Original Paper

Decreased mental time travel to the past correlates with default-mode network disintegration under lysergic acid diethylamide

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Abstract

This paper reports on the effects of LSD on mental time travel during spontaneous mentation. Twenty healthy volunteers participated in a placebo-controlled crossover study, incorporating intravenous administration of LSD (75 µg) and placebo (saline) prior to functional magnetic resonance imaging (fMRI). Six independent, blind judges analysed mentation reports acquired during structured interviews performed shortly after the functional magnetic resonance imaging (fMRI) scans (approximately 2.5 h post-administration). Within each report, specific linguistic references to mental spaces for the past, present and future were identified. Results revealed significantly fewer mental spaces for the past under LSD and this effect correlated with the general intensity of the drug's subjective effects. No differences in the number of mental spaces for the present or future were observed. Consistent with the previously proposed role of the default-mode network (DMN) in autobiographical memory recollection and ruminative thought, decreased resting-state functional connectivity (RSFC) within the DMN correlated with decreased mental time travel to the past. These results are discussed in relation to potential therapeutic applications of LSD and related psychedelics, e.g. in the treatment of depression, for which excessive reflection on one's past, likely mediated by DMN functioning, is symptomatic.

Keywords

Altered states of consciousness, lysergic acid diethylamide, psychedelics, mental time travel, episodic past memory, mentation reports, default-mode network, self

Introduction

Lysergic acid diethylamide (LSD) is a semi-synthetic tryptamine hallucinogen or classic 'psychedelic' with a rich pharmacology. Its characteristic psychological effects are thought to be mediated by serotonin 2A receptor agonism (Nichols, 2004). However, the connections between the neurobiological and the psychological effects of LSD are complex and still poorly understood. To help bridge this gap, the current study sought to integrate neurobiological data from functional brain imaging with data derived from mentation reports collected 2.5 h after administration of LSD and (separately) placebo. Linguistic analyses of mentation reports have previously been used to quantify psychological phenomena such as motor imagery, hallucinations, and recently mental time travel to the future (Speth and Speth, unpublished; Speth et al., 2013, 2015, 2016). The present crossover study used a linguistic tool to analyse references to mental time travel under LSD and placebo in the language of the mentation reports.

Mental time travel refers to the ability of humans to mentally project themselves backwards and forwards in time, to recollect aspects of past autobiographical episodes or imagine future experiences (Schacter et al., 2007; Suddendorf and Corballis, 1997, 2007; Tulving, 1984, 2002, 2005). Previous research has linked spontaneous mental time travel, as it occurs during mind-wandering, to a particular brain network, known as the default-mode network (DMN: Mason et al, 2007; Raichle, 2015). The DMN is a network of hub regions that show strong structural and functional connections associated with various meta-cognitive processes (Spreng et al., 2009), including autobiographical memory retrieval and envisioning of the future (Addis and Schacter, 2008; Buckner et al., 2008; Schacter et al., 2012; Spreng and Grady, 2010; Wagner et al., 2005). The frequency of incidences of mental time travel has been found to correlate positively with DMN resting-state functional connectivity (RSFC; Andrews-Hanna et al., 2010). More frequent mind-wandering has been found to correlate with low mood (Killingsworth and Gilbert, 2010). Increased DMN RSFC has been found in depression (Greicius et al., 2007), particularly in relation to ruminative thought (Berman et al., 2011), which typically takes the form of reflecting

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on one's self in the past. Conversely, decreased DMN RSFC has been observed in the psychedelic state (Carhart-Harris et al, 2012a; Palhano-Fontes et al., 2015); and current investigations are underway into the antidepressant potential of psychedelics (Baumeister et al., 2014; Osorio Fde et al., 2015).

An often reported feature of the psychedelic experience is a breakdown or decomposition of the sense of 'self' particularly at higher doses. This phenomenon is also known both colloquially (Turton et al., 2014) and academically (Lebedev et al., 2015), as 'ego-dissolution' or 'ego-disintegration'. However, defining and quantifying this phenomenon is a challenge (Carhart-Harris et al., 2015; Lebedev et al., 2015). The results of the present study may help these investigations, especially in terms of shedding light onto a possible reduction in mental time travel to the past under LSD. The dependence of a sense of identity on the continuing access to and rehearsal of autobiographical information has been well documented (Pasupathi and Hoyt, 2009). A secure sense of self or ego may therefore depend on a continuing input or 'feed' from autobiographical memory into consciousness (Fivush and Nelson, 2006; Turton et al., 2014). Recent neurophysiological evidence suggests that LSD reduces functional connectivity within the DMN (Carhart-Harris et al., 2015). Since the DMN appears to be closely involved in mental time travel (Buckner et al, 2009; Spreng et al., 2009), in particular to the past (Buckner et al., 2009), but is 'disintegrated' under psychedelics (Carhart-Harris et al. 2012a; Palhano-Fontes et al., 2015) it was predicted that participants would engage less in mental time travel under LSD than placebo and that this effect would correlate with DMN disintegration.

Method

Quantitative linguistic analysis was conducted on transcriptions of participants' verbally delivered mentation reports collected after LSD or placebo administration. This third person method of analysis is intended to objectively measure mental events as they become expressed in the natural language of the first person report (for further explanation see Speth and Speth, unpublished, in press; Speth et al., 2013, 2015, 2016). This study investigated whether the mentation reports differed in the number of linguistic constructs (referred to as 'theta roles' and 'mental spaces', see below for definitions) that indicated references to mental time travel to the past or future, or thoughts about the present. Six raters were instructed to analyse a total of 77 mentation reports. The raters were blind in so far as they were not informed to which condition (LSD or placebo) the individual reports referred.

Participants

Twenty healthy volunteers, recruited to the study via word-of-mouth, participated in the study (four females, mean age=30.9±7.8, range=22–47), and 19 volunteers were included in the analyses reported below (one male was excluded due to an absent report from the LSD condition). Due to the potentially anxiogenic effects of classic psychedelics in a neuroimaging environment, all participants were required to have had at least one previous experience with a classic psychedelic drug (mean estimated LSD uses=14±17.8, range=0–70, see below for other psychedelics) but not within 14 days of the first dosing session (mean last use of LSD=899.3±1363, range=14–5400 days). Self-estimates of other drug use were as follows (mean±standard deviation (SD), range): weekly alcohol units=10.3±9; daily cigarettes=0.3±1.1, 0–5; cannabis uses=705±639, 30–2000; 3,4-methylenedioxy-methamphetamine (MDMA) uses=27±24, 2–100; psilocybin/magic mushroom uses=9.4±7.8, 1–35; ketamine uses=3.6±5, 0–20; cocaine uses=9.6±9.4, 0–30. Previous drug use did not correlate with the primary study outcomes.

Experimental design

The current study was placebo-controlled and used a within-subjects/cross-over, balanced-order design. The study received a favourable opinion from the National Research Ethics Service (NRES) ethics committee London-West London and was conducted in accordance with Good Clinical Practice guidelines, the National Health Service Research Governance Framework, and complied with the ethical standards of the declaration of Helsinki (1975, revised 2008). Imperial College London sponsored the research and a Home Office license was obtained for research with Schedule I drugs. All volunteers were sent a study information sheet and asked to read it before their screening visit.

Volunteers made three study visits that comprised screening, dosing session one, and dosing session two. Dosing sessions were separated by at least two weeks in every case and the order of receipt of LSD was balanced, i.e. half of the volunteers received LSD in dosing session one and half in dosing session two. Volunteers were blind to the dosing order but the research team were not. Dosing order was determined sequentially so that all odd-numbered volunteers (i.e. S1 was the first volunteer recruited and S20 was the last) received LSD in dosing session one, whereas all even-numbered volunteers received it in dosing session two.

Screening

Prior to study enrolment, volunteers attended a screening visit at the Wellcome Trust Clinical Research Facility (WTCRF) at the Hammersmith Hospital in West London. The study design, procedures, and psychological effects of LSD were explained and signed informed consent was taken. Key exclusion criteria were: <21 years of age, personal history of diagnosed psychiatric illness, immediate family history of a psychotic disorder, an absence of previous experience with a classic psychedelic drug (e.g. LSD, mescaline, psilocybin/magic mushrooms or dimethyltryptamine/ayahuasca), pregnancy, problematic alcohol use or a medically significant condition rendering the volunteer unsuitable for the study.

Experimental procedure

Participants were asked to arrive at the study centre (Cardiff University's Brain Research Imaging Centre) at a specific time at or before 09:00. A urine test for drugs abuse and pregnancy (where relevant) was carried out. Participants were re-briefed about the procedures for the day and any recent drug and alcohol use was documented. The study physician inserted a cannula into a vein in the antecubital fossa in preparation for intravenous dosing and the volunteer was encouraged to relax prior to drug/placebo administration. The dose of LSD was 75 µcg (i.v.) in 10 mL saline. Previous research has found this dose to produce robust psychological effects that are generally well tolerated (Carhart-Harris et al., 2015). Placebo was 10 mL saline (i.v.). Both solutions were infused over 2 min.

After dosing, volunteers completed a functional neuroimaging protocol. In brief, subjects spent a period habituating to a scanner environment in a mock magnetic resonance imaging (MRI) scanner before entering a real MRI scanner (one hour post-dosing). The MRI scanning session lasted for one hour after which the first of two structured interviews was performed.

The present analyses are concerned with the mentation reports obtained from participants at the beginning of structured interviews, performed soon (within 30 min) after the functional MRI (fMRI) scanning, ~2.5 h post-dosing. Participants were prompted to report on their mentation by means of four different question asked successively by the investigator ('What was it like in the scanner?', 'Did you daydream in the scanner, and if so, what did you daydream?', 'Was the experience dreamlike at all, and if so, how?', 'Did you experience any personal thoughts or feelings at any point?').

The size of the subjective effect of LSD was assessed by a visual analogue scale with 20 increments. The subjective effects of LSD were detected approximately 10 min post-infusion, peaked approximately 120 min post-infusion (towards the end of the first scan, prior to the first interview), and subsided to a negligible level approximately 7–8 h post-infusion. Participants were discharged by the study physician when they were considered to be functioning normally. Volunteers were either picked-up by a friend or partner, ordered a taxi or were accompanied home by the research team as far as was feasible. Volunteers were asked to contact a researcher via phone or text message once they had arrived home safely. A study psychiatrist was present for the duration of each dosing session and one researcher was allocated to each participant to assist them throughout the day. For each participant, the same researcher was present for both dosing days.

fMRI

fMRI was performed on a 3T GE HDx system. Two blood-oxygenlevel dependent (BOLD)-weighted fMRI scans were acquired using a gradient echo-planar imaging sequence, repetition time (TR)/echo time (TE)=2000/35 ms, field-of-view=220 mm, 64×64 acquisition matrix, parallel acceleration factor=2, 90° flip angle. Each of the two BOLD scan was 7:20 min in duration. Conditions were eyes-closed and task-free, with the instructions: 'Please keep still with your eyes shut at all times and try not to fall asleep'. Detailed descriptions of the pre-processing involved in these analyses will be reported in a separate publication and can be found in the Supplementary Material.

A template DMN was acquired by using independent component analysis (ICA) performed on data derived separately as part of the Human Connectome Project (HCP) (Glasser et al., 2013). All scans were band-passed filtered (0.01–0.08 Hz) and Multivariate Exploratory Linear Optimized Decomposition into Independent Components, as implemented in FMRIB Software Library was used to extract 20 ICA components. A single canonical DMN was identified and used in subsequent calculations of intra-DMN connectivity. DMN maps for the two conditions (LSD and placebo), were calculated and contrasted. Paired *t*-tests were used to calculate the difference in intra-DMN RSFC between conditions. Reductions in intra-DMN RSFC by LSD, i.e. as changes in *z*-scores, were defined as DMN disintegration and used in subsequent correlation analyses. Five participants' data could not be included in these analyses due to one participant not completing the fMRI scan and four others showing excessive motion artefacts.

Mentation reports

Specific linguistic references to mental time travel to the past or future, as well as thoughts about present scenarios, were quantified in the participants' transcribed mentation reports. The linguistic tool developed for this quantification process is partly grammatical and partly cognitive-semantic. The grammatical part of the tool is based on linguistic theta theory (Gruber, 2001; Reinhart, 2002, Reinhart and Siloni, 2005) and measures grammatical agency connected to the semantic field of cognition. It has been used in a different context to successfully link numbers of linguistic references to simulated motor activity in mentation reports with motor cortical activation of the respective state of consciousness (Speth et al., 2013), to investigate the effect of transcranial direct current stimulation (tDCS) on motor imagery (Speth et al., 2015), and to measure auditory verbal hallucinations (AVHs) as well as memory in different states of consciousness (Speth and Speth, unpublished; Speth et al., 2016). The second part of the current tool is based on the cognitive-semantic theory of mental spaces by Fauconnier and Turner (Fauconnier, 1994; Fauconnier and Turner, 1997): the method of mental spaces analysis was developed to measure if instances of grammatical cognitive agency introduced references to past, present and future scenarios.

Analysis of mental spaces hosting past, present or future scenarios

In linguistic theta system theory, the initiator of an event takes on a specific thematic (theta) role within a sentence or phrase (Gruber, 2001; Reinhart, 2002, Reinhart and Siloni 2005). He or she is the *agent* who performs an action. In the phrase 'Mimi throws a ball', *Mimi* is the agent. The agent is defined through his or her relationship to the predicate of a phrase: He or she is *performing* the action described by the predicate. Mimi is the one who is *doing something*. The agent is described by a noun phrase, but the agent does not necessarily correlate with the grammatical subject. Consider the following phrases, where Mimi is the agent in both (a) and (b), but the syntactic subject only in the active version (a).

(a) Mimi opens the box.
(b) The box is opened by Mimi.

The current study focuses on a special variety of agency: cognitive agency, which is defined as such agency that is related to the semantic field of cognition. The cognitive agent is the one who is carrying out a cognitive act such as thinking, imagining, remembering or planning. The following phrases (c) to (i) contain instances of (simulated) cognitive agency as they occur in mentation reports:

(c) I was thinking, you know, just thinking about things.
(d) I just realized that I missed my Italian class yesterday.

(e) Trying to figure out what went wrong during my date the other day.
(f) Just relaxing, contemplating if I… should I be helping Anna and Jill with the dishes or be at the gym instead of sitting around.
(g) Thinking about the people in Africa, and what they must feel like fearing that Ebola virus.
(h) Asking myself if Mimi is going to enjoy the party.
(i) Wondering if I can ace the exam tomorrow.

Often cognitive agents build what linguists call mental spaces (Fauconnier, 1994; Fauconnier and Turner, 1997). The notion of mental spaces is borrowed from the philosophical concept of possible worlds – although mental spaces are understood as essentially cognitive scenarios that are not necessarily attributed a specific metaphysical value, and nor do they have to be logically consistent. Mental spaces can host past, present and future scenarios. Examples (c), (d), and (e) present cognitive agencies building a mental space for the past. The cognitive agencies in (f) and (g) each host a mental space for the present, and the cognitive agencies in (h) and (i) host mental spaces for the future.

Mental spaces are marked via (a) grammatical clues ('going to enjoy the party'), (b) immediate semantic clues ('yesterday', 'the other day', 'tomorrow'), or (c) contextual clues (someone is 'sitting around' pondering if he or she should rather be active in terms of 'helping Anna and Jill' or by being 'at the gym' – or someone is picturing the current situation in Africa, contemplating what it must be like for the Africans). In this study, a space built by the cognitive agent is defined as a past, present or future scenario in relation to the cognitive action carried out during the mentation period on which he or she is reporting.

Report rating instructions

All raters were asked to judge all reports. Raters were given a hard copy of the transcribed reports and an instruction manual in which they were asked to identify instances of cognitive agency and ensuing mental spaces in the reports. The instruction manual contained the brief definitions of cognitive agency and mental spaces that are given above. Raters were issued with a rating table which contained different columns in which raters were asked to further classify instances of the grammatical perspective of the cognitive agency (first person singular or plural, second person singular or plural, third person singular or plural). The mental spaces were to be classified as past, present, or future mental spaces, in relation to the cognitive agency itself, according to the definitions given in the instruction manual. Raters were informed that mentation reports are often transcribed in a way that the original, natural speech is preserved. They would therefore encounter elliptical or grammatically ill-formed sentences, and there would be cases where they would be unsure about their rating decisions. Raters were asked to use their best judgment and decide how to deal with such particular phrases, as not all possible instances of cognitive agency and ensuing mental spaces possible in natural speech can be predefined. Importantly, mentation reports did not provide overt statements regarding the study condition (i.e. whether the report was delivered under LSD or not) that would have compromised the raters' blind.

Statistical analyses

Word count per report was compared between LSD and placebo condition by means of a repeated-measures student's *t*-test. Identified instances of cognitive agency were aggregated for every report, separately for every rater. By calculating the mean rating of all raters for each report, one single rating value was assigned for each report. A one-way repeated-measures multivariate analysis of variance (MANOVA) was conducted to test for an omnibus effect of LSD on the number of cognitive agencies referring to the present, past, and future. Where appropriate, repeated-measures student's *t*-tests were used post-hoc to investigate any interactions. In addition, a planned comparison was carried out to assess the effect of LSD on cognitive agencies referring to the past to elucidate the potential relationship between the psychedelic effect of 'ego-dissolution' (Lebedev et al., 2015) and the hypothesised dependence of a sense of identity on the conscious access of autobiographical information (Fivush and Nelson, 2006; Turton et al., 2014). Pearson's correlation coefficient was used for correlational analyses.

Results

A total of 38 mentation reports were collected approximately 2.5 h post dosing (of either LSD or placebo), 19 reports were collected from the LSD condition, and 19 from the placebo condition. Raters identified a mean of 2.03 (SD=1.67) cognitive agencies per report. The agreement on the number of cognitive agencies per report between the six raters was very high (Cronbach's $\alpha=0.92$). Linguistic samples from reports collected after LSD and placebo can be seen in Table 1.

In general, participants delivered longer reports (in terms of word count) after LSD (Mean, M=252.11, SD=146.88) than after placebo (M=155.578, SD=114.77; $t(18)=2.618$, $p=0.017$, $d=0.73$). An omnibus analysis for the effect of LSD on mental spaces for the past, present, and future did not reach significance ($F(3,16)=1.91$; $p=0.168$). The planned comparison, however, showed a significant effect of LSD on mental spaces for the past ($t(18)=2.5$, $p=0.022$, $d=0.85$). Contrary to the effect of LSD on general report length, there were fewer references to the past after LSD (M=0.079, SD=0.2) than after placebo (M=0.71, SD=1.04) (see Figure 1). There were no significant differences in the number of references to the present (placebo: M=1, SD=0.9; LSD: M=1.04, SD=0.79; $t(18)=-0.114$, $p=0.911$) and future (placebo: M=0.64, SD=0.63; LSD: M=0.51, SD=1.08; $t(18)=0.5$, $p=0.624$).

A correlation analysis was run to look at the relationship between the overall intensity of the subjective effects of LSD, rated during MRI scanning, and the effect on reduced cognitive agencies connected to mental spaces for the past in the post-MRI interview. The correlation was in the predicted direction (i.e. more intense subjective effects predicting fewer cognitive agencies connected to mental spaces for the past) and almost reached significance in a two-tailed *t*-test ($r=0.34$, $r^2=0.17$, $p=0.076$).

A further correlational analysis was run to look at the relationship of between-condition differences in within-DMN RSFC or 'integrity' and between-condition differences in the number of cognitive agencies connected to mental spaces for the past. Again, the correlation was in the predicted direction (i.e. greater

Table 1. Report samples from post-lysergic acid diethylamide (LSD) and placebo interviews. Cognitive agencies are given along with the mental spaces to which they are connected.

Condition	Sample	Cognitive agencies and mental spaces
LSD	Things went in different directions, there wasn't really a theme, I was in space definitely, most solitary, but not feeling alone… the intensity was pretty high in that I could go off and all these inner experiences but it wasn't like… I was hurled up against the cosmos and everything and I'm feeling very powerful… It was fun and fascinating and absorbing	N/A
	I did get a lot of fantasies… some of them were about future events, I was thinking about the possibility of like a trance, like a future event, a party, maybe a festival, it was like a festival, but really psychedelic, in the future	2 cognitive agencies + future space
	Lots of different colours, lots of animals, a lot of lions… the strongest thing was just a woman, it felt really sensual almost… feminineness… I wasn't asleep but it felt like waking from a dream, but I was still sort of here… not so much physical, very much in the mind, not many patterns or colours or anything…	N/A
Placebo	Yeah a little bit about the flat I'm living in, a couple of people that I met recently… a little bit vaguely about the next few months, what I'll be doing in the next few months	1 cognitive agency + present space 1 cognitive agency + past space 2 cognitive agencies + future space
	I firstly started to think about family memories.	1 cognitive agency + past space
	Thinking about… random stuff which happened in the last few days, stuff I'm going to do in the next few days	1 cognitive agency + past space 1 cognitive agency + future space
	I sort of felt a bit like, I wonder what I'll have for dinner later, I can't wait to see my kittens, thought a little bit about a random incident that happened in work yesterday	1 cognitive agency + future space 1 cognitive agency + future space 1 cognitive agency + past space

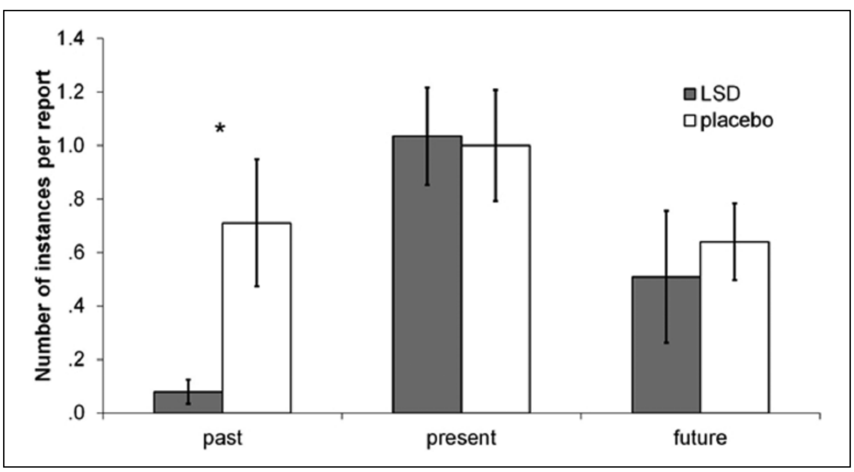

Figure 1. Mean number of instances of cognitive agency referring to past, present or future spaces per report ~2.5 h after lysergic acid diethylamide (LSD) or placebo administration. Error bars indicate standard error of the mean. *$p<0.05$.

DMN disintegration under LSD predicted fewer cognitive agencies connected to mental spaces for the past under the drug) and almost reached significance in a two-tailed *t*-test ($r=0.51$, $r^2=0.26$, $p=0.054$), see Figure 2.

Lifetime uses of LSD, psilocybin and cannabis and time since last-use of these drugs did not correlate with the between-condition differences in mental time travel to the past ($p>0.05$), nor DMN integrity ($p>0.05$). Weekly alcohol-use and time since last drink also did not correlate with the main outcomes ($p>0.05$).

Discussion

This study sought to assess the effects of LSD on spontaneous mental time travel and relate this to the drug's neurobiological effects. Results revealed a selective reduction in the number of linguistic references to mental time travel to the past under LSD. Moreover, there was a relationship between the general intensity of LSD's subjective effects and the reduction in mental time travel to the past, further supporting the assumption that the effect was driven by LSD. Results provide insight into the underlying mechanisms of this effect, as decreased DMN integrity correlated with reduced mental time travel to the past.

Prior research links the DMN to autobiographical memory (Spreng et al., 2009) and self-reflection (Gusnard et al., 2001), as psychological functions relevant to the notion of the self or ego (Carhart-Harris and Friston, 2010). This fits in with the present data on the correlation between decreased integrity within this particular brain network and reduced time travel to the past. The

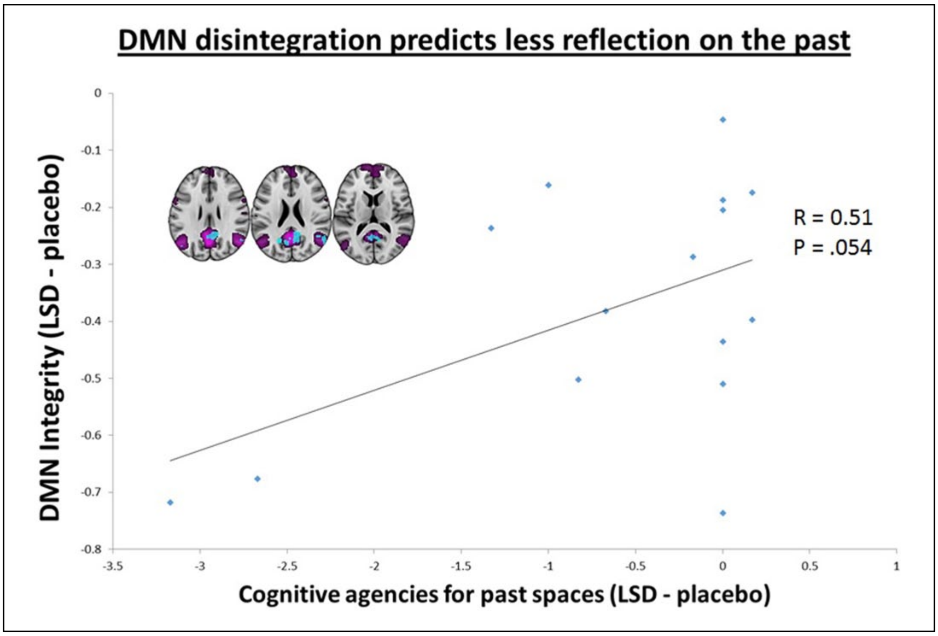

Figure 2. Decreased default-mode network (DMN) integrity predicts fewer cognitive agencies connected to mental spaces for the past under lysergic acid diethylamide (LSD) (r=0.51, p=0.054). The DMN template is shown in purple on the three axial slices and the decrease in DMN integrity under LSD is shown in light blue (cluster-corrected, p<0.05).

DMN appears to subserve spontaneous cognition and particularly cognition that has an introspective and itinerant (i.e. freely-wandering) quality (Andrews-Hanna et al., 2010).

Many brain networks receive a driving input from the external world (e.g. for the visual system this input is light activating cells in the retina) and therefore possess a relatively secure anchor point. The DMN, however, does not possess such an obvious anchor point. If an equivalent 'driving input' was to exist for the DMN, it would likely have an endogenous or intrinsic origin (e.g. a structure or system already within the brain) and be hierarchically inferior (e.g. evolutionarily older) to the cortical DMN. The DMN is known to possess strong anatomical and functional connections with the hippocampus, via the parahippocampal cortex (Ward et al., 2014). Hippocampal to cortical-DMN RSFC has been found to correlate with the prevalence of mental time travel (Andrews-Hanna et al., 2010); moreover, given the classic association between the hippocampus and autobiographical memory (e.g. Fletcher et al., 1997), it seems logical to suspect that the hippocampal-DMN circuit is important, not just for autobiographical memory recollection, but for the preservation of the sense of self or ego. Support for this hypothesis is provided by evidence that the hippocampal-DMN circuit undergoes significant development during maturation (Supekar et al., 2010; Xiao et al., 2015), and that the psychedelic, psilocybin, decreases parahippocampal to cortex RSFC in a manner that correlates with ego-dissolution (Lebedev et al., 2015). Further work is required to test and develop the hypothesis that the hippocampus-DMN circuit is important for the maintenance of one's sense of self and its reliance on autobiographical information.

The present results may help to extend our knowledge of the psychological effects of LSD and could inspire a new perspective on the construct of 'ego-dissolution'. Ego-dissolution is an abstract construct, yet it is generally considered to be an important feature of the psychedelic experience, especially at higher doses, and it is often described by users of psychedelics (Turton et al., 2014). Moreover, the phenomenology of psychedelic-induced ego-dissolution overlaps with the phenomenology of ego-disturbances in early psychosis (Lebedev et al., 2015; Nelson et al., 2012; Schneider, 1959), as well as classic accounts of 'self-loss' in spontaneous religious, spiritual or mystical experiences (James and Bradley, 2012). However, although the experience of ego-dissolution is often described in relation to the psychedelic experience, it is not always clear what is meant by this. It has yet to be investigated if the experience of ego-dissolution under psychedelics is conceptually similar to ego-disturbances in psychosis: Self-disorder in psychosis focuses on a basic, minimal, or core self, also known as ipseity (Nelson et al., 2014; Zahavi, 2005). Further studies could compare phenomenological similarities and differences between the concept of ego disturbances and the concept of ego dissolution, using the linguistic tool presented in the current study. If similarities were to be observed, this would substantiate the LSD state as a model of psychosis (Carhart-Harris et al. 2015).

The notion of 'the narrative self' and 'narrative identity' (Habermas and Bluck, 2000) may be particularly relevant to the findings of the present study and how they relate to psychedelic-induced ego-dissolution. The importance of accessing and rehearsing autobiographical information for the development of a narrative self has been well demonstrated (Pasupathi and Hoyt, 2009). Thus, the existence of a secure sense of self or ego may depend on a regular input or 'feed' from autobiographical memory into consciousness (Fivush and Nelson, 2006), and if this feed is suspended, then the self/ego may collapse (Turton et al., 2014). Based on prior findings (Lebedev et al., 2015), we speculate that the hippocampal-DMN circuit may be an important part of such a 'feed'.

The therapeutic potential of LSD for psychotherapy is currently being revisited (Gasser et al., 2014). LSD has a history of use as an adjunct to psychotherapy, and was originally thought to lower psychological defences and facilitate emotional insight and release, i.e. 'catharsis' (Cohen, 1967; Kaelen et al., 2015). The present finding of decreased mental time travel to the past under LSD may seem contradictory when one considers that a major rationale for using LSD in psychotherapy is that it can facilitate emotional insight, often via stimulating personal memories and associated affect (Cohen, 1967). Indeed, patients undergoing psychedelic-assisted psychotherapy often report re-experiencing past memories with an unusual vividness, an experience sometimes referred to as 'reliving' (Grof, 1979; Sandison, 1954) and facilitated recollection of positive episodic memories was demonstrated in a controlled experiment with psilocybin (Carhart-Harris et al., 2012b).

How can such improved access to autobiographical memory be reconciled with the present finding of less spontaneous reflections on the past under LSD? An explanation for this paradox may be found in the nature of the phenomena themselves, as well as how they are tested and measured. For example, spontaneous recollections or relivings that occur in early psychedelic-psychotherapy often relate to highly salient, personal themes, e.g. familial and/or intimate relationships and highly salient and/or traumatic events that may be temporally remote, e.g. sometimes dating back to childhood (Grof, 1979; Sandison, 1954), such as the following:

> Standing about 4 yards away was my father with his fishing rod…. The sun was shining and the whole scene was peaceful and lovely… all the rest of the day and ever since that picture has remained with me as something too precious to part with because my father has died just before my illness. That is three years this year, and owing to his illness we hadn't fished for some two years…. (Sandison et al., 1954: 497).

Yet the kind of comments coded as reflections on the past in the present study appear to be less emotionally potent and are typically more recent: 'Thinking about… random stuff which happened in the last few days' (Placebo example, Table 1). Thus, during normal waking consciousness, mental time travel to the past may occur with greater regularly than in the psychedelic state; however, the content of these reflections may be more anodyne and (ego) syntonic or unthreatening. Moreover, it should be acknowledged that psychedelic-psychotherapy occurs in a relatively distinctive context, i.e. a patient with mental health problems receives treatment with a psychotherapeutic focus. Further work is required to investigate whether the present findings in healthy volunteers can be replicated in a patient population in a therapeutic context.

Where facilitated autobiographical memory recollection has been demonstrated in controlled research with a psychedelic (Carhart-Harris et al., 2012b), participants were explicitly cued to recollect positive episodic memories. This is quite a different procedure to coding natural speech for spontaneous reflections on the past, present and future, and thus, the outcomes derived from these two different approaches cannot be easily compared. One should also consider that individuals demonstrate hypersuggestibility under psychedelics (Carhart-Harris et al., 2015), and thus, reports of psychedelic-enhanced autobiographical memory recollection in controlled studies (where hypotheses may be easy to intuit) may be biased or, at least confounded, by enhanced suggestibility (Carhart-Harris et al., 2015). Measures of spontaneous cognition (as were employed here) may be particularly useful and informative in this regard, since the experimental aims and hypotheses motivating these measures are effectively hidden.

The raters using the tool of quantitative linguistic analysis in this study evaluated it as easy to apply, and indeed the inter-rater reliability was very high. This tool has been used effectively in previous studies to differentiate between (altered) states of consciousness (e.g. in sleep and waking states, and under electrostimulation; Speth and Speth, unpublished, in 2016; Speth et al., 2015) as well as here with LSD. This helps to develop its utility as a means to quantify markers of different states of consciousness.

Mentation reports produced post-LSD were longer and more elaborate than those given post-placebo. This ties in with findings from other studies of altered states of consciousness, and especially dream research: mentation reports conceived after forced awakenings from rapid eye movement (REM) sleep are known to be longer than reports conceived after non-REM sleep or sleep onset (Stickgold et al., 2001). This was one of the reasons why REM dreams have been interpreted as emotionally richer and more vivid. Their hallucinatory quality has been compared to acute states of psychosis (Hobson, 1997, 2004), as has the psychedelic state (Carhart-Harris, 2007, Carhart-Harris et al., 2014). It is thus not surprising that a (hallucinatory) psychedelic waking experience likewise results in longer reports than a normal relaxed waking experience. It could prove fruitful to consciousness research if the similarities and differences between spontaneously occurring hallucinatory states (e.g. REM dreaming or hypnagogic hallucinations) and pharmacologically induced hallucinatory states (e.g. after LSD or psilocybin) were further explored by applying quantitative linguistic analysis and related quantitative tools, ideally in physiology-monitored experimental settings and within-subject designs (Carhart-Harris and Nutt, 2014).

It is important to highlight some limitations of the present study. One of these relates to the fact that participants were intoxicated on LSD when asked to deliver their retrospective accounts of their experience in the MRI scanner. This makes it difficult to determine whether the main effects reported here (i.e. reduced mental time travel to the past) are reflective of the acute intoxication state (which we assume) or the content of the participants' descriptions about their experiences in the scanner, and so the nature of their retrospective thinking. Since the present analyses cannot make this differentiation, one way to address it in future studies might be to ask participants about their present state, e.g. with questions such as 'How do you feel right now?'.

There is also an important limitation which is related to the correlation analysis. It has been argued before that sample sizes in neuroimaging studies are commonly too small to yield reliable, replicable findings and that many reported positive outcomes may therefore be false positives (Button et al., 2013). It would be sensible to caution therefore that the present study's sample size of n=15 (for the fMRI) may be too small to demonstrate a reliable relationship between individual differences in DMN connectivity and mental time travel and greater sample sizes are therefore advised for future studies.

Another important limitation of the present study's findings must be considered. Namely, it could be inferred that the observed reduction in reflection on the past under LSD is not the result of a specific action of the drug on this specific measure but rather a product of a more general effect of LSD on cognition. If this interpretation were true, any intoxicant (i.e. not just LSD) that alters cognition in a profound way, might impact on mentation about the past. However, if this were true, then it might also apply to mentation about the future, but there was no effect of LSD on this measure. Moreover, the reduced mentation about the past was not caused by participants simply reporting less in their interviews on LSD; in fact, LSD interviews were significantly more elaborate and lengthy than the placebo ones (see Supplementary Material for a fuller discussion of this matter). This alternative explanation for the present results could be explored by examining the effects of other intoxicants, with quite different psychological effects to LSD (e.g. alcohol or amphetamine), on the same measures, to see whether consistent results are observed. Beyond pharmacological manipulations, the effects of other exhilarating experiences on the same measures might also be investigated. These important validity checks would inform on whether the effect of psychedelics on past-focused mentation is indeed exclusive to this class of drugs, or rather something more generally associated with intoxication and/or exhilarating experiences.

If the reported effect of LSD on past-focused reflection is relatively exclusive to psychedelics, then this may say something more interesting about them. The therapeutic potential of psychedelics is currently being revisited, with promising preliminary results (Bogenschutz et al., 2015; Gasser et al., 2014; Grob et al., 2011; Osorio Fde et al., 2015). Inspired by the findings of neuroimaging research with psychedelics (Carhart-Harris et al., 2014), our team are currently investigating the antidepressant potential of psilocybin-assisted psychotherapy for treatment-resistant depression, and again, the initial results are very promising. fMRI studies with psilocybin (Carhart-Harris et al., 2012a), ayahuasca (Palhano-Fontes et al., 2015) and LSD (Carhart-Harris, 2015) have all shown decreased DMN RSFC, as have fMRI studies with meditation (Brewer et al., 2011; Farb et al., 2007; Hasenkamp et al., 2012), whereas DMN RSFC has been found to be elevated in depression (Greicius et al., 2007), and to correlate positively with ruminative thinking (Berman et al., 2011).

The present analyses found a decrease in mental time travel to the past under LSD. Previous work has shown that daydreaming about the past is associated with low mood (Killingsworth and Gilbert, 2010) and popular treatments for depression, such as mindfulness-based psychotherapy, encourage patients to adopt a more present-focused style of thinking (Shapiro et al., 2006). It is intriguing to consider whether psychedelics work in a similar way to mindfulness-based therapies; promoting a mental state that is less focused on the past and therefore less unhappy (Killingsworth and Gilbert, 2010) – and there is some recent evidence to support this (Soler et al. 2016). It would be interesting to extend this work to enquire whether any mindfulness-promoting effects of psychedelics are be mediated by decreases in intra-DMN functional connectivity.

The present study has found decreased mentation on the past in conjunction with decreased DMN integrity under the acute effects of LSD; however, further work is now required to test whether the same effect can be observed after the acute effects of LSD have subsided. If the results of previous controlled studies with psychedelics (Griffiths et al., 2008), as well as subjective reports of participants from our own previous studies (Carhart-Harris et al., 2012a) are considered, then such enduring effects seem likely:

> Ever since [the psilocybin session on] Thursday, I'd say I have found it much easier to engage in the moment – to attend to the here and now. Whether this be watching water in a fountain, or sitting in science talks and meetings this morning. There were some fountains in Cardiff and the water was being blown by the wind, allowing the sun to highlight the spray. I could have watched it for ages – somehow the beauty was enhanced…. Whatever it was, it has lasted – like the sun shining through the leaves this morning, it made me slow down my walk to work and enjoy the experience of it flickering over my face.

Conclusion

In conclusion, the present study sought to investigate the effect of LSD on mental time travel to the past, present and future. Results revealed a selective effect of LSD on mental spaces linked to the past, i.e. there were significantly fewer cases of mental time travel to the past under LSD than placebo, and this effect correlated with the general intensity of LSD's subjective effects. These outcomes shed light on the phenomenon of ego-dissolution and specifically a decomposition of the 'narrative-self' or 'narrative identity', which is strongly associated with autobiographical thought (Pasupathi and Hoyt, 2009). A specific hypothesis was tested that this phenomenon relates to decreased DMN integrity, and this was supported by the data. The findings were discussed in relation to potential therapeutic applications of psychedelic drugs, with a particular focus on depression. Further research is required to investigate the robustness, reliability and specificity of the reported findings.

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References

Addis DR and Schacter DL (2008) Constructive episodic simulation: Temporal distance and detail of past and future events modulate hippocampal engagement. *Hippocampus* 18: 227–237.

Andrews-Hanna JR, Reidler JS, Huang C, et al. (2010) Evidence for the default network's role in spontaneous cognition. *J Neurophysiol* 104: 322–335.

Baumeister D, Barnes G, Giaroli G, et al. (2014) Classical hallucinogens as antidepressants? A review of pharmacodynamics and putative clinical roles. *Ther Adv Psychopharmacol* 4: 156–169.

Berman MG, Peltier S, Nee DE, et al. (2011) Depression, rumination and the default network. *Soc Cogn Affect Neurosci* 6: 548–555.

Bogenschutz MP, Forcehimes AA, Pommy JA, et al. (2015) Psilocybin-assisted treatment for alcohol dependence: A proof-of-concept study. *J Psychopharmacol* 29: 289–299.

Brewer JA, Worhunsky PD, Gray JR, et al. (2011) Meditation experience is associated with differences in default mode network activity and connectivity. *Proc Natl Acad Sci U S A* 108: 20254–20259.

Buckner RL, Andrews-Hanna JR and Schacter DL (2008) The brain's default network: Anatomy, function and relevance to disease. *Ann NY Acad Sci* 1124: 1–38.

Button KS, Ioannidis JP, Mokrysz C, et al. (2013) Power failure: Why small sample size undermines the reliability of neuroscience. *Nat Rev Neurosci* 14: 365–376.

Cardena E, Jonsson P, Terhune DB, et al. (2013) The neurophenomenology of neutral hypnosis. *Cortex* 49: 375–385.

Carhart-Harris R (2007) Waves of the unconscious. The neurophysiology of dreamlike phenomena and its implications for the psychodynamic model of the mind. *Neuropsychoanalysis* 9: 183–211.

Carhart-Harris R and Nutt D (2014) Was it a vision or a waking dream? *Front Psychol* 5: 255.

Carhart-Harris RL (2015) The neural correlates of the LSD state as determined by multimodal functional brain imaging. Submitted.

Carhart-Harris RL and Friston KJ (2010) The default-mode, ego-functions and free-energy: A neurobiological account of Freudian ideas. *Brain* 133: 1265–1283.

Carhart-Harris RL, Erritzoe D, Williams T, et al. (2012a) Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. *Proc Natl Acad Sci U S A* 109: 2138–2143.

Carhart-Harris RL, Kaelen M, Whalley MG, et al. (2015) LSD enhances suggestibility in healthy volunteers. *Psychopharmacology (Berl)* 232: 785–794.

Carhart-Harris RL, Leech R, Tagliazucchi E, et al. (2014) The entropic brain: A theory of conscious states informed by neuroimaging research with psychedelic drugs. *Front Hum Neurosci* 8: 20.

Carhart-Harris RL, Leech R, Williams TM, et al. (2012b) Implications for psychedelic-assisted psychotherapy: Functional magnetic resonance imaging study with psilocybin. *Br J Psychiatry* 200: 238–244.

Cohen S (1967) *The Beyond Within: The LSD Story*, New York: Atheneum.

Farb NA, Segal ZV, Mayberg H, et al. (2007) Attending to the present: Mindfulness meditation reveals distinct neural modes of self-reference. *Soc Cogn Affect Neurosci* 2: 313–322.

Fauconnier G (1994) *Mental Spaces: Aspects of Meaning Construction in Natural Language*. Cambridge: Cambridge University Press.

Fauconnier G and Turner M (1997) *Mappings in Thought and Language*. Cambridge: Cambridge University Press.

Fivush R and Nelson K (2006) Parent-child reminiscing locates the self in the past. *Br J Dev Psychol* 24: 235–251.

Fletcher PC, Frith CD and Rugg MD (1997) The functional neuroanatomy of episodic memory. *Trends Neurosci* 20: 213–218.

Gasser P, Holstein D, Michel Y, et al. (2014) Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. *J Nerv Ment Dis* 202: 513–520.

Glasser MF, Sotiropoulos SN, Wilson JA, et al. (2013) The minimal preprocessing pipelines for the Human Connectome Project. *Neuroimage* 80: 105–124.

Goyal M, Singh S, Sibinga EM, et al. (2014) Meditation programs for psychological stress and well-being: A systematic review and meta-analysis. *JAMA Intern Med* 174: 357–368.

Greicius MD, Flores BH, Menon V, et al. (2007) Resting-state functional connectivity in major depression: Abnormally increased contributions from subgenual cingulate cortex and thalamus. *Biol Psychiatry* 62: 429–437.

Griffiths R, Richards W, Johnson M, et al. (2008) Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. *J Psychopharmacol* 22: 621–632.

Grob CS, Danforth AL, Chopra GS, et al. (2011) Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Arch Gen Psychiatry* 68: 71–78.

Grof S (1979) *Realms of the Human Unconscious: Observations from LSD Research*, London: Souvenir Press.

Gruber JS (2001) Thematic relations in syntax. In: Baltin M and Collins C, eds. *The Handbook of Contemporary Syntactic Theory*. Oxford: Blackwell, pp. 257–298.

Gusnard DA, Akbudak E, Shulman GL, et al. (2001) Medial prefrontal cortex and self-referential mental activity: Relation to a default mode of brain function. *Proc Natl Acad Sci U S A* 98: 4259–4264.

Habermas T and Bluck S (2000) Getting a life: The emergence of the life story in adolescence. *Psychol Bull* 126: 748–769.

Haken H (2004) *Synergetics: Introduction and Advanced Topics*. Berlin: Springer.

Hasenkamp W, Wilson-Mendenhall CD, Duncan E, et al. (2012) Mind wandering and attention during focused meditation: A fine-grained temporal analysis of fluctuating cognitive states. *Neuroimage* 59: 750–760.

Hobson A (2004) A model for madness? *Nature* 430: 21.

Hobson JA (1997) Dreaming as delirium: A mental status analysis of our nightly madness. *Semin Neurol* 17: 121–128.

James W and Bradley M (2012) *The Varieties of Religious Experience: A Study in Human Nature*. Oxford: Oxford University Press.

Kaelen M, Barrett FS, Roseman L, et al. (2015) LSD enhances the emotional response to music. *Psychopharmacology* 232: 3607–3614.

Killingsworth MA and Gilbert DT (2010) A wandering mind is an unhappy mind. *Science* 330: 932.

Lebedev AV, Lovden M, Rosenthal G, et al. (2015) Finding the self by losing the self: Neural correlates of ego-dissolution under psilocybin. *Hum Brain Mapp* 36: 3137–3153.

Mason MF, Norton MI, Van Horn JD, et al. (2007) Wandering minds: The default network and stimulus-independent thought. *Science* 315: 393–395.

Nelson B, Parnas J and Sass LA (2014) Disturbance of minimal self (ipseity) in schizophrenia: Clarification and current status. *Schizophr Bull* 40: 479–482.

Nelson B, Thompson A and Yung AR (2012) Basic self-disturbance predicts psychosis onset in the ultra high risk for psychosis 'prodromal' population. *Schizophr Bull* 38: 1277–1287.

Nichols DE (2004) Hallucinogens. *Pharmacol Ther* 101: 131–181.

Osorio Fde L, Sanches RF, Macedo LR, et al. (2015) Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: A preliminary report. *Rev Bras Psiquiatr* 37: 13–20.

Palhano-Fontes F, Andrade KC, Tofoli LF, et al. (2015) The psychedelic state induced by ayahuasca modulates the activity and connectivity of the default mode network. *PLoS One* 10: e0118143.

Pasupathi M and Hoyt T (2009) The development of narrative identity in late adolescence and emergent adulthood: The continued importance of listeners. *Dev Psychol* 45: 558–574.

Raichle ME (2015) The brain's default mode network. *Annu Rev Neurosci* 38: 433–447.

Reinhart T (2002) The theta system. *Theor Linguist* 28: 229–290.

Reinhart T and Siloni T (2005) The lexicon-syntax parameter: Reflexivization and other arity operations. *Linguist Inq* 36: 389–436.

Sandison RA (1954) Psychological aspects of the LSD treatment of the neuroses. *J Ment Sci* 100: 508–515.

Sandison RA, Spencer AM and Whitelaw JD (1954) The therapeutic value of lysergic acid diethylamide in mental illness. *J Ment Sci* 100: 491–507.

Schacter DL, Addis DR and Buckner RL (2007) Remembering the past to imagine the future: The prospective brain. *Nature* 8: 657–661.

Schacter DL, Addis DR, Hassabis D, et al. (2012) The future of memory: Remembering, imagining, and the brain. *Neuron* 76: 677–694.

Schneider K (1959) *Clinical Psychopathology*. New York: The Classics of Psychiatry and Behavioral Sciences Library, Special edition, 1993.

Sessa B (2012) Shaping the renaissance of psychedelic research. *Lancet* 380: 200–201.

Shapiro SL, Carlson LE, Astin JA, et al. (2006) Mechanisms of mindfulness. *J Clin Psychol* 62: 373–386.

Soler J, Elices M, Franquesa A, et al. (2016) Exploring the therapeutic potential of Ayahuasca: Acute intake increases mindfulness-related capacities. *Psychopharmacol (Berl)* 233: 823–829.

Speth J and Speth C (2015) As we fall asleep we forget about the future. A quantitative linguistis analysis of mentation reports from hypnagogia. Unpublished.

Speth J and Speth C (2016) Memory for the future appears inhibited in sleep. Unpublished.

Speth C and Speth J (2016) The borderlands of waking: Quantifying the transition from reflective thought to hallucination in sleep onset. *Conscious Cognit* 41: 57–63.

Speth J, Frenzel C and Voss U (2013) A differentiating empirical linguistic analysis of dreamer activity in reports of EEG-controlled REM-dreams and hypnagogic hallucinations. *Conscious Cogn* 22: 1013–1021.

Speth J, Speth C and Harley TA (2015) Transcranial direct current stimulation of the motor cortex in waking resting state induces motor imagery. *Conscious Cogn* 36: 298–305.

Speth J, Speth C and Harley TA (in press) Auditory verbal experience and agency in waking, sleep onset, REM, and non-REM sleep. *Cognit Sci*.

Spreng RN and Grady CL (2010) Patterns of brain activity supporting autobiographical memory, prospection, and theory of mind, and their relationship to the default mode network. *J Cogn Neurosci* 22: 1112–1123.

Spreng RN, Mar RA and Kim AS (2009) The common neural basis of autobiographical memory, prospection, navigation, theory of mind, and the default mode: A quantitative meta-analysis. *J Cogn Neurosci* 21: 489–510.

Stickgold R, Malia A, Fosse R, et al. (2001) I. Longitudinal field study of sleep/wake factors influencing mentation report length. *Somnologie (Berl)* 24: 171–179.

Suddendorf T (2013) Mental time travel: Continuities and discontinuities. *Trends Cogn Sci* 17: 151–152.

Suddendorf T and Corballis MC (1997) Mental time travel and the evolution of the human mind. *Genet Soc Gen Psychol Monogr* 123: 133–167.

Suddendorf T and Corballis MC (2007) The evolution of foresight: What is mental time travel, and is it unique to humans? *Behav Brain Res* 30: 299–351.

Supekar K, Uddin LQ, Prater K, et al. (2010) Development of functional and structural connectivity within the default mode network in young children. *Neuroimage* 52: 290–301.

Sussman S and Arnett JJ (2014) Emerging adulthood: Developmental period facilitative of the addictions. *Eval Health Prof* 37: 147–155.

Tolle E (2005) *The Power of Now: A Guide to Spiritual Enlightenment*. London: Hodder Mobius.

Tulving E (1984) Précis of Elements of episodic memory. *Behav Brain Res* 7: 223–268.

Tulving E (2002) Episodic memory: From mind to brain. *Annu Rev Psychol* 53: 1–25.

Tulving E (2005) Episodic memory and autonoesis: Uniquely human? In: Terrace HS and Metcalfe J (eds) *The Missing Link in Cognition: Origins of Self-Reflective Consciousness*. Oxford: Oxford University Press, pp. 3–46.

Turton S, Nutt DJ and Carhart-Harris RL (2014) A qualitative report on the subjective experience of intravenous psilocybin administered in an FMRI environment. *Curr Drug Abuse Rev* 7: 117–127.

Wagner AD, Shannon BJ, Kahn I, et al. (2005) Parietal lobe contributions to episodic memory retrieval. *Trends Cogn Sci* 9: 445–453.

Ward AM, Schultz AP, Huijbers W, et al. (2014) The parahippocampal gyrus links the default-mode cortical network with the medial temporal lobe memory system. *Hum Brain Mapp* 35: 1061–1073.

Washington SD and Van Meter JW (2015) Anterior-posterior connectivity within the default mode network increases during maturation. *Int J Med Biol Front* 21: 207–218.

Xiao Y, Zhai H, Friederici AD, et al. (2015) The development of the intrinsic functional connectivity of default network subsystems from age 3 to 5. *Brain Imaging Behav*. Epub ahead of print 11 Mar 2015.

Zahavi D (2005) *Subjectivity and Selfhood: Investigating the First-Person Perspective*. Cambridge, MA: MIT Press.