



## Out of the box: A psychedelic model to study the creative mind

K.P.C. Kuypers

Department of Neuropsychology and Psychopharmacology, Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, The Netherlands



### ARTICLE INFO

#### Keywords:

Psychedelics  
Psilocybin  
Divergent flexible thinking  
Brain networks  
Creativity  
Psychedelic model

### ABSTRACT

Our creativity is challenged daily when facing new situations asking for novel solutions. Creativity, a multi-component construct includes flexible divergent and rigid convergent thinking. Psychedelic drugs like psilocybin can enhance creativity and affect state of mind (mood, empathy, openness). Of note, flexible thinking is disturbed in psychopathological conditions like anxiety disorders and depression and preliminary findings have shown psychedelics to be efficacious in the treatment of those conditions.

The question how psychedelics induce this state of enhanced flexible thinking remains to be answered and investigating the neurobiology underlying this phenomenon will not only help in understanding why psychedelics are of use in the therapeutic setting but also in other settings where flexible thinking is challenged. A model including neuronal networks, neurotransmitters and personal factors playing a role in this process will be proposed which can be put to the test by means of placebo-controlled pharmaco-imaging studies in healthy volunteers.

### Introduction

In daily life people are challenged by situations of all kinds asking for creative problems solving skills [1,2]. Being able to come up with alternative solutions to a problem is one aspect of creativity which is called (flexible) divergent thinking. It is different from (rigid) convergent thinking which is about finding the best solution to a problem. Divergent thinking has been shown to be a more useful estimate of creative thoughts in daily life than convergent thinking [3]. Flexible thinking is also known to be decreased in certain psychopathological conditions like depression, anxiety, and post-traumatic stress disorder (PTSD) [4–10].

Interestingly, anecdotal evidence, historical examples and (quasi-) experimental studies suggest that psychedelic drugs like LSD, psilocybin and ayahuasca enhance creative flexible thinking in the neuro-typical population [11–16]. In addition, the therapeutic potential of these substances is now being investigated in the treatment of aforementioned mental disorders [17–19]. Preliminary findings in patient samples are promising showing beneficial therapeutic outcomes lasting up to a few weeks after treatment [20–22]. It is hypothesized that these effects are due to a shift from rigid thinking patterns to more flexible thinking patterns, facilitating psychotherapeutic interventions [15].

The question how psychedelics induce this state of enhanced flexible thinking remains to be answered and investigating the neurobiology underlying this phenomenon will not only help in understanding why psychedelics are of use in the therapeutic setting but also

in other settings where flexible thinking is challenged. A model including neuronal networks, neurotransmitters and personal factors playing a role in this process will be proposed which can be put to the test by means of placebo-controlled pharmaco-imaging studies in healthy volunteers.

### Creativity and brain networks

The biological base underlying creativity has been suggested to consist of a dynamic interplay between several brain regions including the three core brain networks, the central executive network (CEN), the default mode network (DMN) and the salience network (SN) [23,24].

The CEN links the dorsolateral prefrontal cortex (dlPFC) and posterior parietal cortices (PPC) and is engaged in higher-order cognitive and attentional control [25]. The DMN has 2 important key nodes, the ventromedial (vm) PFC, implicated in self-referential processing, and the posterior cingulate cortex (PCC), a critical connector hub to all regions of the DMN [25–28]. The SN consists of the anterior insula (AI) and the dorsal anterior cingulate cortex (dACC), both implicated in empathy [25,29–31]. It monitors events occurring outside of the body as well as internal consciousness, and is able to direct attention to whatever is more important at a certain moment in time.

Increased coupling between DMN and SN regions was demonstrated at the beginning of a divergent thinking task, followed by increased coupling between DMN and CEN regions at later stages [32]. It is suggested that the shifts between these externally (CEN) and internally

E-mail address: [k.kuypers@maastrichtuniversity.nl](mailto:k.kuypers@maastrichtuniversity.nl).

<https://doi.org/10.1016/j.mehy.2018.03.010>

Received 8 February 2018; Accepted 22 March 2018

0306-9877/© 2018 The Author. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

(DMN) oriented cognitive networks, facilitated by SN, are very important in the process of divergent thinking [24]. Of note, it has been shown that the SN becomes active shortly before an insightful solution is reached [33]. Furthermore, the DMN is considered to be involved in daydreaming and self-reflection and responsible for the capacity to imagine past, future, or hypothetical scenarios [25,27,28]. A positive association between divergent thinking and resting state functional connectivity in the vmPFC and the PCC was demonstrated [27].

In sum, this activity pattern suggests that divergent flexible thinking involves cooperation between brain networks linked to cognitive control and spontaneous thought, which may reflect focused internal attention and top-down control of spontaneous cognition during creative idea production [32].

### Creativity, networks and neurotransmitters

It has been shown that the three core networks interact during divergent thinking via cortico-striatal–thalamo-cortical loops [24,34–36]. The extensive connectivity between the SN and CEN, and subcortical structures like the dorsomedial thalamus and the putamen on the one hand and the anterior thalamus and the dorsal caudate nucleus on the other hand being important in this light [25].

It has been shown that the thalamus, one of the aforementioned subcortical structures, together with the dopamine 2 (D<sub>2</sub>) receptor system, play an important role in divergent thinking. Decreased D<sub>2</sub> receptor densities are suggested to lower thalamic gating thresholds, increasing thalamo-cortical information flow, which might lead to enhanced performance on divergent thinking tests [36]. The role of dopamine (DA) in creative thinking has been suggested by multiple studies [37–39] with too high levels being linked with impaired divergent thinking and medium levels to high levels of flexible thinking [37–39].

Of note, the activity of DA neurons in the SN, more specific the ventral tegmental area (VTA), is under the excitatory control of serotonin (5-HT) 2A receptors in the PFC [25,40]; the 5-HT<sub>2A</sub> receptors being the principle site via which psychedelics exert their effects [17].

### Psychedelics and creativity networks

A decrement in the functional connectivity in parts of the DMN was demonstrated after administration psychedelics [41,42]. A hypothesized consequence of this effect being enhanced cognitive flexibility and creative thinking [43]. Furthermore, the increased frontal activation and divergent prefrontal-subcortical activation pattern induced by psychedelics might be attributed to a disruption of thalamic gating of sensory and cognitive information. Thalamic gating is under the control of glutamatergic cortico-striatal pathways projecting to thalamic nuclei [13]. It is known that psychedelics have secondary effects on glutamatergic, dopaminergic, and noradrenergic pathways [13,14] and that stimulation of the 5-HT<sub>2A</sub> receptors, can lead to an alteration of thalamo-cortical transmission [13,44,45].

### Psychedelics, personal factors and creativity

Psychedelics generate positive mood effects in healthy participants [12,46] which lead to openness to novel experiences [47,48], and increases in empathy [49]. The ‘facilitatory theory’ proposes that positive mood states tend to result in activation of a rich and complex set of positive memories and thoughts, which promotes flexibility and innovation [50–52]. Furthermore two personality traits, *openness to experience* and *empathy* have been linked with enhanced divergent thinking [48,53].

### Psychedelics, personal factors, creativity and brain networks

The induction of positive mood has been associated with increased activity in the left dlPFC [52], a brain regions which has been

associated with enhanced divergent thinking and the goal-directed planning of novel solutions [54–56]. Numerous studies have reported a positive relationship between creativity and openness [27,48,57] and the trait has been studied in relation to the neurobiological basis of creativity [28]. Apparently both openness and creativity are associated with increased functional connectivity in the DMN [28]. With respect to empathy a positive relation between levels of empathy and creativity has been shown [58]. Both divergent thinking and empathizing have been associated with the DMN [25] and activity in this network has shown to be increased during high-level social cognitive tasks [30,59,60].

### Psychedelics, personal factors, creativity and neurotransmitters

Openness seems to facilitate awareness of both one’s own and others’ emotions and is related to empathy [28]. Research has shown that empathy [61,62] and openness to experience [63] are positively related to oxytocin levels; intranasal administration of oxytocin led to higher levels of empathy in response to positive and negative valence stimuli [61] and to higher self-ratings of openness [63]. Interestingly, De Dreu and colleagues (2014) showed that intranasal application of oxytocin can also lead to enhanced divergent thinking and creative performance [64].

It is suggested that the link between creativity and oxytocin is mediated by DA [64]. The interaction between oxytocin and DA systems is supported by animal research where co-located oxytocin and D<sub>2</sub> receptors in the striatum played an important role in social and emotional behavior [65,66]. Elevated striatal DA is often associated with reduced DA in the PFC and reduced latent inhibition [67]. Latent inhibition is a filtering mechanism which tags novel information as relevant. When this mechanism is reduced, known stimuli or information is treated as novel, independently of the number of times we have seen it before. This reduced filtering has been associated with elevated creativity [2,68].

### Psychedelic model to study the creative mind

Psilocybin has been shown to produce a well-controllable altered state of consciousness marked by stimulation of affect, enhanced ability for introspection, increased empathy [69,70]. It has been widely used in psychopharmacological research without reports of severe adverse events [46,70,71]. Placebo-controlled *mechanistic* experimental studies in healthy volunteers being administered psilocybin in combination with a D<sub>2</sub>R, 5-HT<sub>2A</sub>R and oxytocin receptors blockers when assessing flexible thinking, mood states, openness and empathy, will shed light on the neurotransmitters involved in the facilitation of psychedelic-induced flexible thinking. Proton magnetic resonance spectroscopy (<sup>1</sup>H MRS), a non-invasive neuroimaging technique that allows in vivo quantification of glutamate-related metabolites in localized brain regions [72], will help determining the role of glutamate in this process. Functional connectivity analysis will allow determining the network underlying psychedelic-induced flexible thinking.

It is hypothesized that blockade of 5-HT<sub>2A</sub> receptors will lead to an absence of effects on glutamatergic levels and divergent thinking. Furthermore it is hypothesized that heightened empathy and openness will lead to enhanced divergent thinking and that D<sub>2</sub>R blockade and/or oxytocin receptor blockade in combination with psilocybin will lead to the absence of an oxytocin response, and no enhancement in divergent thinking.

Psilocybin as tool to investigate the neurobiology underlying the creative mind will help to answer the question why psychedelics can be beneficial in the treatment of psychopathologies in which flexible thinking is disturbed.

Download English Version:

<https://daneshyari.com/en/article/8515621>

Download Persian Version:

<https://daneshyari.com/article/8515621>

[Daneshyari.com](https://daneshyari.com)