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Striatal dopamine D2 binding correlates with locus of control: Preliminary evidence from $[^{11}C]$raclopride Positron Emission Tomography

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ABSTRACT

The ability to exert control has been widely investigated as a hallmark of adaptive behaviour. Dopamine is recognized as the key neuromodulator mediating various control-related processes. The neural mechanisms underlying the subjective perception of being in control, or Locus of Control (LOC) are however less clear. LOC indicates the subjective tendency to attribute environmental outcomes to one's actions (internal LOC) or instead to external incontrollable factors (external LOC). Here we hypothesized that dopamine levels also relate to LOC. Previous work shows that dopamine signaling mediates learning of action-outcome relationships, outcome predictability, and opportunity cost. Prominent theories propose dopamine dysregulation as the key pathogenetic mechanism in schizophrenia and depression. Critically, external LOC is a risk factor for schizophrenia and depression, and predicts increased vulnerability to stress. However, a direct link between LOC and dopamine levels in healthy control had not been demonstrated. The purpose of our study was to investigate this link. Using $[^{11}C]$raclopride Positron Emission Tomography we tested the relationship between D2 receptor binding in the striatum and LOC (measured with the Rotter Locus of Control scale) in 15 healthy volunteers. Our results show a large and positive correlation: increased striatal D2 binding was associated with External LOC. This finding opens promising avenues for the study of several psychological impairments that have been associated with both dopamine and LOC, such as addiction, schizophrenia, and depression.

1. Introduction

Life is full of dilemmas. Humans need to learn which life choices will lead to the most fulfilling results, which habits are the healthiest, and generally which behaviors are the most adaptive. Navigating such a complex scenario of opportunities requires several cognitive skills, amongst which the ability to exert control. This skill has been extensively studied in psychology and neuroscience research. Control includes the ability to overcome automatic responses in favor of an unusual yet more appropriate response (cognitive control, (Alexander and Brown, 2010; Botvinick et al., 2001), the ability to learn and select actions leading to better outcomes (Holroyd and Coles, 2008; Silvetti et al., 2014), the ability to perform challenging and effortful tasks when necessary to achieve a goal (effortful control Silvetti et al., 2018; Vassena et al., 2017a; Vassena et al., 2017b; Verguts et al., 2015), the ability to face unexpected events (Alexander and Brown, 2011; Silvetti et al., 2011), and the ability to refrain from unnecessary or maladaptive behavior (self-control, Maier et al., 2015). Partially dissociable underlying neural mechanisms have been implicated in these aspects of control, including the medial prefrontal cortex (MPFC, Braver, 2015; Chong et al., 2017; Klein-Flügge et al., 2016; Vassena et al., 2014a; Vassena et al., 2014b) and the lateral prefrontal cortex (LPFC, Bahlmann et al., 2015; Braver, 2012; Miller and Cohen, 2001; Vassena et al., 2018).

The above-described studies provided a detailed understanding of the *objective* aspects of control exertion. *Subjective control,* i.e. the perception of control that an agent has over its environment, received substantial attention in psychological and neuroscience research. For example, several studies investigated perception of control through intentional binding paradigms. This line of studies investigates the likelihood that an agent will infer a causal link between an action and an outcome due to their temporal contiguity, and its relationship with

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the feeling of agency, i.e. having generated the outcome (Kühn et al., 2013; Moore and Obhi, 2012; Vastano et al., 2018).

Personality psychology takes an individual differences perspective toward subjective control, conceptualized as resulting from a process of causal attribution. In this framework, external events can be perceived as caused by external and uncontrollable factors, or they can instead be perceived as the consequence of internal factors. This attributional process is termed Locus of Control (LOC, Rotter, 1966). People with an external LOC mainly attribute events to external forces over which they have no control, such as fate or chance. People with an internal LOC mainly consider themselves and their own actions as causes of events, and believe to be in control of their lives.

The concept of feeling control over the environment has also been investigated in affective and behavioral neuroscience. Here, controllability reflects the belief that external events follow from one's actions (similarly to internal LOC) (Huys and Dayan, 2009). Lack of perceived control has an important effect on affective processing. For example, uncontrollability affects reaction to stress (Bollini et al., 2004; Sanchís-Ollé et al., 2019). Exposure to an uncontrollable stressor is a classic experimental protocol used to induce learned helplessness in animal research, as a model for depression (Maier, 1984). Conversely, perceived control over a situation is experienced as valuable, and elicits neural activity in the brain reward system, including the ventral striatum (Leotti and Delgado, 2014; Ly et al., 2019; Wang and Delgado, 2019).

Despite the extensive empirical evidence gathered on the subjective perception of control, a mechanistic understanding of how LOC is determined (and how it interacts with objective control and with affect) is still lacking. As a step toward resolving this, we here investigated the neural correlates of LOC. In particular, we hypothesized dopamine (DA) as key neuromodulator involved in determining LOC. DA signals originate in the midbrain and are relayed to the cortex via the striatum. DA signaling mediates several (objective and subjective) control-related processes, which have been investigated focusing on both phasic (fast) and tonic (slow) time scales. Phasic DA firing plays a key role in linking outcomes to actions (Schott et al., 2008; Schultz et al., 1997a), learning which actions are rewarded (Bromberg-Martin et al., 2010; Schultz et al., 1997b), and selecting actions based on a cost-benefit trade off (Silvetti et al., 2018). In line with these findings, reward signaling, including coding of subjective value of stimuli or actions, also elicits striatal activity (Sescousse et al., 2013). Phasic DA signaling is also thought to support striatal gating of information in and out cortical working memory representations (Badre and Frank, 2012; Frank and Badre, 2012).

Besides these phasic DA effects, also tonic DA signaling may relate to (objective and subjective) control. Tonic DA has been proposed as biological driver of response vigor (Niv et al., 2007). In this view, DA levels reflect opportunity cost: any action is costly, because the time spent on it is time taken away from alternative and potentially rewarding actions. Therefore, a very rewarding environment will lead the agent to respond more vigorously because the time spent on any single response is more costly (equals foregoing more rewards). Further, it has been proposed that perceived control is tightly linked to the reward structure of the environment and reward predictability, with a putative key role of DA (Ly et al., 2019). A convergent Bayesian framework defines control based on the degree of entropy of action-outcome associations (Huys and Dayan, 2009). When the association is deterministic (one action is always followed by the same outcome), entropy is low; if additionally the low-entropy outcomes are also rewarding, there is more control. When outcomes cannot reliably be predicted from actions (high entropy), there is less control. Finally, tonic DA level has been related to the willingness to exert control in exchange for rewards, by offsetting the cost of control expenditure (Westbrook and Braver, 2016; Froböse et al., 2018). Critically, each of these theories proposes DA signaling as a core underlying substrate of control.

From an individual-differences perspective, variability in DA levels in the striatum have been associated with inter-individual variation in (phasic or tonic) control-relevant processes, including working memory (van der Schaaf et al., 2013), impulsivity (Trifilieff and Martinez, 2014), cognitive flexibility (van Holstein et al., 2011) and reversal learning (Cools et al., 2009; van der Schaaf et al., 2014). Striatal DA levels have also been linked to altered decision-making, particularly in the case of risk-taking behaviors, such as pathological gambling (Ojala et al., 2018; van Holst et al., 2018). Finally, one previous study reported a correlation between white matter volume in the striatum and LOC (Hashimoto et al., 2015).

The reviewed literature points toward a key role of striatal DA in objective (phasic and tonic) aspects of control exertion, as well as in accounting for inter-individual variability in such control-related processes. We hypothesize that striatal DA mediates inter-individual variability in subjective perception of control as well, as measured by the LOC questionnaire.

Besides the relation between objective control and DA, two other lines of evidence are suggestive of a connection between subjective control (LOC) and DA. First, earlier studies observed a link between LOC and two proxy measures of DA baseline levels, namely blink rate (Declerck et al., 2006b), and DA metabolites (De Brabander and Declerck, 2004; reviewed in Declerck et al., 2006a). Second, the LOC trait also interacts with affective processing, for example by mediating how people react to stress, a process also modulated by DA (Cabib and Puglisi-Allegra, 1996; Trainor, 2011). Internal LOC is associated with lower cortisol response during a stressor when people could control stressor intensity (Bollini et al., 2004). Internal LOC is a protective factor for psychopathology, associated with good health and lower risk of depression (Gale et al., 2008). Conversely, external LOC is a risk factor for developing psychotic symptoms and depression (Sullivan et al., 2017). External LOC also increased the risk of developing depressive symptoms in adolescents with a history of socio-economic adversity (Culpin et al., 2015). External LOC increases the likelihood of psychotic-like experiences in people with previous traumatic life events (Gibson et al., 2018). Patients with psychotic symptoms, and particularly schizophrenia, show external LOC. Intriguingly, abnormal levels of striatal DA have been observed in psychosis, and especially D2 receptor binding. An influential theory on the neural basis of schizophrenia indeed proposes that the disorder may follow from dopaminergic dysregulation (hypersensitivity) (Deserno et al., 2016; Grace, 2016; Seeman, 2013). Animal studies suggest that this abnormality would be triggered by excessive upregulation of D2 receptors in the striatum (Simpson and Kellendonk, 2017). In humans, it is proposed that such dopaminergic dysregulation would lead to increased vulnerability to stressful events, eventually triggering the onset of schizophrenia (Howes et al., 2017). One recent study investigating DA synthesis capacity in the striatum also found increased levels for schizophrenic (as well as bipolar) patients compared to controls (Jauhar et al., 2017).

Overall, evidence from research on different forms of control points toward an important role of DA. However, direct evidence of a link between DA and LOC is missing. In this study we aimed at investigating this link. Using Positron Emission Tomography (PET) with the radioactive tracer [^{11}C]raclopride, we sought to determine whether baseline levels of DA binding in the striatum, especially to D2 receptors, are associated with inter-individual differences in LOC in healthy individuals.

2. Methods

2.1. Participants

Fifteen healthy male subjects participated in this study (age range 20–25 years old, average age 22.4, SD = 1.60). Sample size was based on previous studies using PET to measure striatal DA levels (Clatworthy et al., 2009; Cools et al., 2009; Lawrence et al., 2013; van Holst et al., 2018). All participants provided written informed consent at the beginning of the session. They were asked not to eat in the 3 h preceding the experiment. None of the participants had a history of psychiatric or neurological conditions, and had normal or corrected-to-normal vision. As a compensation for their participation, each subject received 86 euros at the end of the experiment. The experimental protocol was approved by the ethical committee of Ghent University Hospital. One participant subsequently reported to have recently used Noxipro. This substance is a dopamine precursor, used as muscle enhancer. Due to potential interference with DA levels, this participant was excluded from further analysis. Two more participants were excluded due to technical failure.

2.2. Data acquisition

We used Positron Emission Tomography (PET), with injection of the radioligand [^{11}C]raclopride to measure DA binding to D2 receptors (Volkow et al., 1994). The goal was to measure baseline D2 receptor binding, and therefore participants were not performing any task during scanning, and were instructed to relax during the session. [^{11}C] raclopride was synthesized by *O*-methylation of the precursor (*S*)-*O*-desmethylraclopride (ABX, Radeberg, Germany) with [^{11}C]methyl triflate using established methods (Van Laeken et al., 2013). The radiochemical purity of all [^{11}C]raclopride used was ≥99% and specific activities at the end of synthesis were 110 ± 45 GBq/μmol. The PET scanner was a Philips Gemini PET/CT imaging system, consisting of a gadolinium oxyorthosilicate full-ring with 5 mm in-plane spatial resolution. At the beginning of the scanning session, a low dose CT of the brain was performed for attenuation correction (16-slice helical scan, 120 kV, 30 mA, FOV 600 mm, 0.5 s rotation time, pitch of 0.9, collimation 16 × 1.5 mm). Then, the injection of a bolus of 200 MBq [11C] raclopride was performed. After the injection, dynamic ET emission data were acquired in list mode. Emission data were reconstructed as 50 frames of 1 min duration using Philips's iterative 3D-RAMLA algorithm (Row Action Maximum Likelihood Algorithm). The duration of the PET scan was 50 min.

In a separate experimental session, participants also underwent a standard T1-weighted anatomical MRI scan (3D MPRAGE, 176 slices, TR = 1550 ms, TE = 2.89 ms, slice thickness = 0.90, resolution = 0.9 × 0.9 mm^2). This anatomical scan was acquired for coregistration with the PET images, to ensure improved anatomical localization. Finally, each participant filled in the Rotter Locus of Control scale (Rotter, 1966), measuring LOC-attribution (Rotter, 1966).

Importantly, this study was part of a larger protocol, investigating different aspects of striatal contributions to cognitive processes.

All participants performed the PET session first. The behavioral session (including tasks and questionnaires) was carried out on a later day (from one day up to one week after the PET session). During the behavioral session, participants performed 3 behavioral tasks. The first task was a visual detection task (these data are reported in Van Opstal et al., 2014). A second task measured working memory capacity. A third task investigated gambling tendencies (adapted from Vassena et al., 2014a). Participants also filled in 2 additional questionnaires: the Dospert (Blais and Weber, 2006) and the Bis Bas (Carver and White, 1994).

2.3. Data analysis

[11C]raclopride binding potential (BPND), was calculated for each voxel with the PMOD's PXMOD software version 3.405 (PMOD Technologies Ltd., Zurich, Switzerland). BPND is the proportion at equilibrium between the bound radioligand and the non-displaceable radioligand in the tissue (Innis et al., 2007). The cerebellum was used as a reference region, given that no specific binding was expected there. We used the simplified reference tissue model 2 (SRTM2, Wu and Carson, 2002), based on the assumption of a one tissue compartment to describe the influx and efflux in the tissue ROI (K$_1$ and k$_2$) and the reference region (K′$_1$ and k'$_2$). This model with 2 parameters is expected to be more robust than the previously used SRTM version with 3 parameters (Lammertsma and Hume, 1996) at high levels of noise in voxel-based parametric imaging. BP$_{ND}$ were calculated according to this formula:

$$BP_{ND} = \frac{K_1/k_2}{K_1'/k'_2} - 1 = R_1\frac{k_2'}{k_2} - 1$$

where the relative delivery constant R1 is the parameter to be estimated. R$_1$ is the ratio of K$_1$ to K′$_1$, and the rate constant k$_2$. SRTM was used to calculate a global k'2 from all voxels in the striatum. To improve spatial precision we manually coregistered the parametric BP$_{ND}$ maps (with one BP$_{ND}$ value per voxel) with their corresponding MR image using the PMOD's PFUS tool. Subsequent analysis was performed with SPM8 (http://www.fil.ion.ucl.ac.uk/spm/software/spm12/) in MATLAB. We normalized the anatomical MR images to the MNI space. The obtained normalization parameters were used to normalize the parametric BP$_{ND}$ maps. The normalized images were then introduced in a second-level analysis with a one-sample *t*-test and LOC as a covariate of interest. This analysis allowed estimating the variability in BP$_{ND}$ explained by variation in LOC in a voxel-wise fashion. Importantly, both possible directions for the correlation were tested, i.e. testing for voxels showing significant increase as a function of higher LOC (external LOC, positive correlation) and voxels showing a significant increase as a function of lower LOC (internal LOC, negative correlation). For significance testing, we applied a voxel-level threshold of $p = .001$ and a whole-brain cluster-level family-wise error (FWE) correction for multiple comparisons of $p = .05$. In order to test the robustness of the hypothesized relationship between DA D2 binding and LOC, we performed 2 additional control analyses. First, we tested for potential relationship with (phasic) reward processing, by including the BAS score from the Bis Bas (which includes a reward sensitivity measure), and a measure of gambling tendencies obtained from the gambling task (Vassena et al., 2014a) as additional covariates. Second, we tested whether the relationship between D2 binding and LOC would still be present when accounting for multiple testing carried out in the full experimental protocol. To this end, we repeated the main analysis including all behavioral scores and all questionnaires collected from the same participants during the project. Both analyses replicated our main results (see supplementary material for a detailed description of methods and results). The same statistical threshold was applied as previously described.

To verify the reliability of our main analysis, we additionally used a jackknife procedure, similar to what suggested by previous studies (Wilke, 2012). We repeated the whole-brain LOC analysis 12 times, each time excluding a different participant with the same parameters. Results of this analysis are shown in Fig. 3 and Table 2.

3. Results

The average LOC score was 13.92 (SD = 3.61). The analysis revealed a significant positive correlation between D2 binding and LOC score. One cluster survived cluster-level FWE correction for multiple comparisons, located in the right striatum (Table 1). This voxel-based approach allows a precise anatomical characterization, showing involvement of the right pallidum and the right putamen (Fig. 1). A higher LOC score, reflecting a more external LOC, was associated with increased D2 binding (Fig. 2). No voxels showed a negative correlation between D2 binding and LOC. The second analysis (including Bis Bas and gambling as covariates) and the third analysis (including all measured questionnaires and behavioral scores) replicated this result, confirming its robustness (see supplementary material for a detailed description).

To further verify the reliability of our results considering the small sample size, we performed an additional reliability test: an iterative

Table 1
Whole brain results for LOC correlation. The columns from left to right indicate the *p*-value for the cluster-level Family-Wise Error (FWE) correction, the *p*-value for the False Discovery Rate (FDR) correction, the number of voxels in the cluster, T values for peak voxels within the cluster, and MNI coordinates of the peaks. These statistics refer to the results displayed in Fig. 1.

Cluster FWE	Cluster FDR	Cluster size	Peak T	MNI (xyz)		
0.000	0.000	1175	6.10	28	−14	−5
			5.79	26	−5	−3
			5.28	20	5	11

jackknife analysis (Van Opstal et al., 2014; Wilke, 2012). We repeated the main analysis on LOC and D2 binding 12 times, each time excluding a different subject. The results and statistics are reported in Fig. 3 and Table 2. In all analyses, we observed a similar cluster as in our main analysis. In 10 out of 12 analyses, the cluster survived whole-brain correction for multiple comparisons. This procedure confirmed the reliability of the observed effect. Fig. 3 displays each of the iterations of the jackknife procedure, demonstrating the consistency of the observed activation cluster.

4. Discussion

In this study, we probe the link between striatal D2 and LOC in healthy individuals, providing evidence that external LOC is associated with increased D2 binding. This result supports a role of striatal DA in determining the subjective perception of control.

Some previous studies provided preliminary evidence for a link between LOC and striatal DA. Eye blink rate (considered a proxy of baseline DA levels) and DA metabolites have been found to correlate with LOC (De Brabander and Declerck, 2004; Declerck et al., 2006a). The current study corroborates these findings with a direct measure of striatal DA, namely D2 receptor binding.

Theoretically, our findings establish a link between previous work on the role of DA in reinforcement learning with the clinically relevant dimension of environmental controllability (Huys and Dayan, 2009). LOC reflects the belief that external events follow from one's actions, which translates to perceived control (or lack thereof) over the environment. Lack of controllability has been related to learned helplessness, an experimental model of depression (Belujon and Grace, 2017; Grace, 2016; Hori and Kunugi, 2013). External LOC has also been linked to increased risk for psychopathology (particularly depression and schizophrenia) and decreased stress resilience (Bollini et al., 2004; Culpin et al., 2015). Our results suggest that increased striatal D2 binding may be linked to the feeling of lack of controllability. This highlights the importance to further specify the link between DA signaling, perceived control, and affective processing and dysregulation.

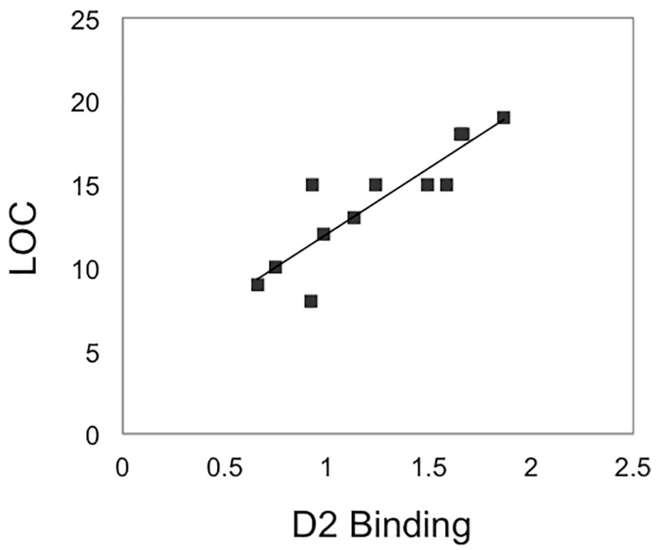

Fig. 2. Increased D2 binding is associated with external LOC. This plot shows the linear relationship between LOC and the D2 binding extracted from peak local maximum of the significant cluster in the whole-brain analysis. Note that this plot is for illustration purposes (no statistical test performed on it).

An influential theory of DA function has proposed a role of tonic DA signals in response vigor (Niv et al., 2007), which may be linked to LOC. In this framework, vigor and rate of behavioral responding are determined by tonic DA, which reflects average reward rate. Specifically, an environment that offers more rewards will result in quicker and more vigorous behavioral responses because of higher opportunity cost of each action (i.e. each action costs time, time that is not spent on gathering reward through alternative actions, Niv, 2007). In this context, average reward rate may determine the perception of

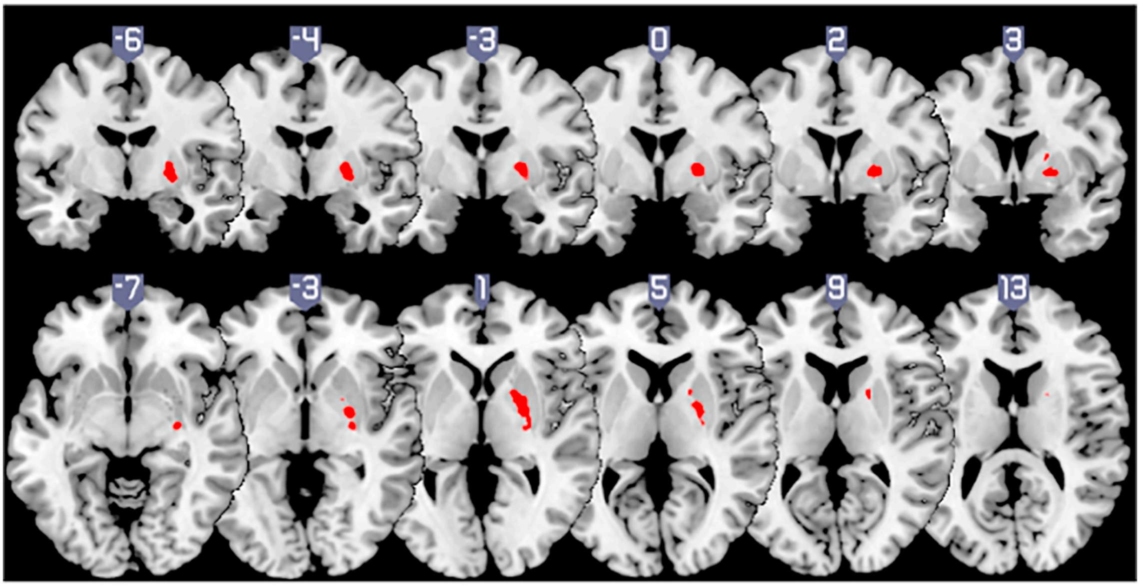

Fig. 1. Voxel-wise analysis showing the cluster where increased D2 binding potential was associated with external LOC. Slice number is displayed above each slice for both coronal (upper row) and axial (lower row) sections.

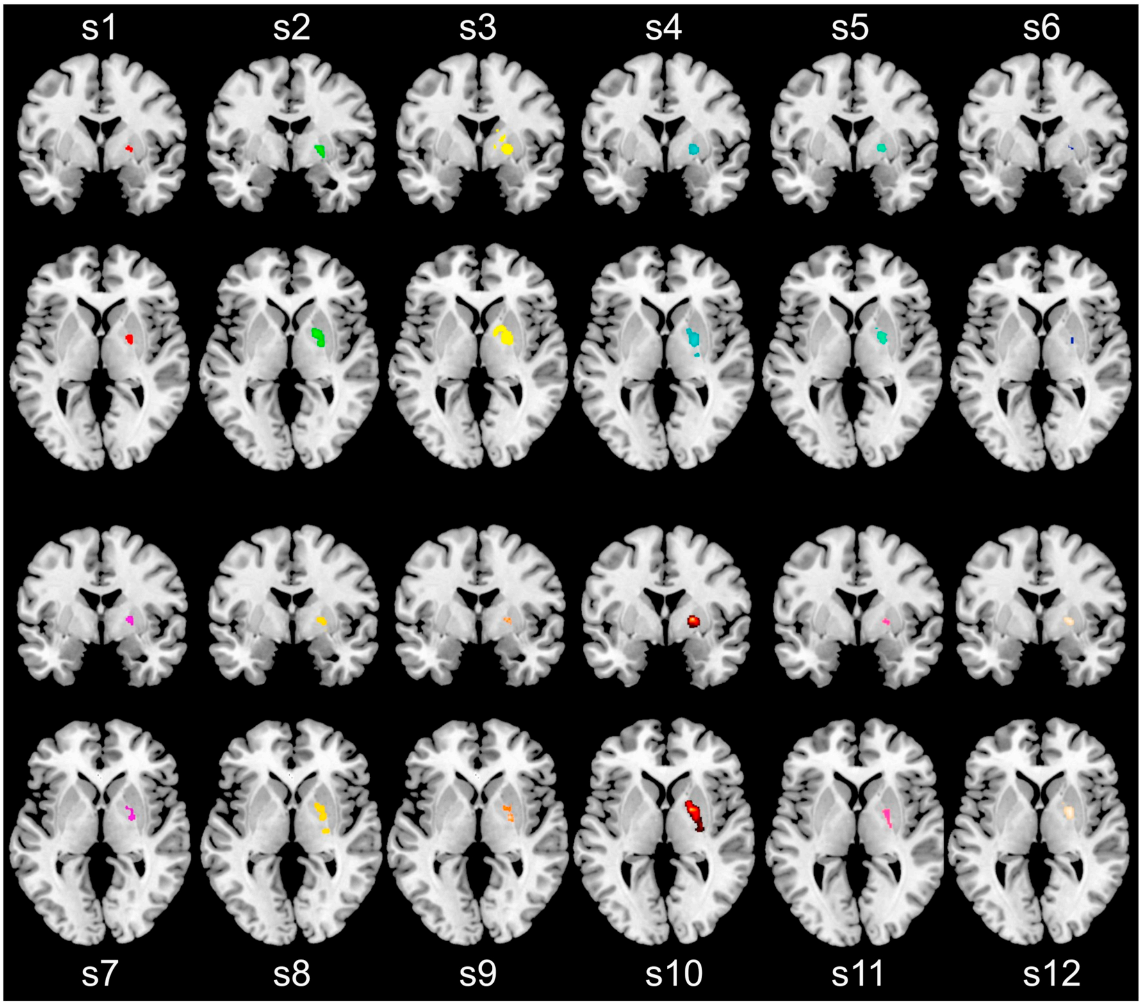

Fig. 3. Results of the reliability test through the jackknife procedure. Each figure indicates the LOC group analysis with one of the subjects excluded (the s indicates the subject number excluded). The coronal slice is for all subjects set at 0 and the coronal slice at 2 (MNI coordinates). All analysis show a comparable cluster, confirming the reliability of the results.

controllability and hence LOC (e.g., in a frustrating environment providing no rewards for one's actions, the agent may infer that action vigor or rate does not matter). In line with this theoretical view, our results link external LOC to lower tonic DA (as indicated by higher D2 binding potential, Badgaiyan et al., 2015).

Clinical perspectives converge in suggesting a link between DA and LOC. Dysregulation of DA signals has been proposed as a pathophysiological driver of depression (Belujon and Grace, 2017; Grace, 2016; Hori and Kunugi, 2013). Further research in this direction may elucidate the role of striatal D2 binding specifically in the development of the disorder. External LOC is also a risk factor for psychosis, especially schizophrenia (Gibson et al., 2018; Sullivan et al., 2017). Prominent theories on the neural basis of schizophrenia propose dysregulation of DA D2 receptors as a core underlying deficit (Deserno et al., 2016; Grace, 2016). Our findings provide evidence for a relationship between LOC and D2 binding in healthy individuals as well, corroborating the relevance of the LOC measure as a risk factor marker.

Overall, this work uncovers a critical relationship between LOC of control, DA levels, and the mediating role of both on affective processing, and particularly dysregulation. Subjective perception of control may be the link between objective cognitive control and affect, and with striatal DA as core underlying substrate.

This study has some important limitations that may be addressed in future research. First, although the observed effect is statistically significant also using a conservative approach (voxel-wise testing with correction for multiple comparison), the sample size is rather small. This is common for PET studies, as this neuroimaging technique is more invasive than fMRI, and carries considerable financial costs. A follow up study with a larger sample size should be conducted to replicate this result.

Second, the age range of the participants was limited to young people (20–25 years old), and only males. These two restrictions were not coincidental. We restricted our sample to young subjects because previous studies reported alterations (especially decline) in DA function associated with aging (Karrer et al., 2017; Zucca et al., 2017), which in extreme cases results in DA degeneration and Parkinson-like motor symptoms (Darbin, 2012). Similarly, we sampled only males because of ovarian hormone cycles relating to DA, and gender-dependent differences in sensitivity to dopaminergic drugs (Barrett et al., 2017). Furthermore, although both men and women show a reduction of D2 receptor density with increasing age, women show higher endogenous DA concentrations (as suggested by decreased D2 receptor affinity) (Pohjalainen et al., 1998). Thus, whether external LOC is associated with increased D2 binding in older subjects and in women, remains to be investigated.

Finally, we observed a relationship that is correlational in nature. DA levels may influence objective control processes, and as a consequence subjective perception of control. Alternatively, DA levels may have a dissociable impact on objective and subjective control. Relatedly, cortical mechanisms implicated in objective and subjective

Table 2

Jackknife procedure. The main analysis was repeated 12 times, each time excluding one of the participants, to test for the reliability of the results. Statistics from each of the 12 iterations are reported in this table, including (left to right) the number of the subject that was excluded in that iteration, the *p*-value for the cluster-level Family-Wise Error (FWE) correction, the *p*-value for the False Discovery Rate (FDR) correction, the number of voxels in the cluster, T values for peak voxels within the cluster, and MNI coordinates of the peaks. In each iteration, we observed a large cluster, overlapping with our main analysis cluster (with some variation of local maximum coordinates and cluster size between iterations). Only 2 iterations resulted in a cluster that did not survive whole-brain correction for multiple comparisons, although the cluster was similarly located as all other analyses. 10 out of 12 iterations returned statistically significant clusters. Overall, this procedure confirmed the reliability of the main result.

Excluded subject	Cluster FWE	Cluster FDR	Cluster size	Peak T	MNI (xyz)
1	0.135	0.050	218	5.14	26 −5 −3
				4.90	21 −2 3
2	0.000	0.000	700	5.47	26 −5 −3
				5.45	20 3 0
				4.98	20 5 11
3	0.000	0.000	1676	7.06	18 7 6
				7.06	20 −3 3
				5.90	13 2 2
	0.390	0.178	158	6.87	28 −14 −5
4	0.000	0.000	1050	6.95	20 5 12
				6.03	29 −14 −6
				5.75	23 −4 0
5	0.004	0.002	447	5.52	26 −5 −2
				4.93	20 2 0
				4.46	24 −10 7
6	0.360	0.141	161	6.53	25 −7 −6
				4.45	23 −2 3
7	0.012	0.007	360	5.62	26 −5 −3
				5.38	22 −3 4
8	0.000	0.000	576	6.22	26 −5 −3
				5.00	20 6 11
				4.98	21 2 1
	0.233	0.065	189	5.87	28 −14 −5
9	0.038	0.027	285	5.05	26 −5 −3
				4.52	21 2 1
10	0.010	0.007	372	5.09	24 −7 6
				5.02	26 −5 −3
				4.68	20 2 0
11	0.010	0.007	372	5.09	24 −7 6
				5.02	26 −5 −3
				4.68	20 2 0
12	0.000	0.000	621	5.47	26 −5 −3
				5.06	21 2 1
				5.05	20 5 11

control perception may interact with striatal DA levels (Westbrook and Braver, 2016). Interestingly, LOC moderates the effect of pharmacological manipulation of dopamine on the exploration/exploitation trade off (i.e. the likelihood to engage in uncertain exploration of new options, rather than sticking to known available reward options (Kayser et al., 2015), which points toward an interaction between striatal and cortical controls systems. Studies exploiting DA pharmacological manipulations may further address the causality direction of the observed relationship, as well as the interaction between cortical and subcortical circuits.

Overall, the present study provides important preliminary evidence of a link between increased D2 binding in the striatum and external LOC. These results elucidate the role of striatal dopamine in subjective perception of control, and relate to the key role of DA (dys)regulation in (lack of) resilience to stress and vulnerability to psychosis.

Declaration of competing interest

The authors have no competing interests to declare.

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Appendix A. Supplementary material

Supplementary material to this article can be found online at https://doi.org/10.1016/j.ijpsycho.2019.09.016.

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