

This file was downloaded from BI Open Archive, the institutional repository (open access) at BI Norwegian Business School <http://brage.bibsys.no/bi>.

It contains the submitted manuscript to the article cited below. It may contain minor differences from the journal's pdf version.

Zhao, D, Corsetti, M, Moeini-Jazani, M, et al. Defecatory urge increases cognitive control and intertemporal patience in healthy volunteers. *Neurogastroenterol Motil.* 2019; 31:e13600. <https://doi.org/10.1111/nmo.13600>

**Copyright policy of *Wiley*, the publisher of this journal:**

Authors are permitted to self-archive the peer-reviewed (but not final) version of a contribution on the contributor's personal website, in the contributor's institutional repository or archive, subject to an embargo period of 24 months for social science and humanities (SSH) journals and 12 months for scientific, technical, and medical (STM) journals following publication of the final contribution.

<http://olabout.wiley.com/WileyCDA/Section/id-817011.html>

**Defecatory Urge Increases Cognitive Control and Intertemporal Patience in Healthy  
Volunteers.**

Dongxing Zhao <sup>\*1,2</sup>,

Maura Corsetti <sup>\*1,3</sup>,

Mehrad Moeini-Jazani <sup>\*4</sup>,

Nathalie Weltens <sup>1</sup>,

Mirjam Tuk <sup>5</sup>,

Jan Tack <sup>1</sup>,

Luk Warlop <sup>#6</sup>,

Lukas Van Oudenhove <sup>#1</sup>

<sup>1</sup>Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium,

<sup>2</sup>Institute for Diabetes Research and Metabolic diseases (IDM), University of Tübingen, Tübingen, Germany

<sup>3</sup>Nottingham Digestive Diseases Biomedical Research Centre, Nottingham University Hospitals NHS Trust, University of Nottingham, Nottingham, UK

<sup>4</sup>Faculty of Economics and Business, University of Groningen, Groningen, the Netherlands

<sup>5</sup>Imperial College London, London, United Kingdom

<sup>6</sup>BI Norwegian Business School, Oslo, Norway

*\*equal contribution as first author, #equal contribution as last author*

**This is a preprint version of the paper accepted at Neurogastroenterology & Motility, April 2019**

Corresponding Authors

Lukas Van Oudenhove, Laboratory for Brain-Gut Axis Studies (LaBGAS), Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, B-3000 Leuven, Belgium, phone: +32 16 33 01 47, e-mail: [lukas.vanoudenhove@kuleuven.be](mailto:lukas.vanoudenhove@kuleuven.be)

Luk Warlop, Department of Marketing, BI Norwegian Business School, N-0484 Oslo, Norway, phone: +47 46 41 01 51, e-mail: [luk.warlop@bi.no](mailto:luk.warlop@bi.no)

# **Defecatory Urge Increases Cognitive Control and Intertemporal Patience in Healthy Volunteers.**

## **Abstract**

Past research has demonstrated that moderate urge to urinate improves inhibitory control, specifically among participants with higher behavioral inhibition sensitivity system (BIS), and the effect was absent when the urge exceeded intolerable level. The present research examines whether rectal distension-induced urge to defecate has similar effects. Moderate and high defecatory urge was induced by rectal distension in healthy volunteers (n=35), while they completed Stroop tasks and monetary delay discounting tasks. The difference of average reaction time between incongruent and congruent trials in the Stroop task (Stroop interference) and the preference for larger-later rewards in the delay discounting tasks were analyzed as the primary outcomes. Participants with high BIS sensitivity (n=17) showed greater ability to inhibit their automatic response tendencies, as indexed by their Stroop interference, under moderate-urge relative to no-urge condition (128±41 ms vs. 202±37 ms,  $t_{64}=-2.07$ ;  $p=0.021$ , Cohen's d: -0.44), but not relative to high-urge condition (154±45 ms,  $t_{64}=-1.20$ ;  $p=0.12$ , Cohen's d: -0.30). High-BIS participants also showed higher preference for larger-later reward in the delay discounting task under high (odds ratio = 1.51 [1.02–2.25],  $p=0.039$ ) relative to no-urge condition, but not relative to moderate-urge condition (odds ratio = 1.02 [0.73–1.42],  $p = 0.91$ ) In contrast, rectal distension did not influence performance on either of the tasks for participants with low BIS sensitivity (n=18). These findings may be interpreted as a 'spill-over' effect of inhibition of the urge to defecate to volitional cognitive control among healthy participants with high BIS sensitivity.

## **Keywords**

defecatory urge, gut-brain axis, inhibitory control, rectal barostat

## **Key Points**

- Defecatory urge improves inhibitory control in healthy volunteers.
- Inhibition of the urge to defecate facilitated cognitive control under moderate urge, and increased preference for larger-later rewards in the delay discounting task under high urge, among healthy humans with high behavioral inhibition sensitivity (BIS), but not among those with low BIS.
- Results show that mechanical signals originating in rectum can improve cognitive control in unrelated domains, and contribute to studies on psychosocial effects of functional GI disorders.

## Introduction

Inhibitory control refers to one's ability to restrain and override impulses to achieve goals of higher importance or with better payoffs<sup>1,2</sup>. A growing body of literature highlights the existence of a common, domain-independent capacity for inhibitory control<sup>3,4</sup>. Specifically, when inhibitory control is activated in one domain, it can facilitate control in other (unrelated) domains. For instance, controlling the urge to urinate facilitates inhibitory control in cognitive domains, specifically in tasks requiring impulse inhibition<sup>2</sup>. It has been proposed that inhibitory control processes across different domains share common neurological pathways<sup>5</sup>, involving brain regions along the cingulate sulcus, with dopamine being the key neurotransmitter<sup>6,7</sup>.

Neurological processes underlying rectal filling are in many ways similar to bladder control processes<sup>5,8-10</sup>. Consequently, in the present research, we propose that defecatory urge should also facilitate inhibitory control. We explore this hypothesis across two self-regulatory tasks by examining the interplay between rectal urge conditions of varying degrees and individuals' chronic differences in behavioral inhibition system (BIS)<sup>11</sup>. Specifically, we hypothesized that, for people with high BIS, experiencing defecatory urge, relative to no-urge, should improve performance on tasks that require inhibitory control. Past research shows that increased urination urge reportedly enhanced inhibitory control only among individuals with high BIS sensitivity<sup>2</sup>. This is consistent with reinforcement sensitivity theory<sup>12,13</sup>, which argues that BIS fosters inhibition of prepotent conflicting behaviors and facilitate self-regulation. Therefore, we expected the positive consequences of controlling defecatory urge on self-regulation to be limited to participants with high BIS sensitivity.

Following past research, we chose the Stroop task and delay-discounting task to measure inhibitory control<sup>14</sup>. In particular, the Stroop task<sup>15</sup> is a robust and well-established method to

measure cognitive control. It measures people's ability to disregard distractions and override impulses in the service of task performance<sup>16,17</sup>. Moreover, delay discounting measures one's ability to resist immediate temptations and to wait for larger-later rewards, an index of patience and self-control. Both of these tasks are commonly used as measures of inhibitory control.

Finally, we used rectal distension technique (barostat) to induce and vary levels of defecatory urge. This is a widely used technique, which enables induction of rectal sensation in a systematic and intensity-controlled manner. This is important because while past research on bladder filling has found that inhibition of urination urge facilitates cognitive control<sup>2</sup>, other findings suggest that extreme urination urge may impair cognitive control<sup>18</sup>. Using a controlled rectal-distension method, therefore, enables us to test our hypothesis across different levels of defecatory urge (e.g., no, medium, and high urge) and to explicate potential boundaries of our hypothesis.

## **Materials and methods**

### ***Participants***

Healthy male, and non-pregnant, non-breastfeeding female participants, aged 18 – 60 years old at the time of consent, were recruited in this randomized, counterbalanced, single-blinded mechanistic interventional crossover study. Candidates with color blindness or those who used any medication or drugs (except contraceptive pills) were excluded. All study visits were conducted in the endoscopy unit, at University Hospital Gasthuisberg of the KU Leuven. The sample size was calculated based on previous results<sup>2</sup> showing a medium-sized effect of moderate urinary urge on Stroop performance in high BIS participants (one-tailed paired t-test,  $\alpha = 0.05$ , Cohen's  $d = 0.50$ , power = 85%). A schematic overview of the study is

presented in *Figure 1*.

### ***Ethical approval and clinical trial registration***

The study was approved by the Medical Ethics Committee of the University Hospitals Leuven; Belgium (ML10139, 17 Aug 2014), pre-registered at ClinicalTrials.gov (NCT02043561: <https://clinicaltrials.gov/>, 23 Jan 2014), and performed in accordance with the Declaration of Helsinki, including written informed consent.

### ***Behavioral Inhibition Sensitivity (BIS)***

The Behavioral Inhibition Sensitivity / Behavioral Activation Sensitivity scale (BIS/BAS)<sup>11</sup> was completed together with screening questionnaires before participants' visit to the lab. Participants were divided into two groups (high BIS group vs. low BIS group) based on a median split on the BIS scale.

### ***Distending device***

Rectal distensions were induced by an intra-rectal balloon (600 ml capacity) and controlled by an electronic barostat (Dual Drive Barostat, Distender Series II; G&J Electronics Inc, Toronto, Ontario, Canada). A personal computer running custom-made software provided by the manufacturer (Protocol Plus, G&J Electronics Inc, Toronto, Ontario, Canada) was used to program the barostat and to continuously record the intra-balloon pressure and volume.

### ***Preparation***

Following an overnight fast and rectal cleansing with tap water enema, a finely folded balloon was introduced in the participants' rectum with the caudal end 6 cm from the anal verge and then connected to the barostat device. Participants were placed in semi-recumbent position on

a bed. The balloon was then unfolded by inflation with 150 ml of air and thereafter completely deflated.

### ***Threshold determination***

The minimal distending pressure (MDP) was first determined, as the pressure level at which respiratory fluctuations were regularly recorded. To determine the individual threshold for defecatory urge, a stepwise pressure-controlled distension procedure (steps of 4 mmHg/30 seconds) starting from MDP was performed<sup>19,20</sup>, following a 15 min accommodation period. After 15 sec into each distension step, participants rated their perceived intensity of defecatory urge and pain, using a 100 mm visual analogue scale (VAS) ranging from “no urge” to “maximal urge” and “no pain” to “maximal pain” on a computer screen. The end of the stepwise distension procedure was established when the participants reported maximal urge (100 on the VAS), or at an intraballoon volume of 500 ml.

Three pressure thresholds were derived from this stepwise distension sequence<sup>20</sup>, and were used during the subsequent parts of the study:

1. no urge (balloon deflated)
2. moderate urge (first pressure step evoking a score of 41 or more on the urge VAS)
3. high urge (first pressure step evoking a score of 81 or more on the urge VAS)

After the stepwise distension, participants went through three tonic distension blocks, in which they were exposed to tonic distension at no urge, moderate urge and high urge pressure thresholds (in counterbalanced order) for 180 seconds and were asked to rate their urge and pain sensations on a VAS every 30 seconds (to ensure that this stimulus length would allow us to achieve stable pressures, volumes and above all ratings of moderate/high urge).



### *Test blocks*

Between the threshold determination and the test blocks, participants rested in bed for 10 min while the rectal balloon was not extubated. During each test block, rectal distension at one of the three individually titrated pressure thresholds, described above, was administered in counterbalanced order, with a 10-minute break in between. During each block, participants performed the Stroop task followed by the delay discounting task. At the end of each block, all participants rated VAS for urge and pain retrospectively.

### *Stroop task*

Stroop task requires participants to indicate the font color of a series of visually presented color words as quickly as possible. In *incongruent* trials, participants should ignore the meaning of the color word, thus override their dominant and impulsive response tendencies, and attend to its font color instead. Performance in the Stroop task is measured by the difference between reaction times (RTs) in incongruent and congruent trials, an index that is referred to as *Stroop interference*. A smaller Stroop interference score therefore indicates greater cognitive ability to disregard distractions and impulses and to stay focused on the goal.

The Stroop task consisted of three types of trials<sup>21</sup>. The “*word naming*” trials in which the color words (e.g., the word RED) were displayed in black font. The “*incongruent*” trials (e.g., the word RED in blue font) and the “*congruent*” trials (e.g., the word RED in red font) were displayed in colors. For congruent and incongruent stimuli, participants were instructed to neglect the meaning of the word, but only respond to the font color of the displayed stimuli. To respond across these trials, participants pressed one of three keys on a keyboard labelled with colors red, blue, or green that corresponded to the word color (i.e., in the word naming

trials) or the font color (i.e., in the congruent and incongruent trials) of the stimuli.

A Stroop trial consisted of the following sequence: a fixation cross for 500 ms, followed by a blank space for 500 ms, and stimulus presentation for 2000 ms. The inter-trial intervals were uniformly distributed between 1500 - 3000 ms. Responses were recorded between the start of stimulus presentation until 1500 ms into the intertrial interval; the stimulus disappeared from the screen as soon as the response was registered. Any response faster than 150 ms was considered abnormal and hence removed prior to the analysis; for each participant, the average reaction time for each trial type (i.e., congruent, incongruent, and word naming) was then calculated. As mentioned earlier, the main dependent variable was Stroop interference which was calculated by subtracting average response times in congruent trials from the average response time in incongruent trials for each participant.

At the beginning of the experiment, participants went through one practice block in which the three trial types were presented with instructions. During the practice block, the three trial types were presented in fixed order: word naming, congruent, and incongruent. Afterwards, at each distension level, participants performed a block of 30 Stroop trials, consisting 10 trials of each type. The 30 trials in each distension pressure level were presented in a random order and no feedback was provided. However, the practice block would repeat until participants responded to all 30 stimuli correctly. Colors were counterbalanced. Presentations were therefore unblocked and uncued within each trial block to ensure the maximal experience of conflict.

#### *Delay Discounting Task*

Immediately after each Stroop trial, participants performed a delay discounting task, consisting of 5 intertemporal monetary choices<sup>22</sup>. For each choice, participants indicated their

preference for either a smaller, sooner or a larger, later monetary reward<sup>22</sup> (e.g., “Would you prefer 24 euro now or 35 euro in 29 days?”). Participants pressed button ‘1’ on the keyboard to choose the immediate but smaller amount, and ‘2’ to choose the larger but delayed amount. Participants’ choices were then treated as binary outcomes in the logistic regression model. Overall, participants' tendency to choose larger, later rewards over smaller, sooner rewards signifies their ability to resist immediate temptations and to wait for larger rewards in future, a critical capacity for self-regulation.

In the informed consent form, and upon completion of the three test blocks all participants signed a document indicating that they would be awarded a fixed amount of money after completing the experiment.

### ***Statistical analysis***

All statistical analysis was done using SAS Version 9.4 (SAS Institute, Cary, NC, USA). Reaction times of the Stroop test were reported as mean  $\pm$  SEM. Differences were considered significant when  $p \leq 0.05$ . The variance-covariance structure providing the best fit was chosen based on the minimum value of Akaike’s Information Criterion (AIC).

The average of Stroop task reaction time was prepared per trial type in each test block using trimming methods<sup>23</sup>. All the erroneous responses, responses faster than 150 ms, and any responses 3SD above or below the mean of each condition were removed. The remaining data were then averaged for each urge and Stroop condition, for each participant. The pre-processed Stroop color naming data were then analyzed in a 3 (urge condition) x 3 (Stroop condition) within-subject mixed model including the urge condition-by-Stroop condition interaction effect in each BIS group separately, with the order of the test blocks, and the subjective pain rating added as covariates. Lower-tailed planned t-contrasts were performed to

test our hypotheses: reaction time differences between incongruent and congruent trials, defined as Stroop interference, decreases under moderate (but not under high urge) condition, compared to no urge condition, in the high BIS group, but not in the low BIS group. To control for effects of urge condition on reaction speed in general (i.e. not related to inhibitory processes), the pre-processed Stroop word naming reaction times (control stimuli) were also analyzed in a separate mixed model. Two-tailed planned t-contrasts were performed based on our hypothesis: the reaction time of Stroop word naming trials did not differ among urge conditions, for neither people with high-BIS nor the ones with low-BIS. .

Participants' choice between a larger later reward and a smaller immediate reward in the delay discounting task was treated as a binary dependent variable in generalized linear mixed models with urge condition as a within-subject factor, and order of the test block and subjective pain rating as covariates<sup>24</sup>, in each BIS group separately. The probability to choose a larger later reward was further compared in high vs. no urge condition, and moderate vs. no urge condition in each BIS group.

## Results

### *Participants*

Thirty-five healthy volunteers [23 (66%) women, age:  $22 \pm 0.3$  years, recruited between 10-Sep-2014 and 03-Sep-2015] participated in the study (*supplementary Figure 1*). Participants were divided into high ( $n=17$ ) and low ( $n=18$ ) BIS groups, based on a median split of their BIS score (median 22 [18, 23]). The demographic characteristics of the participants are presented in *Table 1*. All participants completed the study and there was no adverse event reported throughout the experiment. The overall error rate in the Stroop task was 2.32%, and all participants completed the Stroop task with more than 90% correction rate. Therefore, no participant was excluded for too many erroneous responses. *Table 2* shows the overall erroneous rate in the Stroop task in each urge condition. Further, statistical analysis was also performed on Stroop interference including the number of errors as a covariate, but the major outcomes did not change.

### *Manipulation check*

The average retrospective urge ratings, measured at the end of each test block, were significantly higher in the moderate ( $41.0 \pm 3.3$  mm) and high ( $67.2 \pm 4.2$  mm) urge conditions compared to the no urge condition ( $20.0 \pm 3.3$  mm), as shown in *Figure 2a* (main effect of urge condition,  $F_{2,34} = 52.65$ ,  $p < 0.0001$ , planned contrast: moderate urge vs. no urge,  $t_{34} = 5.08$ ,  $p_{\text{Holm}} < 0.0001$ , high urge vs. no urge,  $t_{34} = 9.48$ ,  $p_{\text{Holm}} < 0.0001$ , high urge vs. moderate urge,  $t_{34} = 7.82$ ,  $p_{\text{Holm}} < 0.0001$ ). These results confirm that our urge manipulation was successful and worked as intended.

Similarly, retrospective pain ratings, measured at the end of each test block, were significantly

higher in the high urge ( $27.3 \pm 4.9$  mm) compared to the no urge ( $5.4 \pm 1.7$  mm) condition. However, no difference between the moderate urge ( $11 \pm 2.9$  mm) and no urge conditions was found (main effect of urge condition,  $F_{2,34} = 14.76$ ,  $p < 0.0001$ , planned contrast, moderate vs. no urge,  $t_{34} = 1.90$   $p_{\text{Holm}} = 0.15$ , high vs. no urge,  $t_{34} = 5.39$   $p_{\text{Holm}} < 0.0001$ , high vs. moderate urge,  $t_{34} = 4.50$   $p_{\text{Holm}} = 0.0002$ ), as shown in *Figure 2b*. Given the differences in pain ratings between the high urge and the other conditions, we controlled for pain ratings in all subsequent analyses.

### ***Stroop interference***

#### *High BIS group*

Consistent with our hypothesis, the Stroop interference was significantly smaller in the moderate urge condition compared to the no urge condition (planned contrast, lower tail, moderate urge  $128 \pm 41$  ms vs. no urge  $202 \pm 37$  ms,  $t_{64} = -2.07$ ;  $p_{\text{Holm}} = 0.021$ , Cohen's  $d: -0.44$ ), indicating that moderate urge improves inhibitory control. However, we did not find a difference in Stroop interference between the high urge and no urge conditions (planned contrast, lower tail, high urge  $154 \pm 45$  ms vs. no urge  $202 \pm 37$  ms,  $t_{64} = -1.20$ ,  $p_{\text{Holm}} = 0.12$ , Cohen's  $d: -0.30$ ).

#### *Low BIS group*

Consistent with our hypothesis, urge conditions did not predict cognitive control among people with low BIS sensitivity. Specifically, we did not find significant differences, neither between the moderate urge and no urge conditions (planned contrast, lower tail, moderate urge  $158 \pm 32$  ms vs. no urge  $168 \pm 24$  ms,  $t_{68} = -0.34$   $p_{\text{Holm}} = 0.37$ , Cohen's  $d: -0.08$ ), nor between the high urge and no urge conditions (planned contrast, high urge  $178 \pm 27$  ms vs. no

urge  $168 \pm 24$  ms,  $t_{68} = 0.72$   $p_{\text{Holm}} = 0.76$ , Cohen's d: 0.17).

*Figure 3* shows the Stroop interference scores as a function of urge conditions in both the high and the low BIS group.

Together, these results are consistent with our hypothesis that (moderate) defecatory urge, improves inhibitory control ability, only in people with high-BIS sensitivity.

### ***Stroop word naming***

Contrary to the Stroop color naming trials, the Stroop word naming trials consisted of color words (e.g., the words, RED, BLUE, and GREEN) displayed in black font. Specifically, in these trials, participants reacted only to the words, instead of font color. As expected, there was no effect of urge on reaction times in this word-naming task, which did not require conflict resolution (planned contrasts, two-tailed, high BIS group: moderate vs. no urge  $t_{68} = 0.49$   $p_{\text{Holm}} = 0.63$  Cohen's d: 0.12, high vs. no urge  $t_{68} = 0.81$   $p = 0.42$  Cohen's d: 0.20; low BIS group: moderate vs. no urge  $t_{68} = 1.04$   $p_{\text{Holm}} = 0.30$  Cohen's d: 0.25, high vs. no urge  $t_{68} = 0.76$   $p_{\text{Holm}} = 0.45$  Cohen's d: 0.18).

### ***Delay discounting task***

#### ***High BIS group***

As shown in *Figure 4*, participants preferred the larger later reward more frequently under high urge compared to no urge ( $z = 2.06$ ,  $p = 0.039$ , odds ratio = 1.51, 95% CI: 1.02 – 2.25). However, participants' preference under moderate urge was not significantly different from their preference in the no urge condition ( $z = 0.11$ ,  $p = 0.91$ , odds ratio = 1.02, 95% CI: 0.73 – 1.42). Overall, these results suggest that increased levels of urge render more patience in intertemporal choices, among people with high BIS.

### *Low BIS group*

As expected, urge conditions did not predict patience in intertemporal choices among participants with low BIS. Specifically, participants' preference under high urge was not significantly different from no urge ( $z = -1.61$ ,  $p = 0.11$ , odds ratio = 0.67, 95%CI: 0.42 – 1.09), nor did their preference differ significantly between the moderate urge and no urge conditions ( $z = -0.21$ ,  $p = 0.83$ , odds ratio = 0.93, 95%CI: 0.50 – 1.75), as shown in *Figure 4*.



## Discussion

Building on past findings suggesting the existence of a common, domain-independent inhibitory control system, we hypothesized and provided empirical evidence that inhibition of defecatory urge facilitates inhibitory control, across both cognitive and financial decision-making (i.e., increased patience in the delay discounting) domains, among individuals with high BIS.

Particularly, with respect to inhibitory control, our findings demonstrate that among participants with high BIS, moderate (but not high) urge significantly reduced Stroop interference, compared to a no urge condition. In other words, high-BIS participants showed improved ability in inhibiting their automatic response tendencies under moderate defecatory urge induced by the rectal balloon. Moreover, we found that high-BIS participants also showed more patience in the intertemporal monetary choices under high (but not moderate) urge, relative to no urge. Furthermore, in line with our reasoning, among individuals with low BIS, increased defecatory urge did not predict enhancement in the Stroop performance, nor did it increase patience in the delay discounting task. Overall, our findings are consistent with the inhibitory “spill-over” effect that was found earlier under increased urge to urinate among high BIS individuals<sup>2</sup>.

While our findings are consistent with the existence of a domain-general inhibitory control system, further research is necessary for explicating the neurological underpinnings of this system. From a neurological perspective, the anterior midcingulate cortex (aMCC, Brodmann 24) and adjacent pregenual anterior cingulate cortex (pACC, Brodmann 32) may be central to the inhibitory “spill-over” effects, given their important role in conflict detection<sup>5,25</sup>. For example, pACC<sup>26,27</sup> has differential responses to incongruent trials (i.e., when the font color mismatches the word meaning) compared to congruent trials in the Stroop task, and those

differential responses further extend over central and parietal brain regions. Moreover, the adjacent regions along the cingulate sulcus implement a domain-general process in inhibitory control<sup>28</sup>, and overlap partly with representations from other functions, such as pain, in the border between the aMCC and posterior midcingulate cortex<sup>29</sup>. Importantly, a meta-analysis by Tillisch *et al.*<sup>30</sup> revealed that the pACC and the aMCC were also activated in response to rectal balloon distension in healthy controls. Furthermore, Amodio *et al.* found a correlation between participants' BIS sensitivity and pACC/aMCC responses to error detection in an electroencephalography study<sup>31</sup>. More specifically, participants with higher BIS had stronger responses in the adjacent area between the pACC and aMCC when they performed a No-Go task, in which they were requested NOT to respond to a certain cue<sup>31</sup>. In our study, the Stroop task, like the No-Go task, also required participants to inhibit their impulsive response tendencies. This might explain the differential effects in the high BIS and low BIS groups in our study. Putting the evidence together, we propose that the brain responses to rectal filling and BIS modulated inhibitory control overlapped in the adjacent cingulate subregions including pACC and aMCC. These regions may serve as an integrative center that mediated the 'spill-over' effect observed in our study.

The delay discounting task consists of a series of choices between a smaller-sooner monetary reward and a larger-later reward. Therefore, the task is often used to measure the ability to control impulsiveness in order to maximize future outcomes. While Stroop performance and delay discounting both tap into self-regulation ability, and both are improved when people simultaneously control the urge to void<sup>2</sup>, our findings suggest that these tasks seem to respond to different experienced levels of defecatory urge. Recent work has also found other dissociations between these tasks<sup>32</sup>. Indeed, in the delay discounting task, brain regions that are related to self-regulation and inhibition were activated when participants made an

impulsive choice, including medial orbital frontal cortex, and medial prefrontal cortex (mPFC)<sup>1,14</sup>, but not including the abovementioned pACC or the aMCC, which are associated with inhibitory control. Further research needs to examine exactly why different tasks are differentially sensitive to urge level. One crucial difference might be that resisting to the lure of immediate financial rewards, and to wait for later large rewards, is a higher order ‘self-control’ task which not only depends on people’s ability to inhibit impulses but also depends on their subjective processing of delay times<sup>33,34</sup>. Therefore, in contrast to the Stroop task, an delay discounting task might involve multiple cognitive operations<sup>1</sup>, and is subject to individual differences in relative salience of saving and spending goals.

Another consideration is that the high urge condition was accompanied by increased pain experience, relative to the two other conditions. Pain could interrupt attention<sup>35</sup>, and might do so more in a basic cognitive control task (e.g., the Stroop task), compared to when people try to exert higher order, motivated, self-control (e.g., in intertemporal choices ). Notably, we used pain ratings as a covariate in all of our analysis, and it did not significantly influence any of the major outcomes. In addition to the effect induced by pain, extremely high urge might also undermine cognitive control. Although we did not extend our investigation to extreme, unbearable, high urges, prior research has found decrements in cognitive performance when the urge (to urinate) increased to a very high, unbearable, level<sup>18</sup>. It is however noteworthy that that the prior research had a rather small sample size (n = 8). Therefore, further investigation is necessary to confirm the differential cognitive responses to moderate and extremely high physiological urge conditions.

In our study, we limited our participants to the healthy normal weight population, and did not include patients with functional bowel disorders such as irritable bowel syndrome (IBS), which is currently viewed as caused by dysregulation of the ‘brain-gut axis’<sup>36</sup>. Moreover,

patients with IBS have shown increased sensitivity<sup>37,38</sup> to rectal distension compared to normal controls, both in terms of urge and pain thresholds. Therefore, it would be interesting to investigate inhibitory control responses to different levels of rectal distension above and below the urge threshold of patients with IBS.

In summary, we found that inhibition of the urge to defecate facilitated inhibitory control, and rendered more patience in the delay discounting task, among healthy humans with high BIS sensitivity. These findings have the potential to improve our understanding of the nature of different volitional cognitive control processes and their interaction.

## **Acknowledgements**

We would like to acknowledge the infrastructural support of Lieselot Holvoet in the Endoscopy Unit, University Hospital Gasthuisberg. We would also like to thank Jessica Biesiekierski and Julie Iven for language editing support, and Mark Phillip Keller for his technical assistance.

## **Funding**

The work was supported in part by a grant from FWO Flanders (Grant No. G.0.396.10.N.10) to Luk Warlop and by a grant (STRT/12/002) from the KU Leuven Special Research Fund to Lukas Van Oudenhove.

## **Disclosures**

DZ, MC, NW, MM-J, MT, LW and LVO designed the research; DZ and MC collected the data; DZ, MM-J, and LVO analyzed data and performed statistical analyses; DZ and LVO wrote the manuscript. MM-J, LW, JT and MC revised the manuscript. LVO and LW had primary responsibility for the final content. All authors read and approved the final manuscript. The authors have nothing to disclose.

## References

1. Hofmann W, Schmeichel BJ, Baddeley AD. Executive functions and self-regulation. *Trends in cognitive sciences*. 2012;16(3):174-180.
2. Tuk MA, Trampe D, Warlop L. Inhibitory spillover: increased urination urgency facilitates impulse control in unrelated domains. *Psychol Sci*. 2011;22(5):627-633.
3. Berkman ET, Burklund L, Lieberman MD. Inhibitory spillover: intentional motor inhibition produces incidental limbic inhibition via right inferior frontal cortex. *Neuroimage*. 2009;47(2):705-712.
4. Fenn E, Blandón-Gitlin I, Coons J, Pineda C, Echon R. The inhibitory spillover effect: Controlling the bladder makes better liars \*. *Conscious Cogn*. 2015;37:112-122.
5. Critchley HD. Neural mechanisms of autonomic, affective, and cognitive integration. *J Comp Neurol*. 2005;493(1):154-166.
6. MacDonald AW, 3rd, Cohen JD, Stenger VA, Carter CS. Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science*. 2000;288(5472):1835-1838.
7. Todd S. Braver JDC. On the control of control: The role of dopamine in regulating prefrontal function and working. Paper presented at: MIT Press. Making Working Memory Work2000.
8. Mertz H, Morgan V, Tanner G, et al. Regional cerebral activation in irritable bowel syndrome and control subjects with painful and nonpainful rectal distention. *Gastroenterology*. 2000;118(5):842-848.
9. Athwal BS, Berkley KJ, Hussain I, et al. Brain responses to changes in bladder volume and urge to void in healthy men. *Brain*. 2001;124(Pt 2):369-377.
10. Cohen JR, Lieberman MD. The common neural basis of exerting self-control in multiple domains. In: Hassin RR, Ochsner KN, Trope Y, eds. *Self-control in society, mind, and brain*. Vol 1. Oxford University Press; 2010:141-160.
11. Carver CS, White TL. Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS scales. *Journal of personality and social psychology*. 1994;67(2):319.
12. Gray JA, McNaughton N. *The neuropsychology of anxiety: An enquiry into the function of the septo-hippocampal system*. Oxford university press; 2003.
13. Corr PJ. Reinforcement sensitivity theory and personality. *Neurosci Biobehav Rev*. 2004;28(3):317-332.
14. McClure SM, Laibson DI, Loewenstein G, Cohen JD. Separate neural systems value immediate and delayed monetary rewards. *Science*. 2004;306(5695):503-507.
15. Stroop JR. Studies of interference in serial verbal reactions. *Journal of Experimental Psychology*. 1935;18(6):643.
16. Kane MJ, Engle RW. Working-memory capacity and the control of attention: the contributions of goal neglect, response competition, and task set to Stroop interference. *J Exp Psychol Gen*. 2003;132(1):47-70.
17. Miyake A, Shah P. *Models of working memory: Mechanisms of active maintenance and executive control*. Cambridge University Press; 1999.
18. Lewis MS, Snyder PJ, Pietrzak RH, Darby D, Feldman RA, Maruff P. The effect of acute increase in urge to void on cognitive function in healthy adults. *Neurourology and urodynamics*. 2011;30(1):183-187.

19. Basilisco G, De Marco E, Tomba C, Cesana BM. Bowel urgency in patients with irritable bowel syndrome. *Gastroenterology*. 2007;132(1):38-44.
20. Kwan CL, Mikula K, Diamant NE, Davis KD. The relationship between rectal pain, unpleasantness, and urge to defecate in normal subjects. *Pain*. 2002;97(1-2):53-63.
21. Floden D, Vallesi A, Stuss DT. Task context and frontal lobe activation in the Stroop task. *J Cogn Neurosci*. 2011;23(4):867-879.
22. Kirby KN, Petry NM, Bickel WK. Heroin addicts have higher discount rates for delayed rewards than non-drug-using controls. *Journal of Experimental Psychology: General*. 1999;128(1):78.
23. Selst MV, Jolicoeur P. A solution to the effect of sample size on outlier elimination. *The quarterly journal of experimental psychology*. 1994;47(3):631-650.
24. Jones J, Sullivan PS. Impulsivity as a risk factor for HIV transmission in men who have sex with men: a delay discounting approach. *J Homosex*. 2015;62(5):588-603.
25. Lieberman MD, Eisenberger NI. The dorsal anterior cingulate cortex is selective for pain: Results from large-scale reverse inference. *Proc Natl Acad Sci U S A*. 2015;112(49):15250-15255.
26. Badzakova-Trajkov G, Barnett KJ, Waldie KE, Kirk IJ. An ERP investigation of the Stroop task: the role of the cingulate in attentional allocation and conflict resolution. *Brain Res*. 2009;1253:139-148.
27. Carter CS, van Veen V. Anterior cingulate cortex and conflict detection: an update of theory and data. *Cogn Affect Behav Neurosci*. 2007;7(4):367-379.
28. Shackman AJ, Salomons TV, Slagter HA, Fox AS, Winter JJ, Davidson RJ. The Integration of Negative Affect, Pain, and Cognitive Control in the Cingulate Cortex. *Nat Rev Neurosci*. 2011;12(3):154-167.
29. Kragel PA, Kano M, Oudenhove LV, et al. Generalizable representations of pain, cognitive control, and negative emotion in medial frontal cortex. *Nature Neuroscience*. 2018;21(2):283.
30. Tillisch K, Mayer EA, Labus JS. Quantitative meta-analysis identifies brain regions activated during rectal distension in irritable bowel syndrome. *Gastroenterology*. 2011;140(1):91-100.
31. Amodio DM, Master SL, Yee CM, Taylor SE. Neurocognitive components of the behavioral inhibition and activation systems: implications for theories of self-regulation. *Psychophysiology*. 2008;45(1):11-19.
32. Scherbaum S, Frisch S, Holfert AM, O'Hora D, Dshemuchadse M. No evidence for common processes of cognitive control and self-control. *Acta Psychol (Amst)*. 2017;182:194-199.
33. Zauberman G, Kim BK, Malkoc SA, Bettman JR. Discounting time and time discounting: Subjective time perception and intertemporal preferences. *Journal of Marketing Research*. 2009;46(4):543-556.
34. Kim BK, Zauberman G. Perception of anticipatory time in temporal discounting. *Journal of Neuroscience, Psychology, and Economics*. 2009;2(2):91.
35. Eccleston C, Crombez G. Pain demands attention: a cognitive-affective model of the interruptive function of pain. *Psychol Bull*. 1999;125(3):356-366.
36. Kennedy PJ, Clarke G, O'Neill A, et al. Cognitive performance in irritable bowel syndrome: evidence of a stress-related impairment in visuospatial memory. In: *Psychol Med*. Vol 44.2014:1553-1566.
37. Tornblom H, Van Oudenhove L, Tack J, Simren M. Interaction between preprandial and postprandial rectal sensory and motor abnormalities in IBS. *Gut*.

- 2014;63(9):1441-1449.
38. Zar S, Benson MJ, Kumar D. Rectal afferent hypersensitivity and compliance in irritable bowel syndrome: differences between diarrhoea-predominant and constipation-predominant subgroups. *Eur J Gastroenterol Hepatol.* 2006;18(2):151-158.



## **Abbreviations**

BIS	behavioral inhibition system
BAS	behavioral activation system
MDP	minimal distending pressure
VAS	visual analogue scale
RT	reaction time
AIC	Akaike's information criterion
aMCC	anterior midcingulate cortex
pACC	pregenual anterior cingulate cortex
mPFC	medial prefrontal cortex
IBS	irritable bowel syndrome

**Table**

*Table 1. Demographic characteristics of participants.*

	<b>High BIS group</b>	<b>Low BIS group</b>		<b>P value</b>
			Chi-squared	
Gender (F/M)	12/5	11/7	0.097	0.76
			t	
Age (year)	23.5±1.4	22.2±0.4	0.84	0.41
BIS score	23.7±0.4 [range: 22,28]	18.4±0.4 [range: 16,21]	9.18	<0.0001

*Table 2. Error rate of Stroop tasks in each Stroop type in each urge condition. Error rate was higher in the incongruent trials compared to congruent or word naming trials. Further, the error rate did not differ between urge conditions. (Friedman's Chi-square test, Stroop type:  $Q=17.6$   $p=0.0001$ , Urge condition:  $Q=1.69$   $p=0.43$ )*

<b>Urge condition</b>	<b>Stroop type</b>		
	incongruent	congruent	word naming
no urge	4.29%	0.86%	2.57%
moderate urge	2.28%	1.14%	2.28%
high urge	4.86%	0.57%	1.71%

## Figure legends

**Figure 1. Schematic overview of the experimental procedure.** (A) overview of a study visit: firstly, a threshold determination involving a stepwise distension session was undertaken, followed by tonic distension blocks to ensure that the stimulus length would allow stable pressure, volumes, and ratings of moderate/high urge. Finally, 3 test blocks were performed (one for each level of urge) in a counterbalanced order. (B) overview of a test block: firstly, instructions were provided, and a Stroop practice session was undertaken, followed by 30 Stroop trials in a randomised order, followed by 5 delay discounting tasks. At the end of each test block, retrospective ratings of urge and pain were collected using visual analogue scales (VAS). (C) an example of a Stroop trial: presented in the following sequence: a fixation cross displayed 500 ms, followed by a blank space for 500 ms, followed by stimulus presentation for 2000 ms, followed by an inter-trial blank space whose display time varied between 1500 and 3000 ms (uniform distribution) until the next trial.

**Figure 2. Rectal barostat successfully induced defecatory urge in both moderate and high urge conditions.** Average VAS (A) urge scores in high and moderate urge conditions were significantly higher than in no urge condition (\*  $p < 0.05$ ), and average VAS (B) pain scores in high urge condition was higher than in no urge condition (\*  $p < 0.05$ ). VAS, visual analogue scale (0 – 100 mm).

**Figure 3. Stroop interference was smaller under moderate (but not high) urge condition, both compared to no urge condition, in the high BIS group (\*  $p < 0.05$ ).** The Stroop interference was not predicted by urge conditions in the low BIS group.

**Figure 4. The probability that participants chose a larger-later reward, and thus show more patience, in the delay discounting task was higher under the high (but not moderate) urge condition, both compared to no urge condition, in the high BIS group (\*p < 0.05). Among participants with low BIS, urge conditions did not significantly predict the choice of larger-later rewards.**

## Figures

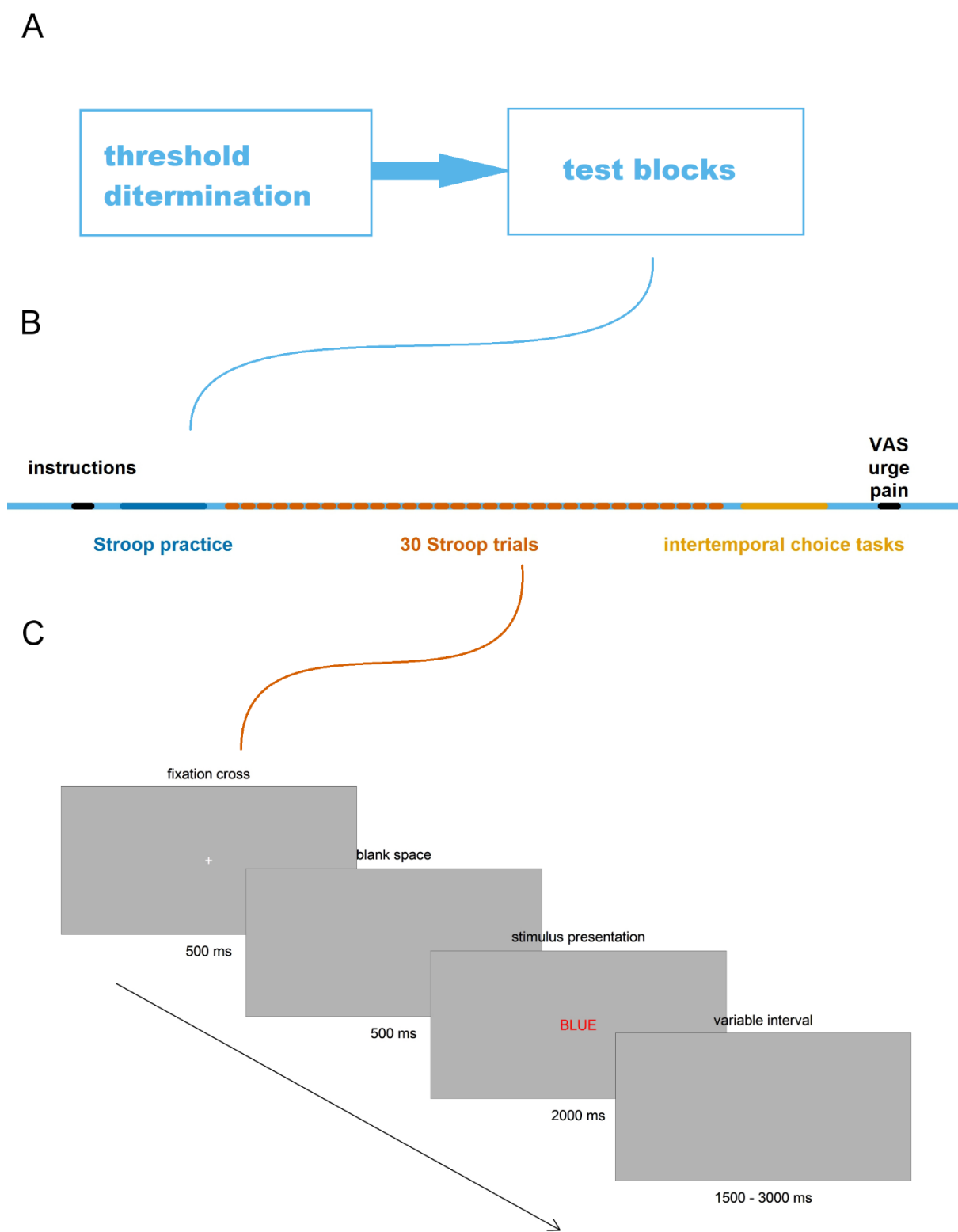


Figure 1

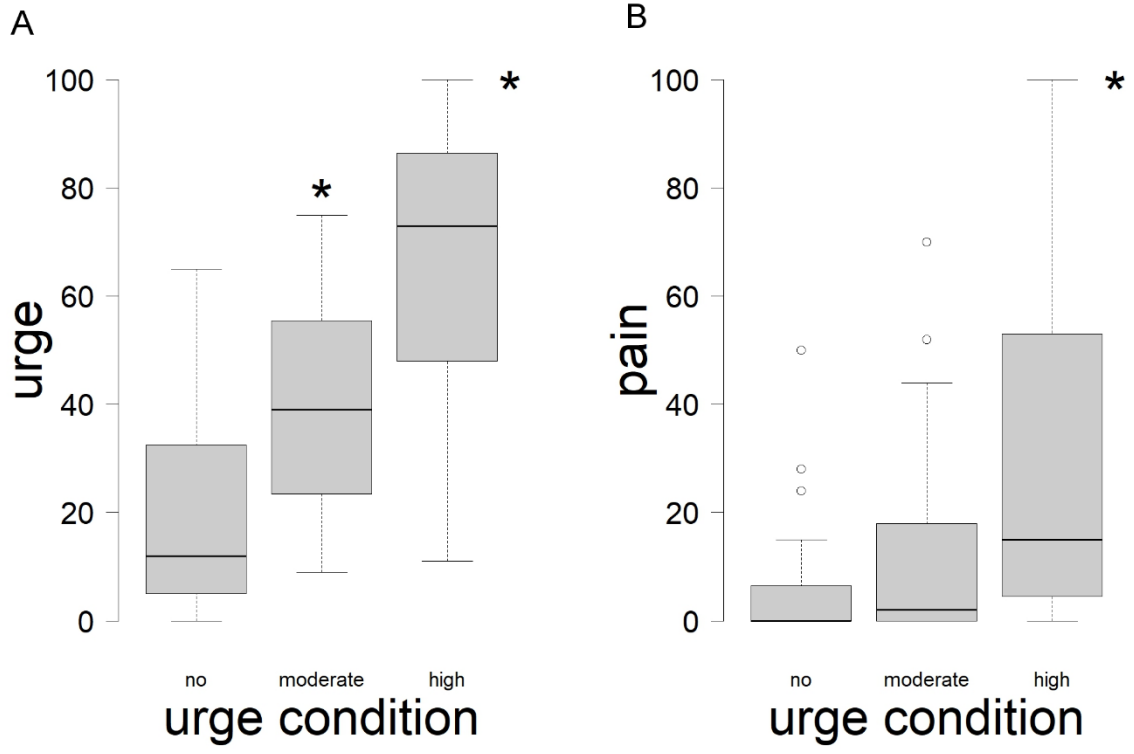


Figure 2

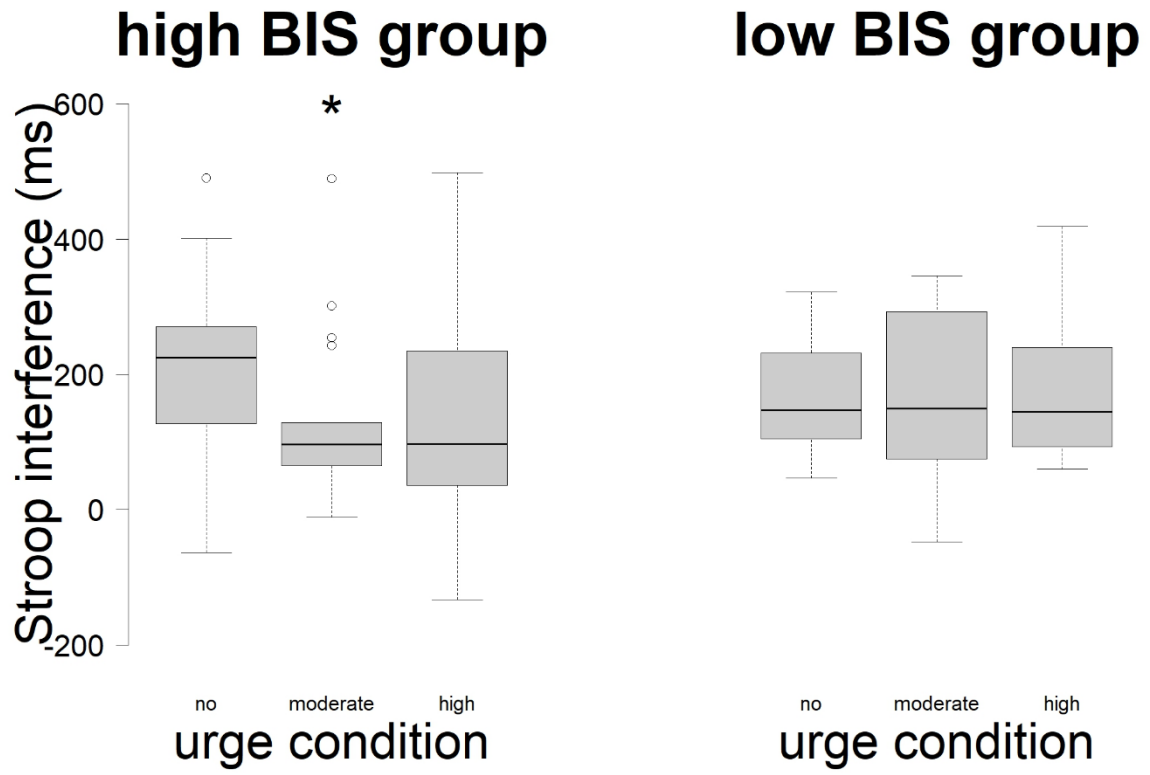


Figure 3



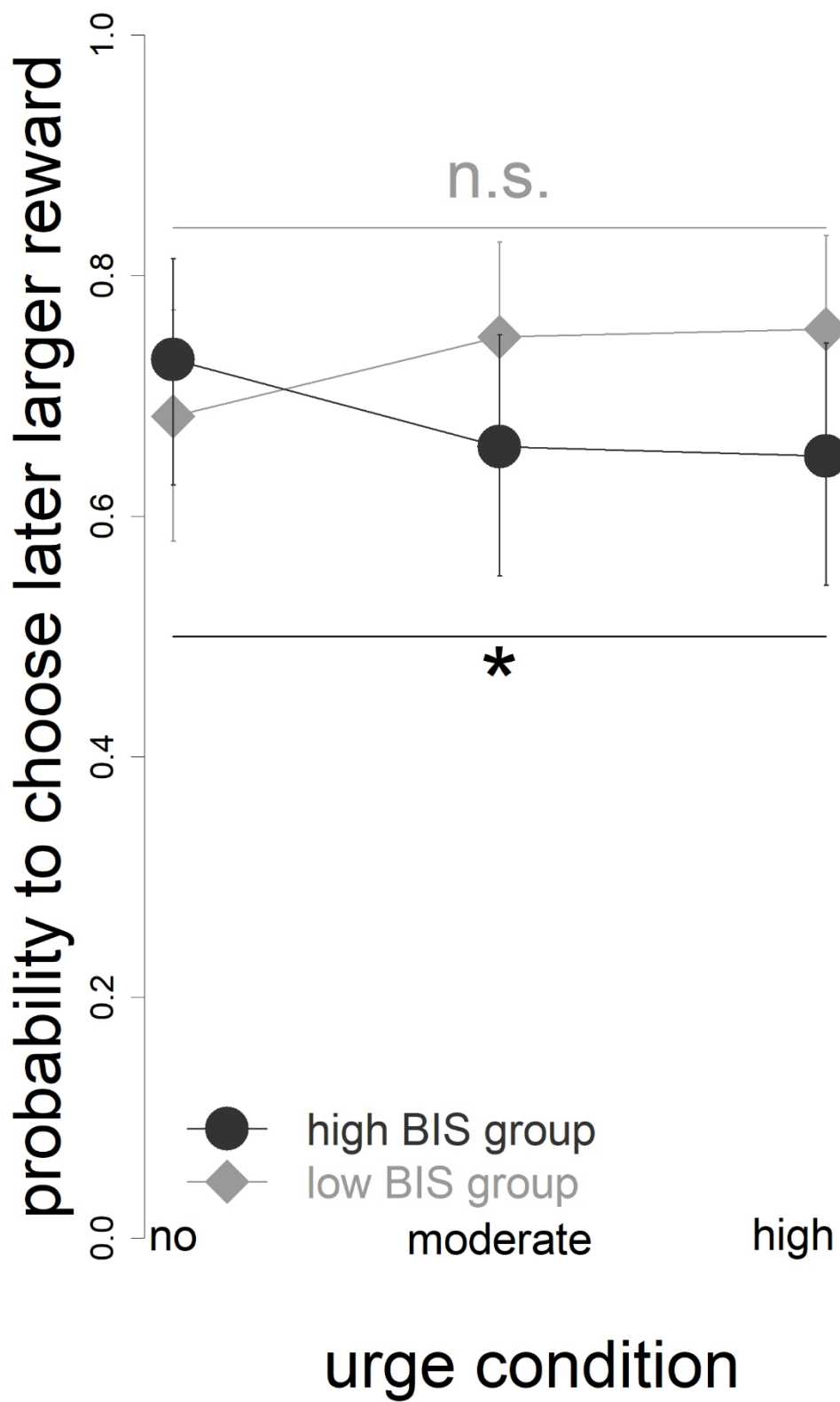


Figure 4