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Short communication

Increased dopamine tone during meditation-induced change of consciousness

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Abstract

This is the first in vivo demonstration of an association between endogenous neurotransmitter release and conscious experience. Using ^{11}C-raclopride PET we demonstrated increased endogenous dopamine release in the ventral striatum during Yoga Nidra meditation. Yoga Nidra is characterized by a depressed level of desire for action, associated with decreased blood flow in prefrontal, cerebellar and subcortical regions, structures thought to be organized in open loops subserving executive control. In the striatum, dopamine modulates excitatory glutamatergic synapses of the projections from the frontal cortex to striatal neurons, which in turn project back to the frontal cortex via the pallidum and ventral thalamus. The present study was designed to investigate whether endogenous dopamine release increases during loss of executive control in meditation. Participants underwent two ^{11}C-raclopride PET scans: one while attending to speech with eyes closed, and one during active meditation. The tracer competes with endogenous dopamine for access to dopamine D2 receptors predominantly found in the basal ganglia. During meditation, ^{11}C-raclopride binding in ventral striatum decreased by 7.9%. This corresponds to a 65% increase in endogenous dopamine release. The reduced raclopride binding correlated significantly with a concomitant increase in EEG theta activity, a characteristic feature of meditation. All participants reported a decreased desire for action during meditation, along with heightened sensory imagery. The level of gratification and the depth of relaxation did not differ between the attention and meditation conditions. Here we show increased striatal dopamine release during meditation associated with the experience of reduced readiness for action. It is suggested that being in the conscious state of meditation causes a suppression of cortico-striatal glutamatergic transmission. To our knowledge this is the first time in vivo evidence has been provided for regulation of conscious states at a synaptic level.

Theme: Neural basis of behavior

Topic: Monoamines and behavior

Keywords: Meditation; Dopamine; Raclopride; Consciousness; Positron emission tomography; Electroencephalography

There are two main, complementary aspects of consciousness [6]: consciousness of our sensory world, and the equally important consciousness of action [12]. Yoga Nidra is a relaxed meditative state in the meditation tradition where these aspects are subjectively dissociated: the mind ‘withdraws’ from wishing to act. This state is not associated with a change in emotional state or willpower. The meditator becomes a neutral observer. He experiences loss of conscious control of his actions and experiences an enhancement of sensory stimulations or imagination [3,9]. This dichotomy seems common to several relaxation meditation techniques, as concluded from a factor analysis of the subjective accounts of 940 persons performing a variety of relaxation techniques [16]. The study revealed that meditation, within or outside the Yoga concept, was characterized by a ‘profound willingness to let go of personal goals on concerns, and an intense absorption of attention’ to the sensory world.

Abbreviations: PET, positron emission tomography; BP, binding potential; EEG, electroencephalography; GABA, gamma-amino butyric acid; MRI, magnetic resonance imaging

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In a previous $H_2{}^{15}O$-PET study we compared the cerebral blood flow activation pattern during Yoga Nidra meditation with the normal restful state in order to localize the neural structures differentially active in the two aspects of consciousness — imagery and attention towards action. Subjectively, Yoga Nidra is characterized by reports of vivid imagery and decreased attention towards action. We found a corresponding relative flow *increase* in occipital and anterior parietal cortical regions known to be active in imagery, and relative flow *decreases* in several regions of the so-called executive system: dorsolateral prefrontal, anterior cingulate, and orbital frontal cortices, striatum, thalamus, brain stem and cerebellum [12]. The prefrontal regions, striatum and thalamus, are thought to be organized in re-entrant loops, of which three seem to be responsible for behavior and cognition [5]. Recent evidence suggests that the cerebellum may be binding this system [2]. The loops pass through the striatum in an anatomically segregated manner [7], although striatal cholinergic interneurons may serve the purpose of synaptic integration [10]. The cortico-striatal connection is subserved by glutamatergic excitatory cortical efferents, which activate the GABAergic medium sized neurons (MSNS) of the striatum. MSNS contribute about 90% of the striatal neurons. Recent anatomic studies have localized both glutamate and dopamine receptors to the dendrites of the MSNS. Dopaminergic activity modulates the postsynaptic potentials of glutamatergic neurotransmission in the prefrontal-subcortical loops [18,14].

We, therefore, hypothesized that the voluntarily induced suppression of the executive system during relaxation meditation [12] could be mediated by the dopaminergic system. This hypothesis would predict reduced binding of ^{11}C-raclopride to D_2 dopaminergic receptors during relaxation meditation, due to increased endogenous dopamine release. In particular, the ventral striatum would be a target as the loops subserving motivation and initiative pass through this structure. The aim of the present study was to test this prediction.

Eight healthy male meditation teachers aged 31–50 from the Scandinavian Yoga and Meditation School, Copenhagen, were investigation at the MRC Cyclotron Building, Hammersmith Hospital, London. Participants were highly experienced, and had practiced meditation for 7–26 years on a daily basis. Six out of eight were strongly right handed, one ambidextrous and one left handed. All volunteered and gave informed consent. The protocol was approved by the Ethics committee, Hammersmith Hospital. Permission to use radio-ligands was obtained from the Administration of Radioactive Substances Advisory Committee of the United Kingdom.

Each participant had ^{11}C-raclopride PET twice on separate days — once when performing Yoga Nidra relaxation meditation and once during rest, in random order. Participants were scanned in an ECAT EXACT3D (CTI/Siemens 966) scanner in a supine position wearing earphones with the head resting in a head holder. An initial transmission scan used for attenuation correction was performed. Participants were guided for 72 min by auditory CDs to either follow a standard relaxation meditation scheme or in the control condition attend to speech conducted by the same voice. Seven minutes after initiation of the auditory stimulation, ^{11}C-raclopride was injected intravenously and scans with a reconstructed spatial resolution of 4.8 mm×4.8 mm×5.6 mm were acquired as 24 time frames over 85 min. The auditory stimulation was terminated approximately 15 min earlier than the scan. The early termination was due to the limited duration of the meditation procedure and was the same in both the meditation condition and the attention condition. Parametric images of ^{11}C-raclopride binding potentials (BP) were generated.

A T_1-weighted volumetric MRI brain scan was performed on each participant. The ^{11}C-raclopride BP and MR images were coregistered and five regions of interest were traced on the MRI: right caudate, left caudate, right putamen, left putamen and ventral striatum.

Electroencephalograms (EEG) were not routinely available in the laboratory. Therefore, a 16-channel portable recording device (Medtronic) was brought into the lab. Due to practical problems with the new equipment, only five of the eight participants had successful EEGs in both of the two conditions. These 10 EEGs were analyzed with spectral analysis using fast Fourier transform on segments of 1 s duration. The average power in the theta frequency band (4–7 Hz) and alpha frequency band (8–13 Hz) was calculated.

After each PET investigation, participants completed a questionnaire with respect to pleasure, relaxation, awakeness, and awareness. Following scans in the meditation condition, the quality, depth and success of the meditation were assessed.

The binding potentials were calculated using the simplified reference tissue model with a cerebellar input function [8]. Changes in mean binding potentials during meditation compared with attention for each of the five regions defined were evaluated using a two-tailed paired Student's *t*-test. Average EEG power spectra were compared using a two-tailed paired Student's *t*-test. The nominal scores from the interview were evaluated using the signed rank sum test.

There was a significant 7.9% decrease in BP in the ventral striatum. The average decrease in binding potential (BP) during meditation is summarized in Table 1, and illustrated by example in Fig. 1.

Spectral analysis of EEG recordings revealed an increase in theta activity during meditation, which correlated significantly with the decrease in ^{11}C-raclopride binding (Fig. 2). The power of the theta activity increased 9% (NS) and the power of the alpha activity decreased 8% (NS) during meditation.

The participants reported a significant decrease in

Table 1
Percentage decrease in binding potential during meditation for all eight subjects in the five regions of interest (right caudate, left caudate, right putamen, left putamen, and ventral striatum). *Significant change ($P<0.013$)

Participant	R caudate	L caudate	R putamen	L putamen	Vent. striatum
1	8.3	−0.4	3.9	3.0	14.8
2	5.7	12.5	4.0	13.5	7.3
3	−5.6	−6.3	−1.6	−13.0	−0.7
4	−3.3	−4.3	−6.1	−7.5	6.8
5	3.5	5.7	6.3	5.3	6.0
6	13.0	12.1	19.9	9.2	8.2
7	2.1	0.0	−3.1	−9.1	1.3
8	4.7	3.5	2.6	8.7	19.3
Mean	3.5	2.9	3.2	1.3	7.9*

readiness for action ($P<0.05$) along with a significantly heightened sensory imagery ($P<0.05$) during active meditation compared with attention to speech (Fig. 3). The feeling of gratification and the extent of relaxation did not differ between the two conditions. The questionnaire showed no significant change in quality, depth and success of meditation compared to that which participants experienced at home.

The major finding of the present study has been the demonstration of increased dopaminergic tone in the ventral striatum during an altered conscious state, as evidenced by decreased D2 receptor availability to ^{11}C-raclopride. The state of relaxation meditation has previously been shown to be characterized by suppression of prefrontal-subcortical activity regulating the executive system along with consciousness for action [12], while brain regions responsible for a complementary aspect of consciousness, sensory perception or imagery, showed relatively increased activity. Subjectively, the meditative state is characterized by a marked decrease in readiness for action and a corresponding increase in the experience of imagery, as seen in Fig. 3.

The 7.9% decrease in ventral striatal ^{11}C-raclopride BP was greater than within participant test–retest variations reported earlier [19]. Microdialysis studies in monkeys have shown that a 1% decrease in striatal ^{11}C-raclopride binding reflects an 8% increase in extracellular endogenous dopamine levels [4]. Therefore, the present results would indicate a rise by approximately 65% of extracellular dopamine release during meditation in the ventral striatum.

The fact that the ventral striatum was the only region in which the decrease in dopamine receptor availability reached statistical significance is of interest. Two of the three frontal-subcortical circuits regulating behavior include structures in the ventral striatum. One originates in the lateral orbital frontal cortex, passes through the ventromedial frontal cortex, ventral striatum, medial and dorsomedial globus pallidus, ventral anterior and medial dorsal thalamus, and back to the orbitofrontal cortex. Dysfunction in this loop may result in an orbitofrontal syndrome with lack of interest and initiative. The other circuit passing through the ventral striatum originates in the anterior cingulate gyrus. It passes through the nucleus accumbens of the ventral striatum, the rostrolateral globus

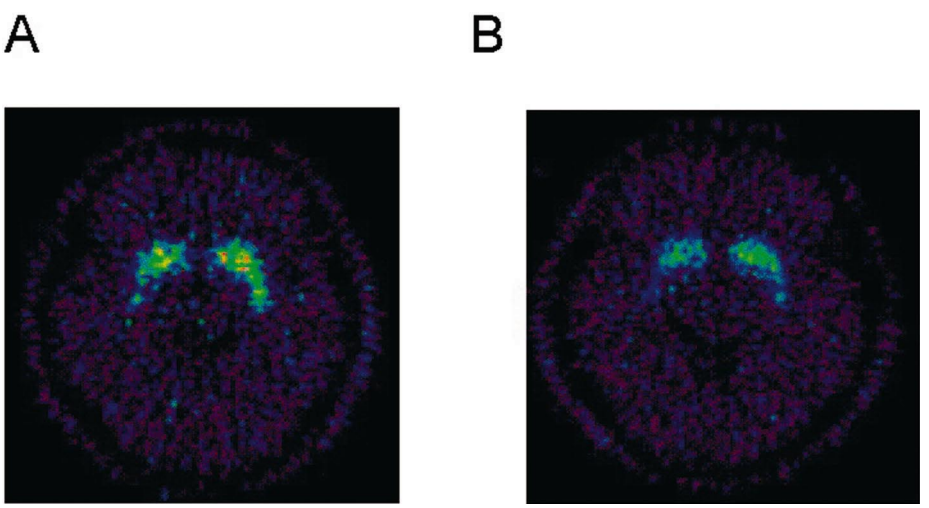

Fig. 1. The ^{11}C-raclopride binding potential images at the level of the striatum for one participant (No. 8) during attention to speech (A) and meditation (B). The reduced ^{11}C-raclopride binding potential in ventral striatum is evidence of increased endogenous dopamine release during meditation.

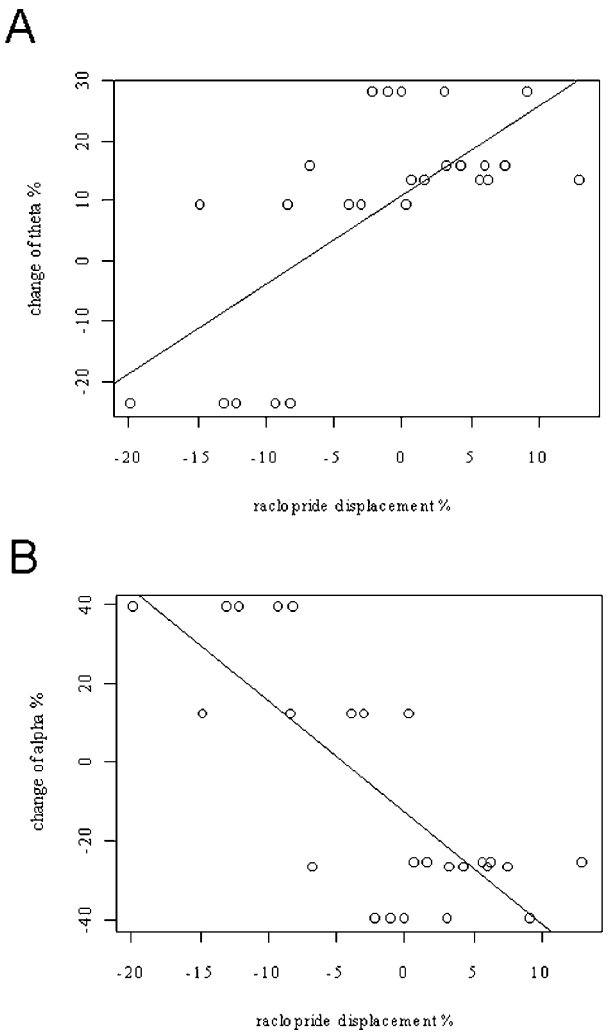

Fig. 2. Correlation between changes in raclopride binding and changes in EEG activity. (A) The correlation coefficient between the relative change of activity in the theta band (4–7 Hz) and changes in raclopride binding (BP) was $r=0.69$. The slope of the regression line is significantly greater than 0. (B) The correlation coefficient between the relative change of activity in the alpha band (8–12 Hz) and changes in raclopride binding was $r=-0.78$. The slope of the regression line is significantly smaller than 0. Thus there is a significant correlation between changes in raclopride binding and changes in activity of these two frequency bands. It has previously been shown that Yoga Nidra meditation is associated with increased activity in the theta band.

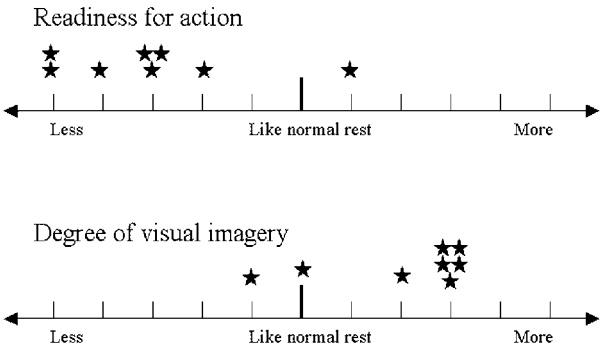

Fig. 3. The reported readiness for action and degree of sensory imagery during meditation compared to normal rest. Each star indicates the response of one subject. Readiness for action was significantly reduced and sensory imagery was significantly increased during meditation ($P<0.05$).

pallidus, the medial dorsal thalamus and back to the prefrontal cortex. Dysfunction in this loop may result in an anterior cingulate syndrome, characterized by apathy, poverty of speech and movement, and no display of emotions. Response inhibition on the go–no go test is impaired [2]. The phenomenology of relaxation meditation with loss of will, emotional disinterest and withdrawal is in fact very similar to the experience of lack of readiness for action (cf. Fig. 3). Functions attributed to a third behavioral loop, the dorsolateral prefrontal loop passing through the dorsal striatum, are working memory and establishments and shifts of preparation for volitional action (motor 'sets').

Our earlier finding of a relatively increased blood flow in the cerebellum compared with striatum during meditation could lead to an overestimate of the non-specific activity of the reference region and thus underestimate the endogenous dopamine release during meditation. In spite of this potential bias we demonstrate a significant 7.9% decrease in ventral striatal ^{11}C-raclopride binding during meditation.

In the striatum, glutamatergic-gated ion channels mediate excitatory responses during synaptic transmission from cortical afferents to the striatal GABAergic spiny neurons. Hence, cortical glutamatergic afferents provide the main excitatory drive for the striatum. In recordings of propionate and kainate-type glutamate receptor-mediated components of excitatory postsynaptic currents (EPSCs), incubation of brain slices in 10 μM dopamine resulted in a reduction of the amplitude by 33±11%. The large variability may reflect activation of different receptor subtypes with opposing effects. In an earlier study, goal-directed behavior (a videogame) was also found to release dopamine in the ventral striatum [11]. At first glance this finding would seem contradictory to the present study where desire for executive function is suppressed. However, the selection of goal-directed actions involves suppression of irrelevant signals from a great number of sources, and the enhancement of only one set of signals. It is now believed that the basal ganglia may play a primary role in the selection of context-dependent actions. This focusing and filtering function is carried out by enhancement of the relevant signals through a direct striatal-thalamic pathway, and by the suppression of irrelevant signals through an indirect pathway. The indirect pathway runs from the striatum through the external segment of the pallidum (GABAergic), subthalamic nucleus (GABAergic), internal segment of the pallidum plus substantia nigra (glutamatergic), and thalamus (GABAergic) [1,15].

A relative increase in theta activity is a common feature of meditation [12,17]. In the present study, EEG monitoring was successful in only five cases. In spite of this shortcoming the decrease in ^{11}C-raclopride binding during meditation correlated positively with increased theta activity, suggesting an association between increased dopamine tone and the characteristic theta activity increase in meditation.

In conclusion, the results of the present study have shown increased dopamine release in the ventral striatum during relaxation meditation, as evidenced by reduced 11C-raclopride binding. This increase in dopaminergic tone, therefore, seems to be associated with the observed reduction in readiness for action during meditation. To our knowledge this is the first time evidence has been provided for regulation of conscious states at a synaptic level.

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