been observed by meticulously time-locking the presentation of task-relevant information to each cardiac phase, here we foster a more natural framework in which participants actively sample information at their own pace. We hypothesised that participants may 'take in' information according to interoceptive signalling (i.e., behaviour produced in synchrony with oscillatory changes in cardiac signalling). To examine this issue, we allowed participants to freely sample the information needed for the task at hand while recording saccades, fixations, and ECG.

We used three different approaches to examine the generation of oculomotor behaviour in two different experimental samples. The results of these approaches converge into showing that participants' oculomotor behaviour was driven by the cardiac cycle. We found a coupling of saccades and subsequent fixations with the heartbeat. These results are in the same order of magnitude than those reported in previous studies examining changes in participants' responses during the diastole and systolic phases of the cardiac cycle (e.g., Garfinkel et al., 2013, 2014; Pramme et al., 2016; Kunzendorf et al., 2018). Overall our results support the idea of visually sampling the environment according to phasic changes in the cardiac cycle. An earlier study has also indicated a link between motor behaviour and autonomic oscillations. Ohl et al., 2016 reported the coupling of microsaccades (i.e., small fixational involuntary eye movements) with the heartbeat. Specifically, they reported more microsaccades in the early period of the systolic phase. The authors suggested that these slow fixational eye movements may be modulated by baroreceptors (i.e., sensors on vessels firing during the ejection

of blood from the heart; systole) via afferent signalling to the superior colliculus. In addition, as suggested by Ohl and colleagues, a more parsimonious explanation is that cardioballistic fluctuations of the ejected blood may exert a direct effect in the muscle activity (Fallon, 2004). In this regard, previous research has shown that the afferent discharge of muscle spindles is indeed modulated by arterial pulsations (Birznieks et al., 2012)

Several saccades are usually produced per second and with each saccade the fovea moves between points of interest. Two notions need to be emphasized here, the first one is that in primates only the central portion of our visual field has the adequate density of receptors to obtain visual information with high resolution. Therefore, we generate saccades to sample elements distributed in the environment, this encompasses changes in object representation, allocentric/egocentric framing, and allocation of attentional resources (Hamker et al., 2008; Ibbotson and Krekelberg, 2011). Second, the generation of saccades allows the gathering of relevant sensory data to test hypotheses or beliefs of how the gathered data is actually caused (see eg., Friston et al., 2012; Parr and Friston, 2018). Here combining perceptual and motor mechanisms allows the reduction of entropy inherent to the environment and its perceived consequences (Friston et al., 2009, 2012; Pickering and Clark, 2014). Interestingly, visual perception is impaired during saccades. Previous research has described the selective suppression of the magnocellular pathway during saccades (Burr et al., 1994; Ross et al., 1996), which is a relevant path to process tasks similar to the currently used here where serial search and scanning of objects seem crucial processes (Cheng et al., 2004). Furthermore, other studies have also described that visual acuity is enhanced during the postsaccadic period (as reviewed by Ibbotson and Krekelberg, 2011).

Our results show that participants generated more saccades during systole than diastole. The systole period is concurrent with baroreceptors' firing and the diastole is the quiescent period. The fixations generated during the task follow the opposite pattern, with shorter fixations during systole compared to diastole. Thus, participants generated more saccades, in which visual perception is dampened, during the occurrence of an additional source of information (i.e., baroreceptors firing during the systolic phase). Conversely, they encoded external information during the quiescent period

of such inner bodily signal. Overall, we believe that in order to reduce uncertainty about the external environment, humans sample the environment by generating more saccades during the systolic phase and the concurrent upstroke of inner bodily signalling. Conversely, they seem to gather visual sensory information during the quiescent period of the cardiac cycle (i.e., in the absence of inner signalling and during the postsaccadic momentum). This idea is coherent with the presence of saccadic enhancement –increase vision before and after saccades (Ibbotson and Krekelberg, 2011), as well as to previous studies that report dampened detection of pain, visual and auditory stimuli during systole compared to an improved perceptual sensitivity in the diastole phase of the cardiac cycle (Edwards et al., 2001, 2007; McIntyre et al., 2006; Pramme et al., 2014).

Conclusion

By coregistration of eye movements and ECG, we found statistical evidence for a significant coupling of saccades and subsequent fixations with the heartbeat. More saccades were generated during the systolic phase and the concurrent upstroke of inner bodily signalling. Contrary to this, longer fixations (and the subsequent absence of saccades) were generated during the quiescent period of the cardiac cycle. Our results are consistent with the hypothesis that the different phases of the cardiac cycle, and potentially the cardioballistic fluctuations concomitant to the ejection of the blood across the body, modulate behaviour. We believe that these results provide original evidence for a mechanism by which humans might sample the world according to our bodily signals. This is congruent with the hypothesis of humans sampling the external environment during quiescent periods of inner bodily signals such as the heartbeat.

Materials and methods

Participants.

A total of 32 healthy adults participated in two experiments (16 in each experiment; 22 females; age range = 18-39). All participants reported both normal or corrected-to-normal vision and normal cardiac condition. All subjects gave informed consent and volunteer to take part in the experiments. Ethical

approval for the methods and procedures were obtained from the UCL research ethics committee. Three participants were excluded from experiment one: two participants due to tachycardic heart rates (>100 bpm) and another participant due to the single recording of the ECG, missing the oculomotor recording.

Task and procedure.

Participants completed five blocks of 20 trials while their electrocardiogram (ECG) and oculomotor behaviour were recorded. Prior to this, they received instructions explaining the task and completed two practice trials. At the start of each block, a standard nine-point calibration procedure was carried out, followed by a validation procedure to align the participants' gaze with the eye tracking system. Once this was completed, participants performed a visual search comparable to a simpler and more controlled version of 'the spot the difference task'. Specifically, participants had to count the number of boxes distinctively coloured across two bilateral arrays having similar spatial configuration along the Y axis of the screen (Figure 1a). To do this, participants compared one by one the colour of the boxes in one array with the colour of the boxes in the other array. The participants moved to the next trial by pressing the space-bar and reporting the number of differences counted. Importantly, the arrays were continuously displayed on the screen. In addition to the coloured boxes, catch trials, consisting of a change of one of the boxes by a small red circle (0.8° x 0.8) were included in 3% of the trials to enforce ongoing attention to the task. Participants had to report the sight of these latter stimuli and count their presence as a difference. All participants reported the presence of these red circles in the catch trials.

Visual display.

The visual arrays were displayed on a 17-inches LCD monitor with a refresh rate of 60 Hz and resolution of 1280 x 800 pixels. Participants were seated in a dimly light room at 66 cm from the monitor with their head stabilised on a chin rest and their forearms rested on the top of a table. The visual arrays were generated and displayed using Matlab R2016b (The MathWorks Inc., Natick, MA, USA) with the Psychtoolbox-3 (Brainard, 1997; Pelli, 1997; Cornelissen et al., 2002; Kleiner et al., 2007). We recorded oculomotor behaviour while participants compared differences in coloration between small coloured

boxes (0.8° x 0.8° each) displayed within two bilateral arrays that were embedded in two rectangular regions (8° x 11°) centred 6° to the left and right side of the screen centre. In each trial the positions of the 12 boxes displayed on the right array were randomised with the restriction that the distance between them was maintained to a minimum of 2.2° (centre to centre). The spatial configuration of the boxes in the left array was similar to that of the right array but shifted to the left side along the X axis. To decide the assignment of colouration in each individual frame, we run several pilot sessions in which we also consider the length of the task and the time spent in each trial, the number of generated saccades, the number of heartbeats recorded, and the difficulty of the task. In each trial of the final experiments used here, each coloured frame was subjected to a combination of the RGB triplet, assigning a .18 probability of obtaining 1 in each individual number of the triplet (see https://bit.ly/2jUvdFd). Overall, this equals to a ~.58 likelihood of obtaining a white coloured frame (approximately 8 differences in average). In the remaining probability a different colour out of the remaining seven RGB combinations was obtained.

Eye tracker recording and pre-processing.

Eye movements were recorded using a video-based eye tracking System (Eyelink 1000 Plus; SR Research, Ottawa, ON, Canada) with a sampling rate of 1000Hz. Before each block, participants' point of gaze on the screen was acquired. To compute this, the correspondence between the position of the pupil in the camera image and nine positions on the display screen were measured. Following this, we validated the recording of the eye movements in a second calibration. If performance was poor (i.e., a deviation of >1° between the participants' gaze and the expected positions on the screen), the calibration/validation procedure was repeated. Lastly, before each trial a single centred target was presented to the participant, this allowed estimating the drift between the current fixation and the above-mentioned calibration. The calibration/validation procedure was launched through the EyelinkToolbox implemented in Psychtoolbox-3 and run in Matlab R2016b. At the onset of each trial, a squared pulse was delivered through a data acquisition box (NI USB-6229; National Instruments Corp., ATX, USA) to a CED Power unit 1401-3A, which signal was recorded in simultaneity to the ECG in Spike2 8.10

434 (Cambridge Electronic Design Limited, Cambridge, UK). This pulse allowed us to align the oculomotor
435 and ECG recordings.

436 In order to detect eye movements during the task we used a parsing system implemented in the
437 Eyelink 1000 Plus and configured to extract oculomotor events (i.e., saccades, fixations, and blinks) in
438 standard cognitive research. A saccade event was detected if the velocity and acceleration of an eye
439 movement reached specified thresholds; these involve motion, velocity, and acceleration, computed as
440 0.1°, 30°/sec, and 8000°/sec^2, respectively. Only oculomotor events without blinks were included in
441 further analyses. Next, we computed the mean length of the fixations generated in the systole and
442 diastole phases of each heartbeat. Given the variability of the fixations' length and the possibility of
443 including erratic data due to track-loss (e.g., loss of measurement, participants turning away, etc.), we
444 rejected heartbeats including fixations that were ±1.25 * the median of the participants' fixation length
445 in diastole or systole. We rejected the same heartbeats in the calculation of the number of saccades
446 generated. Note that the overall percentage of oculomotor data included after this step was over 85%.

447 *ECG recording and pre-processing.*

448 ECG was recorded using a D360 8-Channel amplifier (Digitimer Ltd, Hertfordshire, UK) in Spike2
449 8.10 at a sampling frequency of 1000 Hz. The electrodes were placed over the right clavicle and left
450 iliac crest according to Einthoven's triangular arrangement. In order to identify the different phases of
451 the cardiac cycle we detected the R peaks in the ECG trace. To do this, we computed vectors with the
452 local maxima (R-peaks) of the ECG; we defined a minimum peak to peak distance of 550 ms and a
453 mean minimum peak height of ~0.7. We visually inspected the detection of the R-peaks returned by the
454 algorithm and applied small adjustments when required. The visual inspection of the data also allowed
455 us to observe small drifts that impaired the correct detection of all the R-peaks –due for instance, to
456 some participants producing small body movements. Given the temporal consistency between R-peaks,
457 these small portions of the ECG trace were found and rejected by detecting peaks separated by a
458 distance ±1.25 * the median of the participants' R to R-peak distance.

459 ***Data analysis.***

Saccades and fixations in time windows bounded to the cardiac phases. Since each participant generates a different number of saccades along the self-paced visual search, we normalised the data by computing the number of saccades that participants produce in a given time (i.e., estimated number of saccades per second in systole or diastole). This approach is based on units of time and it allows normalising data irrespectively of the time windows' length. Specifically, it was applied here by dividing the number of saccades in each time window and heartbeat by the value obtained when dividing the length of the time window by 1000 (number of saccades in diastole or systole / (length of time window/1000)). Moreover, we also calculated the percentage of time that participants spent fixating on the stimuli in each time window. We normalised these data by dividing the length of the fixations by the length of the time windows used in each cardiac phase (length of fixations in diastole or systole / length of time window).

Saccades and fixations over the whole cardiac phases. We calculated the participants' heart rate in a heartbeat per heartbeat basis. We then made use of the parameters described in (Mao et al., 2003) who examined the length of the diastole and systolic phases in more than 800 participants, noting the percentage of these phases relative to the whole cardiac cycle according to the participants' heart rate. Following this, similar to the above-mentioned analysis, we calculated the number of saccades generated per second in systole and diastole, as well as the percentage of time that participants spent fixating in each whole cardiac phase.

Number of saccades over time. The previous analyses did not allow examining the number of saccades generated over time, namely, a potential interaction between the number of saccades and time. To this aim, we computed histograms by calculating the number of saccades in consecutive bins from -200ms to 700ms after the R-wave. We applied a moving window of 200ms averaging the number of generated saccades over time. The time bins depicted in figure 3 show the results of the centred histograms after applying this moving window (i.e., -100 to 800ms). We normalised these data by dividing the number of saccades in each bin by the total number of saccades generated in the whole task. Furthermore, we compared the number of saccades produced in each bin against the expected uniform distribution after normalisation of the data (i.e., each bin *vs.* 0.1).

Last, in all those analyses using paired student t-test, normality was checked and Wilconxon signed-rank test was used when it was violated. Likewise, Mauchly's W was computed to check for violations of the sphericity assumption and Greenhouse–Geisser adjustments to the degrees of freedom were applied when appropriate. The P values were corrected for multiple comparisons using Bonferroni correction.

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Competing interests:

The authors declare no competing financial interests.

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