SPONTANEOUS CONFABULATION AND THE ADAPTATION OF THOUGHT TO ONGOING REALITY

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Confabulation — the production of fictitious stories — has puzzled clinicians for over a century. Recent studies have singled out spontaneous confabulations as a distinct disorder that is characterized by an inability to adapt thought and behaviour to ongoing reality, so that patients act according to presently inappropriate memories. Lesions that lead people to confabulate always involve anterior limbic structures. Studies on healthy subjects and on patients with lesions of this type indicate that the orbitofrontal cortex, through subcortical connections, suppresses presently irrelevant memories even before their content is consciously recognized. The studies indicate that the monitoring of ongoing reality in thought might be a capacity of the brain's reward system.

ILLUSORY RECOGNITION
False familiarity with items that have not been presented in a memory task.

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Confabulations have intrigued clinicians for over a century. Korsakoff observed that many alcoholic patients with amnesia would produce detailed accounts of events that had never happened[1,2]. These 'pseudo-reminiscences'[3] were soon called 'confabulations'[4–7], of which different forms were recognized. Some patients would react to questions with invented responses, as if trying to avoid embarrassment caused by their lack of memory. Others would produce elaborate, fantastic stories that seemed to exceed the need to hide a gap in memory. Confabulations were subsequently recognized in other diseases[1,5,8–10], but both their anatomical basis and their underlying mechanisms remained elusive for decades.

Here, I discuss current interpretations of confabulations. I present evidence that allows spontaneous confabulation to be singled out as a distinct form of false memory after anterior limbic (in particular orbitofrontal) damage. Patients with lesions in these areas produce stories that seem to be invented, but always contain elements of true events. The stories seem to reflect the patients' honest view of ongoing reality, and often guide their behaviour. The study of these subjects has revealed an anterior limbic mechanism for selecting memories of current relevance, and has provided models to explore how the healthy human brain adapts thought and behaviour to ongoing reality.

Forms of confabulation

Confabulation has been defined as "falsification of memory occurring in clear consciousness in association with an organically derived amnesia"[11] or as "spontaneous narrative reports of events that never happened"[12]. The intensity of confabulation can vary from one patient to another. Several authors have distinguished between momentary confabulations, which are produced to avoid embarrassment, and fantastic or productive confabulations[4,13]. Another distinction has been made between provoked confabulations, which can be elicited by questions, and spontaneous confabulations, which patients produce without a recognizable motive[7]. Modern authors often mix these characteristics and extend the description of spontaneous confabulations to 'fantastic, productive, sustained, wide-ranging, grandiose, readily evident in the subject's everyday conversation', with the assumption that they represent a more severe form of the same disorder as provoked confabulations[11,14–17]. Recent theories have tried to explain both provoked and spontaneous confabulations, sometimes together with ILLUSORY RECOGNITION, within a common framework[12,18–20].

My colleagues and I tested the association between different forms of false memories in a group of patients with brain damage that had similarly severe retrieval failure in a verbal memory test[21]. Patients were classified

as spontaneous confabulators if they produced confabulations with no external trigger, if they seemed to be convinced about the veracity of their stories, and if they occasionally acted according to them (as proof of the spontaneity and the patients' conviction about the veracity of the confabulations). Similarly to other authors[15], we measured provoked confabulations as the number of false words (intrusions) when subjects recalled a previously learned word list, and as the number of false ideas when recalling a story. It is noteworthy that other authors have distinguished between confabulated stories and intrusions, while still considering them within the same framework[12,19,22]. We measured false recognition as the number of falsely recognized words (lures) in a verbal memory test, and as false positives in a continuous picture recognition task. No limitation as to the aetiology of brain damage was made.

We found that these three types of false memories were not associated[21,23]. On the contrary, there was a DOUBLE DISSOCIATION between spontaneous confabulation and both provoked confabulation and false recognition, showing that spontaneous confabulation is independent of the other two types of failure of memory. This finding is compatible with the observation that provoked confabulations can be induced in healthy subjects when they are pushed to retrieve details of an inaccurate memory (for example, details of a holiday[20]). Illusory recognition can also be induced in healthy subjects when they are asked to recognize an item (such as a word) that was not presented before among previously learned, closely related items[24,25]. By contrast, the profound confusion of ongoing reality that characterizes spontaneous confabulation only occurs after brain damage.

Presentation of spontaneous confabulation

Spontaneous confabulations reflect a profound derangement of thought. Patients are admitted to neurorehabilitation services as a result of memory failure after brain damage. Just like other amnesics, they might appear normal to the uninformed person. Accounts of their recent doings and their plans for the day might be entirely cogent. Only a trained person might realize that the patients' discourse is inappropriate and does not take into account their hospitalization and brain damage. For example, a 58-year-old woman that was hospitalized after rupture of an ANEURYSM of the ANTERIOR COMMUNICATING ARTERY was convinced that she was at home and had to feed her baby, but her 'baby' was over 30 years old at the time[21]. A tax accountant with extensive traumatic destruction of the orbitofrontal cortex (OFC) inadvertently left the hospital under the conviction that a taxi was waiting downstairs to take him to a meeting with the county's financial director[21,26]. A dentist who was hospitalized after aneurysm rupture repeatedly left the hospital under the conviction that patients were waiting for him at his clinic[27].

Similarly to healthy people, most patients have preferred topics in their thinking[8,9,21,23,28,29]. The mother cited above was regularly concerned about her baby, the tax accountant repeatedly thought he had a business meeting, and the dentist was consistently concerned about his patients. Although it might seem that a patient has just one topic of confabulation[3,28], conversation usually reveals that the patient's concept of reality is deranged in a general fashion. Questioning reveals that the patients are disoriented; they confuse the place and time (they typically antedate it), and are unaware of the hospitalization and the reason for it[29–31]. They often deny having a memory failure. When confronted with evidence contradicting their beliefs, they can be surprised and search for explanations, but fail to adapt their ideas about reality[3,21,27]. A patient, who was convinced he was in Bordeaux (rather than Berne), admitted that the view from the window indeed did not resemble Bordeaux, but added "I am not crazy, I know that I am in Bordeaux!"

Confabulations are usually limited in time; they relate to the recent past, the present and the future. So, patients fabricate stories about their recent doings and recent events, and produce plans for the future that are incompatible with their current state[21,29,31]. General knowledge and remote autobiographic memory is typically, but not always[32], preserved[27,29,31,33]. Exceptionally, confabulations can extend over many years: one of our patients with extremely severe spontaneous confabulation mixed elements of events that had occurred over 25 years into the narrative of what he remembered as one single episode[23]. The confabulations therefore seemed bizarre and incoherent, corresponding to what has been called 'wild fabrications'[34]. Nonetheless, similarly to virtually all spontaneous confabulators, the elements of his discourse were plausible and could be traced back to actual events[34,35]. This feature is typical of confabulations in general[3,8,9,21,29,35–38]. Spontaneous confabulation, as discussed here, constitutes a syndrome of profound derangement of thought, in which the concept of ongoing reality in thinking and planning is dominated by a patient's past experiences and habits, rather than by true ongoing reality. It seems that, for the patients, confabulations are the honest narrative of their perceived reality, rather than invented stories[3,9,21,28,29,31].

Mechanisms of confabulation

Confabulations have been interpreted in many ways, but few authors have distinguished separate forms[13]. An early observation was that amnesia alone was not sufficient for confabulations to occur[4,6,7]. Additional factors were proposed — suggestibility[7], personality traits ("disturbed balance between introversion and extroversion"[37]) and impaired judgement[7]. An early interpretation states that confabulations emanate from an (unconscious) desire to fill gaps in memory[4,6,7,9], an interpretation that still appears in modern texts[39]. However, in comparison with non-confabulating amnesics, confabulators do not have an increased tendency to answer questions about non-existent items for which they have a true 'gap in memory' (Where is Premola? Who is Princess Lolita? What is a waterknube?)[21,40]. Some confabulators do not even have a gap in memory. Although all of them fail common memory tests, particularly when recalling previously learned information after a delay, some confabulators show normal storage capacity in a conceptually simple recognition task[21].

DOUBLE DISSOCIATION
A double dissociation is observed when two different conditions (lesions or tasks) lead to complementary patterns in behaviour or brain activation; task X is normal in patient A but not in patient B, whereas task Y is normal in patient B but not in patient A.

ANEURYSM
A pouch formed by the dilation of the wall of a blood vessel that is often filled with fluid or clotted blood.

ANTERIOR COMMUNICATING ARTERY
Part of the circle of Willis that allows blood flow between the left and right anterior cerebral arteries.

An influential suggestion has been that confabulations are based on the combination of amnesia with frontal EXECUTIVE FAILURES, including control over thinking (self-monitoring)[14,16,17,41–44]. Indeed, in a select group of patients with basal forebrain damage after rupture of an anterior communicating artery aneurysm[17] and in an unselected sample of patients with brain damage[43], the intensity of confabulations correlated with executive failures. These studies, which did not distinguish between different forms of confabulation, indicated an association between the severity of brain damage and the occurrence of false memories, but they do not necessarily reveal the mechanism of a distinct form of confabulation. My colleagues and I found that common executive failures did not distinguish spontaneous confabulators from non-confabulating patients with similarly severe amnesia[21,23,45]. Also, executive failures did not reliably parallel the course of spontaneous confabulations[26]. By contrast, we found that provoked, but not spontaneous, confabulation correlated with relatively better word recall in a memory task and with better performance in a verbal idea-production task (verbal fluency), reviving Bonhoeffer's suggestion that provoked confabulation requires some degree of 'geistige Regsamkeit' ('mental agility')[4]. Provoked confabulations seem to be the trade-off for increased item recollection.

Many authors have suggested that confabulations emanate from a failure of memory retrieval, rather than encoding or storage[12,19,20,40,46–50]. Schacter[12] suggested that cues that are necessary for the retrieval of memories might match and activate stored experiences other than the episode that is sought. Confabulation would occur if a process relevant to focusing were defective, resulting in recollection of information that does not pertain to the target episode[12]. Other authors have also suggested that confabulations result from a failure to focus the search in memory and to monitor the veracity of retrieved memories[19,20,40,46–50]. None of these proposals have specifically explained the reality confusion that is typical of spontaneous confabulation or the criteria that the brain would use to monitor the veracity of a retrieved memory. A more specific proposal by Johnson and her colleagues[18,19,48] holds that confabulations, illusory memory and other false memories reflect an inability to retrieve the precise circumstances of memory acquisition; that is, whether a memory relates to a true or an imagined event, a capacity referred to as reality or source monitoring. Failure of reality monitoring might result from defective encoding of information or defective monitoring at retrieval. Source-memory deficits have been found in spontaneous confabulators[22,29,31], but also in non-confabulating, non-amnesic subjects[51]. Although it seems intuitively plausible that the inability to distinguish between true and imagined events might lead to confabulations and false recognition, it is difficult to imagine how this failure would explain the conviction that spontaneous confabulators have with respect to their beliefs about present reality. According to the mechanism that I propose later in this review, source-memory deficits might be explained as a possible correlate, rather than a cause, of spontaneous confabulation.

A final view stems from the early observation that confabulations seemed to be temporally loose combinations of real memories[8,13]. It was therefore suggested that confabulating patients confuse the temporal order and the context of memory acquisition[8,13,29,36]. Spontaneous confabulators typically fail in tasks that probe conscious knowledge about the recency or temporal sequence of previously presented information[22,29]. However, this failure is not specific to confabulators; even non-confabulating amnesics and patients with dorsolateral frontal lesions (who have no discernible memory failure) can fail such tasks[22,52–57]. So, lack of knowledge about when and where information was acquired in the past does not explain spontaneous confabulation. By contrast, a variant of the temporal-order hypothesis seems to address many characteristics of spontaneous confabulation. Dalla Barba has suggested that confabulators have an impaired awareness of the flow of time in memory — a loss of 'personal temporality', which makes it impossible for them to refer their thinking to the true present[31,58–61]. The theory does not distinguish between different forms of confabulation and is mainly derived from observation; no experimental model has been suggested to test it. In accordance with this theory, we found that spontaneous confabulators, in comparison with non-confabulating amnesics, fail to make temporal distinctions down to the range of seconds[45] (the temporal frame designated as 'immediate present'[62]). The mechanism that I present in the following sections is compatible with this theory, but has the advantage of being derived from an experimental model that reliably separates spontaneous confabulators from non-confabulating amnesics. These experiments not only provided a neurobiological explanation for spontaneous confabulation and disorientation, but also generated testable hypotheses on the healthy brain's capacity to adapt thought to ongoing reality.

Confusion of memory traces

A striking feature of spontaneous confabulations is that they can virtually always be traced back to elements of actual events in the patient's past; the patient seems to re-experience an earlier episode, or even an imagined event, as if it were real and occurring now[3,8,21,29,31,35,36,38]. Why do presently irrelevant memories dominate thought in such a way that they are perceived as ongoing reality?

In our studies, we used variations of an experiment that measures the ability to distinguish between memories that pertain to ongoing reality and memories that do not. No explicit knowledge about the recency of last appearance or the temporal relationship between pieces of information is required[21] (FIG. 1). Subjects make a first run of a continuous recognition task in which they are asked to indicate in a long series of pictures those that reappear during the course of the run. In the first run, any item that seems familiar can be assumed to be a repetition; that is, a target. So, the first run measures ability to learn and recognize new information. We found that most, but not all, spontaneous confabulators and non-confabulating amnesics were impaired in this run, indicating a similarly impaired capacity for new learning[21,23].

EXECUTIVE FAILURES
Impairments in the operation of the 'executive functions' — a cluster of high-order capacities that includes selective attention, behavioural planning and response inhibition, and the manipulation of information in problem-solving tasks.

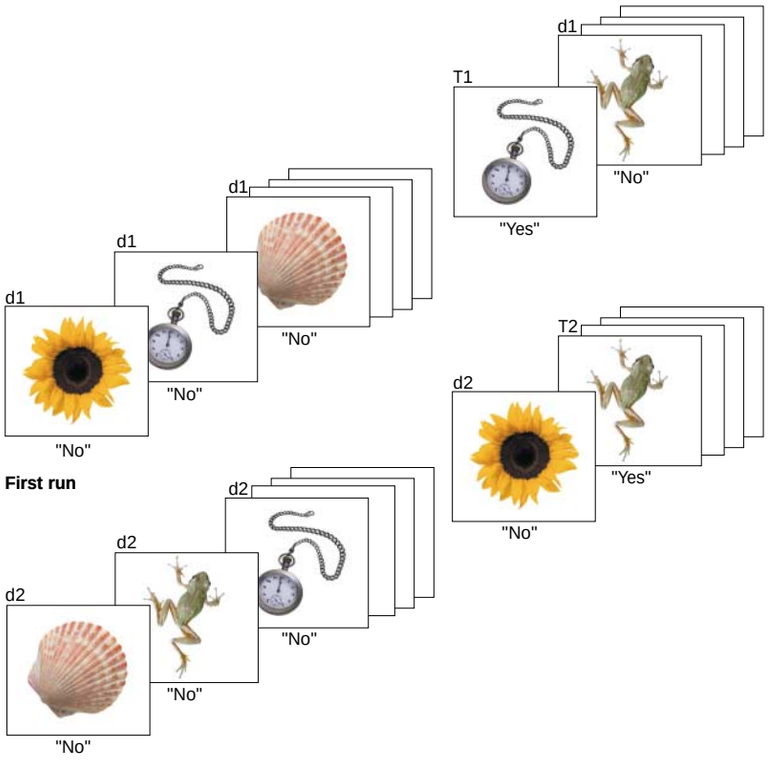

Figure 1 | **The experimental task.** In the first run, subjects see a long series of pictures, among which several are repeatedly presented. Subjects must indicate picture recurrences. This run measures learning and recognition of new information. The second run is composed of precisely the same picture series, arranged in different order. Subjects are asked to forget that they have already seen all pictures and to indicate picture recurrences only within the second run. d1, d2, first presentation of a picture in run 1 and run 2, respectively (distracters); T1, T2, picture recurrences within run 1 and run 2, respectively (targets). "Yes" and "No" denote correct responses.

The decisive part of the experiment lies in the repetition of the task. Subjects are shown the same picture series, arranged in a different order. They are asked to forget that they have already seen all of the pictures and to indicate picture recurrences only within this second run. As all pictures have been presented previously, the task cannot be undertaken on the basis of familiarity judgements alone. Instead, task performance now depends on the ability to sense whether the memory evoked by the presentation of an item refers to the ongoing reality of the current run or to the past reality of the previous run. An inability to make this distinction was expected to lead to poorer performance (decreased number of hits or increased number of false positives).

The results confirmed the hypothesis. Whereas healthy controls and non-confabulating amnesics maintained their performance at the level of the first run, the performance of all spontaneous confabulators was markedly poorer in the second run, which was undertaken one hour after the first run. Without exception, spontaneous confabulators showed a greater increase in false-positive responses than any non-confabulating amnesic or healthy subject[21]. So, spontaneous confabulators specifically failed to distinguish between memories pertaining to the present (the ongoing run) and memories pertaining to the past (the previous run). This observation is compatible with the idea that spontaneous confabulators have a failure of personal temporality[31]. Notably, the task had no predictive value for provoked confabulations[21].

Subsequent studies corroborated the biological validity of the task. First, performance in the task was also highly predictive of disorientation, which is always present in the early stage of spontaneous confabulation[21,30,31]. Orientation (tested with 20 questions[63]) in a group of amnesic patients was only moderately correlated with performance on the first run. That is, the amount of information that subjects can store is a weak predictor of their ability to maintain orientation. By contrast, poor performance on the second run correlated highly with orientation in time, place and circumstances[30]. So, orientation depends primarily on the ability to sort presently pertinent information from memory; it therefore seems to share a common mechanism with spontaneous confabulation.

A second observation that underscores the validity of the task was that it precisely paralleled the clinical course of spontaneous confabulation[26]. Of eight patients that were followed over five years, only those who regained the ability to refer thought to ongoing reality (and therefore ceased to confabulate) showed a normalization of performance on the second run. Persistent spontaneous confabulation was associated with continued failure of the task. No other measure of explicit memory or executive capacities had comparable reliability[26].

Mechanism of 'now' confusion in memory. Why do spontaneous confabulators confuse presently relevant and irrelevant memories? One possible explanation is that the patients fail to represent new, incoming information with normal saliency in memory, such that old, firmly established memories dominate thinking[21,29]. A difficulty with this interpretation is that it does not explain why patients with extremely severe amnesia and no measurable storage capacity do not normally confabulate[64–66], and why patients occasionally also confabulate about long-past events[23,32,49]. An alternative explanation is that spontaneous confabulators cannot maintain a normal contrast between representations of ongoing reality and memories that refer to the past because they fail to suppress activated but presently irrelevant memory traces.

To test these possibilities, we used an adapted version of the continuous recognition task (FIG. 1) with 4 consecutive runs separated from each other by 1, 5 and 30 minutes, respectively[23]. The idea was that a failure to strongly represent incoming information would be mirrored in defective detection of item recurrences within a run, and should result in spontaneous confabulators producing fewer hits. However, if temporal confusion resulted from an inability to suppress presently irrelevant memories, spontaneous confabulators should produce increasing numbers of false-positive responses from run to run relative to non-confabulating amnesics.

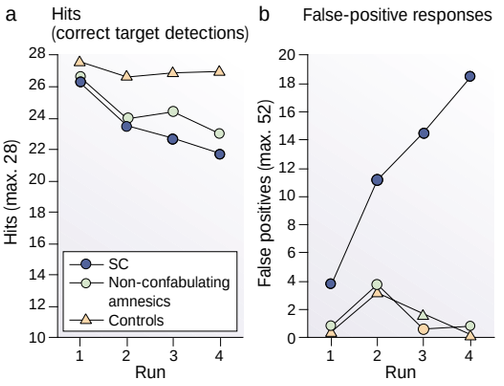

Figure 2 | **Suppression failure in spontaneous confabulation. a** | Number of correct recognitions of repeated items in four runs of the task described in FIG. 1. Runs 2, 3 and 4 were separated by 1, 5 and 30 minutes, respectively. Spontaneous confabulators (SC) and non-confabulating amnesics were similarly impaired in comparison with healthy subjects. **b** | False positives increase from run to run in spontaneous confabulators, whereas non-confabulating amnesics perform like healthy controls. So, an inability to suppress the interference of presently irrelevant memories distinguishes spontaneous confabulators from both non-confabulating amnesics and normal subjects. Modified, with permission, from *Nature Neuroscience* REF. 23 © (1999) Macmillan Magazines Ltd.

The result supported the second hypothesis. In comparison with healthy controls, both spontaneous confabulators and non-confabulating amnesics had difficulty detecting target items, but they did not differ from each other (FIG. 2a). So, failure to represent incoming information saliently is typical for amnesia in general, but it does not explain spontaneous confabulation. By contrast, only spontaneous confabulators showed a steep increase in the number of false-positive responses from run to run, and failed to suppress this interference even when the interval between 2 runs was 30 minutes (FIG. 2b). In comparison, healthy subjects and non-confabulating amnesics gave few false-positive responses and only in the second run, which was performed one minute after the first run. So, spontaneous confabulation seems to result from failure to suppress (inactivate) evoked memories that do not pertain to ongoing reality. This failure then leads to continued, inappropriate saliency (activity) of presently irrelevant memories[23].

Anatomy of spontaneous confabulation

Confabulations were first described in alcoholic people[2,4], but were soon recognized in patients with chronic infections[1,8], traumatic brain injuries[8,9], subarachnoid haemorrhages[10], brain tumours[5] and other diseases. Their anatomical basis remained a mystery; until the 1950s, they were thought to emanate from 'diffuse brain damage'[37,67,68].

Provoked confabulations have no specific anatomical basis, but they are more frequent after brain damage[21,69]. Provoked confabulations can also be induced in healthy subjects[20]. By contrast, spontaneous confabulation does have a distinct anatomical basis. Productive, presumably spontaneous confabulations were repeatedly reported in people with lesions of the basal forebrain and posterior OFC[17,22,27,28,31,34,44], similar to the lesions shown in FIG. 3a. Other lesion sites that lead to confabulation have been occasionally reported. They include the hypothalamus[70] and the dorsomedial thalamic nucleus (DMT)[71], the main relay station of subcortical projections to the prefrontal lobe. It is possible that spontaneous confabulation in KORSAKOFF'S SYNDROME[3,32] also results from destruction of the DMT[72].

Our studies indicated that spontaneous confabulation can result from diverse lesions, the common feature of which is that they either involve the posterior OFC itself or anterior limbic structures directly connected with it[26,30] (FIG. 3b, bottom). The most common lesion site was the posterior OFC together with the basal forebrain. Some spontaneous confabulators had isolated medial OFC damage. Single patients had lesions of the amygdala on one side and the perirhinal cortex on the other side[21,73], or of the anteromedial hypothalamus[74], structures that are directly connected with the posteromedial OFC. Another patient had an infarct of the right capsular GENU, which carries the projections of the DMT to the posterior OFC[29].

This lesion extension clearly differed from the lesions of non-confabulating amnesics, which overlapped on the medial temporal area but might also involve neocortical sites such as the dorsolateral prefrontal cortex (FIG. 3b, top). Damage to the posterior limbic system (medial temporal area) has long been known to produce amnesia[64–66,75–79].

The dichotomy between the anterior and posterior limbic systems was corroborated in an imaging study with healthy subjects (FIG. 3c): when they performed the first run of our task, the hippocampal area was activated (FIG. 3c, top). In the second run, which requires subjects to distinguish between presently relevant and presently irrelevant memories, they exhibited circumscribed posteromedial OFC activation[73] (FIG. 3c, bottom). An interesting observation in this study was that the task was considered by the subjects to be somewhat challenging only when repeated runs were made in immediate succession. So, whereas failure of the anterior limbic suppression mechanism leads to intrusion of memories that were pertinent for behaviour weeks or even years before, intact suppression seems to synchronize thought rapidly (from seconds to minutes) with ongoing reality.

Rehabilitation and clinical course

Spontaneous confabulation is a pervasive disorder that represents a great challenge to any rehabilitation team. There is no controlled study on its rehabilitation. Early clinicians proposed avoiding memory training — such as repeated questions about orientation — with patients and engaging them in common everyday activities, accepting their false interpretation of reality as much as possible[3,4]. Our studies support such an approach. Knowing that any cue can activate a memory[12,80,81] and provoke a presently inappropriate action, patients should receive information about their hospitalization,

KORSAKOFF'S SYNDROME
Anterograde and retrograde amnesia with confabulation that commonly occurs in association with alcoholism, results from thiamine deficiency, and affects primarily the mammillary bodies in the hypothalamus.

GENU
Latin: 'knee'. A general term to describe any structure that is bent like the knee, such as the angle formed by the union of the two limbs of the internal capsule (the genu of the internal capsule) and the ventral curve at the anterior end of the body of the corpus callosum (the genu of the corpus callosum).

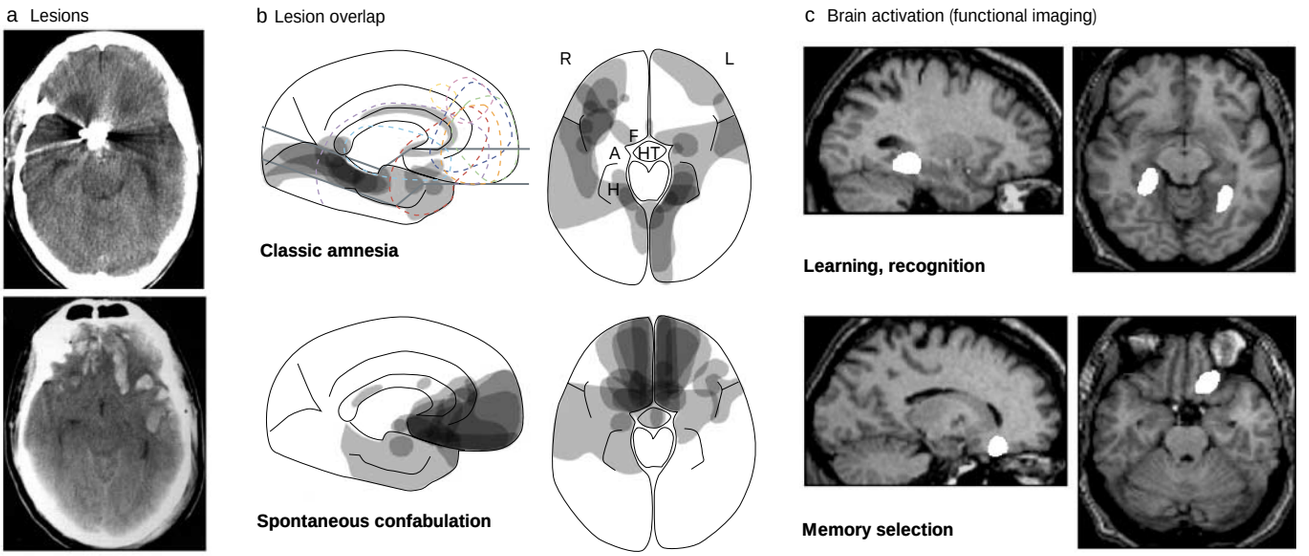

Figure 3 | **Anatomy of spontaneous confabulation and reality monitoring. a** | Typical lesions that lead to the production of spontaneous confabulations. Top, lesion of the basal forebrain and posterior orbitofrontal cortex (OFC) after rupture of an aneurysm of the anterior communicating artery in a 58-year-old woman (discussed in the text). Bottom, traumatic brain injury that led to medial OFC and temporal pole contusions in a 48-year-old tax accountant (described in the text). **b** | Lesion overlap of patients examined in different studies[21,23,30]. The diagrams at left show sagittal views of the brain. Shaded areas indicate paramedian lesions; dashed lines indicate lateral lesions. The straight, parallel lines in the lower part of the upper sagittal view indicate the composite axial slice used to show lesions of the amygdala (A), basal forebrain (F), hippocampus (H), hypothalamus (HT) and OFC in the diagrams at right. Top, the lesion overlap in patients with classic amnesia was primarily in the medial temporal lobe (hippocampal area) and the neocortex (insular cortex or dorsolateral prefrontal lobe). None of these patients has a medial OFC lesion. Bottom, the lesions of spontaneous confabulators primarily overlapped in anterior limbic areas, particularly in the posteromedial OFC and basal forebrain. Isolated lesions involved the hypothalamus, or the amygdala and the perirhinal cortex. **c** | Functional imaging in healthy subjects. Top, the first run in the task described in FIG. 1 induced medial temporal activation. Bottom, the following run, which required suppression, induced posterior OFC activation. Modified, with permission, from REF. 73 © (2000) Society for Neuroscience.

but their false ideas about current reality should not constantly be corrected. It is easier for a mother to accept that her baby has already received food than to convince her that her baby is over 30 years old. The tax accountant accepts more readily that his meetings have been postponed than the fact that he is at the hospital because of brain damage. A memory booklet with information about the circumstances of the hospitalization and feedback to the patients about their own actions might be helpful[28], but many patients fail to use it in a prospective way.

Most patients with spontaneous confabulation eventually stop confabulating. In a follow-up study of eight spontaneous confabulators, all but one stopped confabulating and regained correct orientation in time and place, as well as the ability to refer thinking and acting to ongoing reality[26]. The cessation of spontaneous confabulation was strictly associated with recovery of the ability to suppress presently irrelevant memories, but not with other executive or memory capacities.

The duration of spontaneous confabulation depended on the lesion site; it lasted only a few weeks after isolated damage of the anterior OFC, but up to 12 months after combined posterior OFC and basal forebrain damage[26]. Persistent confabulation has also been described after basal forebrain damage[82]. In our series, only one patient with extremely extensive OFC damage that reached up to the anterior horn of the lateral ventricles — therefore interrupting projections from the DMT to the whole prefrontal cortex — still produced spontaneous confabulations after more than five years[26]. Six of eight patients remained amnesic, but five of these lead independent lives. Vocational outcome was generally poor. Two of three patients with isolated anterior OFC damage had apparently complete neuropsychological recovery, although subtle personality changes with social failures persisted in one of them[26].

Monitoring ongoing reality in thought

Spontaneous confabulation is characterized by unduly dominant intrusion of memory traces that do not pertain to ongoing reality into current thought and behaviour. This observation alone shows that activation of memory bears the risk of eliciting presently irrelevant mental associations. This conclusion is compatible with current neurobiological models which posit that perceptual or internal cues could activate even distant mental associations[80,81,83], some of which would be inadequate guides for current behaviour. Reconstructive processes have been proposed to control the retrieval of memory[12,80]. Our studies indicate that one such mechanism, which is specifically concerned with the adaptation of thought and behaviour to ongoing reality, is mediated by the anterior limbic system (particularly the posterior OFC) and acts by suppressing activated memory traces that do not pertain to ongoing reality (FIG. 4).

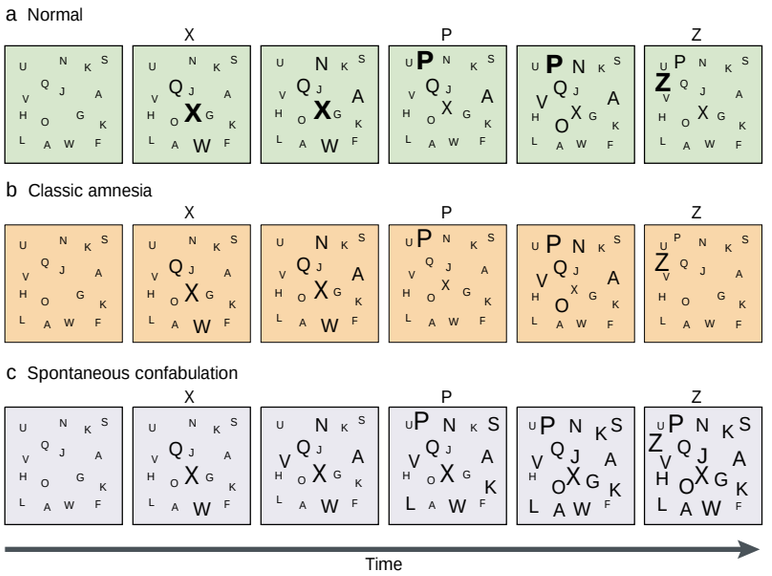

Figure 4 | **Model of 'now' representation and suppression in thinking.** Any letter indicates an event (X, P, Z) or memory trace (letters within squares). The size of the letters indicates their saliency in thinking. **a** | In a healthy person, new incoming information (the reality of 'now') is thought to attain high saliency in cortical representation (X) and to provoke mental associations. Some of these associations might lack connection with ongoing reality; they might be fantasies. The next pieces of incoming information (P, Z) again attain high saliency and provoke mental associations. In addition, previous associations, which do not refer to current reality, are being suppressed (deactivated). **b** | In classic amnesia with no spontaneous confabulation, a new event attains high saliency and provokes mental associations. In contrast to healthy subjects, however, previously encountered information cannot be normally retained (consolidated). So, 'now' is unequivocally represented in thinking, but the information is subsequently forgotten. **c** | In spontaneous confabulation, new information is thought to provoke mental associations, as in a healthy brain. However, when new pieces of information are processed (P, Z), those associations, which no longer refer to the current reality, are not inactivated. Any activated memory trace, whether or not it is pertinent to ongoing reality, could therefore guide thinking and behaviour. Modified, with permission, from REF. 45 © (2000) Elsevier Science.

So, this mechanism does not determine which memory traces are activated in response to a cue (associative processes are left to the cortex); it only filters out those that fail to match the cues that represent ongoing reality. The requirements for such cues are unknown. Temporally coherent activity of multiple sensory and motor areas might be a requirement, as indicated by experiments in animals[83] and by the observation of patients with schizophrenia[84]. It is not suggested that failure of this mechanism explains other thought aberrations characterized by false convictions, such as psychotic thought, or mis-identification of people or places[85]. These disorders might directly emanate from defective cortical processing[84–86].

Despite this limitation, spontaneous confabulation can be considered as a model to study how the brain adapts thought and behaviour to ongoing reality. Given the specificity of our experimental task for spontaneous confabulation, we have used it to explore how this mechanism works in the healthy brain.

Suppression as an early process. The demonstration that spontaneous confabulators fail to suppress presently irrelevant mental associations does not explain the absolute conviction they hold about what they perceive as ongoing reality[12,31]. The same mystery relates to healthy thinking. Why are we so convinced about the 'now'? Why is it impossible to alter consciously our concept of ongoing reality? The easiest way to explain these facts would be that, before the content of an evoked memory (mental association) is recognized, its relation with ongoing reality has been checked. This indeed seems to be the case. We used spatio-temporal analysis of evoked potentials while healthy subjects performed a task similar to the one we had used with patients. Knowing that spontaneous confabulators had specifically failed to suppress false-positive responses in the second run of the task[23,26] (FIG. 2), we were particularly interested in the cortical response to these stimuli ('distracters' of run 2).

We found that correct suppression of these stimuli is associated with distinct alteration of cortical activity after 220–300 milliseconds (FIG. 5a,b). By contrast, learning and recognition — as derived from the differences between the electrical responses to the first and repeated presentation of stimuli in the first run — were associated with cortical amplitude modulation after 400–480 milliseconds[87] (FIG. 5a,b). So, by the time the content of a mental association is recognized and consolidated, its cortical representation has already been adjusted according to whether it relates to ongoing reality or not. This sequence not only explains the conviction that healthy subjects and spontaneous confabulators have about their interpretation of ongoing reality, it also explains our ability to distinguish between the memory of a true and an imagined event. By the time these evoked memories enter the stage of recognition and new encoding, their representation has already been adapted according to their relationship with ongoing reality. This mechanism might therefore be a prerequisite for later source or reality monitoring[18,19,48].

Reality in thinking and reward processing

Spontaneous confabulators act on the basis of presently inadequate memories; that is, on the basis of expectations that have no present potential of being satisfied. A similar failure has been described in other primates. Monkeys with ablations of the posteromedial OFC continue to react to stimuli that are no longer rewarded; they have a severe extinction deficit[88]. In addition, they have difficulty learning new stimulus–reward associations[89]. That is, monkeys with posteromedial OFC ablation fail to update their anticipations to ongoing reality, and continue to act on the basis of the now irrelevant memory that a given cue was previously followed by reward. The posteromedial OFC of monkeys contains neurons that specifically increase their firing rate when an expected reward is not delivered; that is, they fire on extinction trials[90,91]. These neurons therefore signal the inconsistency of a memory with ongoing reality.

How might such neurons in the posteromedial OFC suppress the influence of presently irrelevant memories on thinking and behaviour? Assuming that activated memories are cortically represented as the synchronous

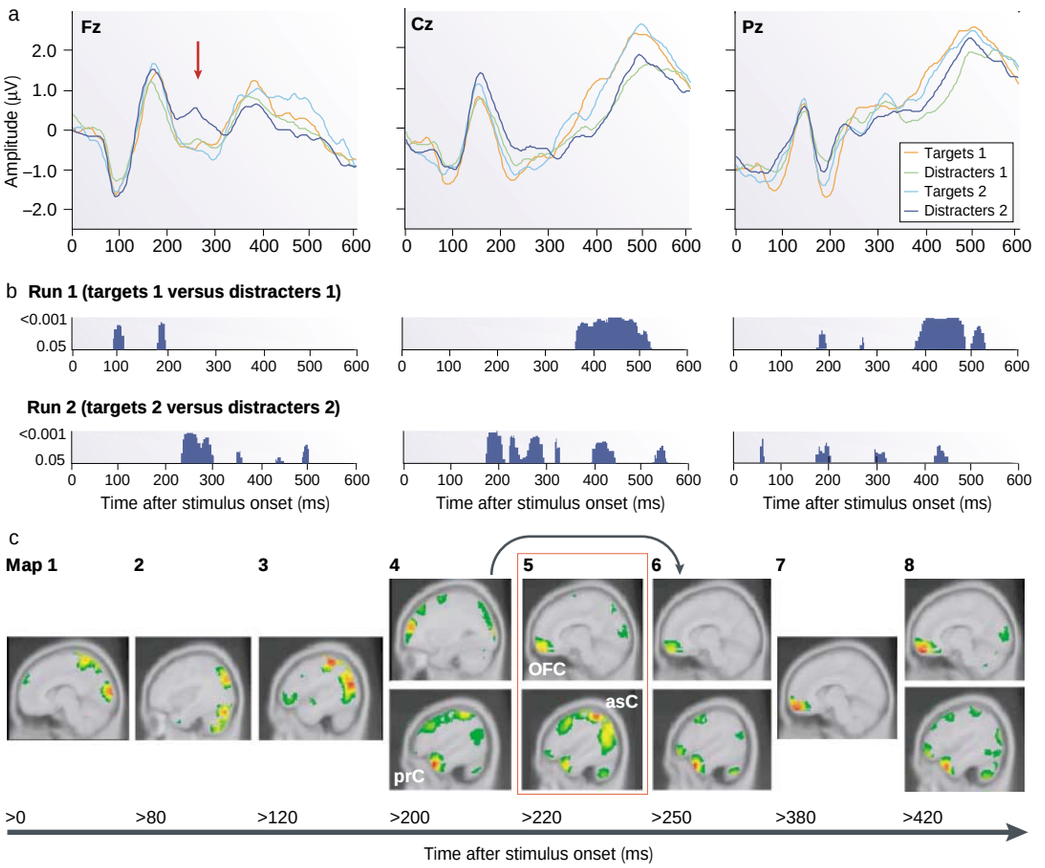

Figure 5 | **Electrocortical manifestation of suppression**. Evoked-potential study[87] with healthy subjects performing the task described in FIG. 1. **a** | Responses over frontal (Fz), central (Cz) and posterior parietal (Pz) electrodes for four stimulus types — targets and distracters in run 1 and run 2. The arrow indicates that the response to distracters of run 2 (stimuli that must be suppressed) differs from all other stimuli at 220–300 ms at electrode Fz. **b** | Statistical comparison of the potential amplitudes of distracters versus targets at each point in time (*p* values, *y* axis). Top, in run 1 (learning and recognition), the main amplitude difference is seen at electrodes Pz and Cz at about 400–500 ms. Bottom, in run 2 (memory selection), the main difference is seen at electrode Fz at about 220–300 ms. **c** | Spatial analysis of the electrical responses over 128 electrodes yielded eight distinct potential maps over 600 ms. Distracters of run 2 differed from the other stimuli by virtue of a significantly shorter and weaker presence of the fifth map[87]. The source localization of these eight maps is shown, using local auto-regressive averaging[101]. The missing configuration when processing the crucial items (that is, the distracters of run 2) is marked in red. The curved arrow indicates that processing of these stimuli proceeds directly from map 4 to map 6 (at about 220–250 ms). Map 5, which is skipped in response to distracters of run 2, is distinct from the subsequent processing stage by virtue of additional neocortical activity. In other words, suppression of presently irrelevant memory seems to be realized by transient inhibition of synchronized neocortical activity[93]. asC, association cortex; OFC, orbitofrontal cortex; prC, perirhinal cortex.

activity of neuronal populations[80,92], suppression of presently irrelevant memories might be exerted by simple desynchronization of these populations[92]. This hypothesis is supported by a source analysis of our evoked-potential data[87], where an INVERSE SOLUTION indicated that suppression differed from the other stimuli by the transient absence of synchronized electrical activity in the association cortex between 220–300 milliseconds[93] (FIG. 5c).

Through what anatomical routes does the OFC induce desynchronization of cortical neuronal networks? How does it communicate with the neocortex? Using positron emission tomography while healthy subjects performed the second run of a more powerful version of our task (four blocks with different types of stimuli), we observed activation of the ventral striatum, the body of the caudate, the substantia nigra and the contralateral medial thalamus, in addition to the left OFC[94]. These findings are entirely consistent with anatomical studies which indicate that communication between the OFC and the neocortex occurs through frontal–subcortical loops that connect the frontal cortex with distinct portions of the striatum, globus pallidus, substantia nigra and thalamic nuclei, before projecting back to the cortex[95,96]. Whereas the loops that emanate from different prefrontal areas seem to be fairly segregated down to the level of the striatum[97], massive cross-communication and convergence of fibres seems to occur at the level of the substantia nigra[98]. The OFC, which initially projects to the ventral striatum[97], might therefore influence the activity of large areas of the neocortex. It is noteworthy that non-delivery of an expected

INVERSE SOLUTION
The localization of the generators of the electromagnetic signal in electro- or magnetoencephalographic recordings.

reward, which elicits increased firing of select neurons in the OFC, phasically inhibits firing of dopaminergic neurons in the ventral striatum, the substantia nigra and the ventral tegmental area at the time when the reward is expected[99]. These neurons, which receive afferents from the posterior OFC, project in turn onto frontal–subcortical loops[100]. These findings are compatible with the idea that the OFC might actively suppress neuronal activity in subsequent sites of the loop, in that the OFC phasically inhibits dopaminergic neurons.

So, whereas studies on the suppression of presently irrelevant memory show participation of structures commonly considered to be part of the brain's reward system[73,94], it also seems that the known properties of this system render it apt to monitor ongoing reality in thought and behaviour. This system prepares the organism for outcomes and signals whether anticipated outcomes actually occur or not. The reward system might therefore be an 'outcome-monitoring system', irrespective of tangible reward.

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