Hypnotic suggestion: opportunities for cognitive neuroscience

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Abstract | Hypnosis uses the powerful effects of attention and suggestion to produce, modify and enhance a broad range of subjectively compelling experiences and behaviours. For more than a century, hypnotic suggestion has been used successfully as an adjunctive procedure to treat a wide range of clinical conditions. More recently, hypnosis has attracted a growing interest from a cognitive neuroscience perspective. Recent studies using hypnotic suggestion show how manipulating subjective awareness in the laboratory can provide insights into brain mechanisms involved in attention, motor control, pain perception, beliefs and volition. Moreover, they indicate that hypnotic suggestion can create informative analogues of clinical conditions that may be useful for understanding these conditions and their treatments.

Despite some understandable misconceptions regarding mind control and choreographed stage shows, hypnosis attracted the attention of a number of eminent thinkers and scientists over the past century (BOX 1). Since the late 1950s, most hypnosis research has employed fairly standard paradigms derived from modern experimental cognitive, social and personality psychology. However, over the past two decades, the scientific investigation and use of hypnotic suggestion have become more closely integrated into mainstream cognitive neuroscience[1–9].

In particular, hypnotic suggestion has been increasingly used as an investigative tool in a range of cognitive and social neuroscience research areas, such as hearing[10], vision[11], synaesthesia[12], volition[13], pain[14–16], and attention and attentional conflict, including the ability to exert substantial control over automatic processes[17–19].

This renewed research interest from the cognitive neurosciences can be divided into two basic groups[2,20]. In the first, which is best described as 'intrinsic', the primary interest lies in acquiring a better understanding of the nature of hypnosis and hypnotically suggested phenomena. Intrinsic studies are largely concerned with what makes some people more responsive to hypnotic suggestions than others, the nature of hypnotic suggestibility, whether suggested hypnotic phenomena are 'real' or are simply 'imagined' and whether hypnosis involves a special state of consciousness. A second, more 'instrumentally focused' group of studies involves the selective use of experimentally and, increasingly, clinically informed suggestions to investigate aspects of normal and abnormal psychological functioning. This more instrumental approach probes challenging issues such as the nature and neural basis of consciousness[21], brain mechanisms underlying visual perception or pain and the putative cognitive origins of clinical symptoms such as medically unexplained paralysis seen in some patients with conversion disorder (hysteria), hallucinations, delusions and alterations in control over thought and action in schizophrenia[6]. A unique advantage of hypnotic suggestion when it is used as a tool for cognitive and clinical neuroscience research is that suggested effects informed by clinical experience can be generated in the laboratory and removed easily and quickly.

Although intrinsic studies have helped to demystify the neurocognitive processes involved in hypnosis, there is now growing interest in exploiting the instrumental use of hypnotic suggestion for a range of normal and abnormal psychological processes. Some of the most interesting include showing how clinical analogue symptoms produced by suggestion in normal subjects might help to reveal compromised neurocognitive systems in relevant clinical conditions. In this Review, we first provide a brief background on the phenomena and practice of hypnosis and hypnotic suggestion, before discussing intrinsic and instrumental studies of hypnosis.

What is hypnosis?

Trance and the hypnotic state. Hypnosis produces a highly focused, absorbed attentional state that minimizes competing thoughts and sensations. It typically involves two processes, induction and suggestion. Induction comprises

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Box 1 | **History and misleading beliefs**

With its origins in mesmerism and associations with mysticism, quackery, literary fiction and stage entertainment, it is understandable that formal research into hypnosis was not always valued, believed or considered worthwhile by mainstream science and consequently has remained less well known[28,54,113]. By contrast, general interest in hypnosis has remained strong. The author Charles Dickens was an enthusiastic amateur mesmeriser[114], and stage hypnosis continues to be a popular form of mass entertainment. An important misconception that has a long history is the popular belief, promoted through stage shows, that hypnosis is a form of sleep. It is also embedded in the word 'hypnosis' itself, which can be traced back to James Braid in the early nineteenth century. Braid argued that the phenomenon he was studying was an example of mental fatigue or 'nervous sleep'. As a result, he termed the phenomenon 'neurypnology' (neurohypnology) and later popularized the term 'hypnosis', both of which are derived from the Greek word for sleep[113]. This particular misconception has been perpetuated in the unfortunate, but still prevalent, habit among researchers of labelling the non-hypnotic control condition as the 'waking state'. Nevertheless, there is good reason for retaining the term 'hypnosis', as it provides the powerful context of positive expectancy that affects the experience that accompanies the induction procedure and that influences both the eliciting of suggested effects[23] and the outcome of therapies in which hypnosis is used as an adjunct[93].

Similarly, the view that hypnosis is related to 'animal hypnosis' has a long and popular history despite being abandoned in hypnosis research. In physiological terms, animal hypnosis — or 'tonic immobility' — seems quite different and is related to defensive antipredation reactions, best exemplified by the 'sham death' reflex in animals[115]. It has recently been persuasively argued, however, that hypnotic ability in humans may have evolved at least in part to allow for the control of pain and anxiety after injury, thereby reducing the likelihood of attack by predators[116].

Despite scepticism from some sectors of the scientific community, a small number of pioneering researchers and clinicians persisted with their interest in hypnosis over the past century. They recognized its intrinsic potential for treatment and for understanding consciousness, normal cognitive processes and possible mechanisms of clinical conditions. These pioneers include Jean-Martin Charcot, Ivan Pavlov, Alfred Binet, Pierre Janet, Sigmund Freud, William James, William McDougall, Clark L. Hull, Ernest Hilgard and, more recently, John Kihlstrom[113,117]. Although Freud famously abandoned the use of hypnosis in his own clinical practice, he continued to discuss it and acknowledged its role in the development of psychoanalysis and its contribution to the theories he formulated[118]. The scientific scepticism regarding hypnosis began to change in particular in the past decade, which has resulted in a resurgence in interest from a neurocognitive research perspective[2–6,54].

a series of instructions that cause the participant to voluntarily adopt a particular mental behaviour (for example, "focus on the sound of your own breathing") or engage in mental strategies, such as guided imagery, that are intended to achieve the desired focused and absorbed attentional state in which suggestions are given. We will use the more traditional term 'hypnotic trance' when referring to this state, although, as discussed later, this term is controversial.

Hypnotic suggestions consist of factual statements describing changes in experience or behaviour that do not require a participant's volitional engagement (for example, "your arm is becoming so stiff that you cannot bend it"). Although the two processes are distinct, implicit suggestions are often deployed during the induction phase: "listen to the sound of your breathing [instruction] and as you do so your mind becomes clearer [suggestion]" or "as you listen to the sound of my voice [instruction] you will begin to notice the muscles in your body becoming less tense [suggestion]". The type of suggestion used as part of the induction procedure is different from the 'targeted suggestions' that are given after the induction procedure is complete and that are intended to create a specific change in perceptual experience or behaviour (for example, "at the sound of a click, you will see the colour drain from the display in front of you" or "when you try to move your leg, you will find you are unable to do so").

Calling a procedure 'hypnosis' and introducing a formal induction procedure could be viewed, however, as a suggestion in itself 'to enter a hypnotic state' (REF. 22). Moreover, suggestions that are embedded in the induction procedure and expectancies derived from cultural beliefs can clearly influence an individual's experience of hypnosis. For example, adding the label 'hypnosis' to an induction procedure that involves focused absorption can increase a subject's responsiveness to suggestion when compared with labelling the same procedure 'relaxation' (REF. 23) . Although 'hypnotic induction' can be considered a form of suggestion[24], it remains useful to retain the notion of an induced hypnotic trance as a state that engages neuropsychological processes that are different from those accompanying targeted suggestions. It is common, particularly in clinical situations, to introduce one or more additional ('deepening') procedures to further increase the participant's focus and attention at the end of the initial induction procedure. The induction procedure also creates a context for the delivery of targeted suggestions. Hypnosis in the absence of targeted suggestions is often described as 'neutral' hypnosis.

The induction procedure and delivery of suggestions typically involve at least two individuals, the experimenter ('hypnotist') and the subject, and this is known as 'heterohypnosis'. However, both induction and suggestion can be effectively used by the subject alone — known as 'self-hypnosis' or 'autohypnosis'. Indeed, there is a well-established view that hypnotic procedures lie on a continuum of autohypnosis and heterohypnosis[25] and that all suggestion ultimately involves self-suggestion ('autosuggestion')[26]. In either case, and like many of our other everyday human experiences, the individual remains unaware of the cognitive processes involved. Although most of the studies described below involve heterohypnosis, the potential experimental and clinical significance of self-hypnosis and autosuggestion should not be overlooked, particularly given their potential role in the aetiology and treatment of clinical symptoms[26,27].

Assumptions and controversies. There are several common misconceptions about hypnosis[28] (BOX 1), but three are particularly worth mentioning. First, relaxation is not an essential component of the hypnotic trance state. There are effective hypnotic induction procedures that emphasize normal or even increased levels of physical and mental arousal and actively focused attention (termed 'active alert' inductions). Nevertheless, most hypnotic induction routines do involve 'relaxation' techniques. Second, many of the striking effects produced by targeted suggestions in hypnosis can be generated without prior hypnotic induction in a substantial number of people[29]. In fact, studies have shown that an individual's

ability to respond to the same suggestions with and without a hypnotic induction procedure is highly correlated and that the difference in effectiveness between the two conditions is relatively small[30]. A third misconception is that hypnosis is a form of sleep (BOX 1).

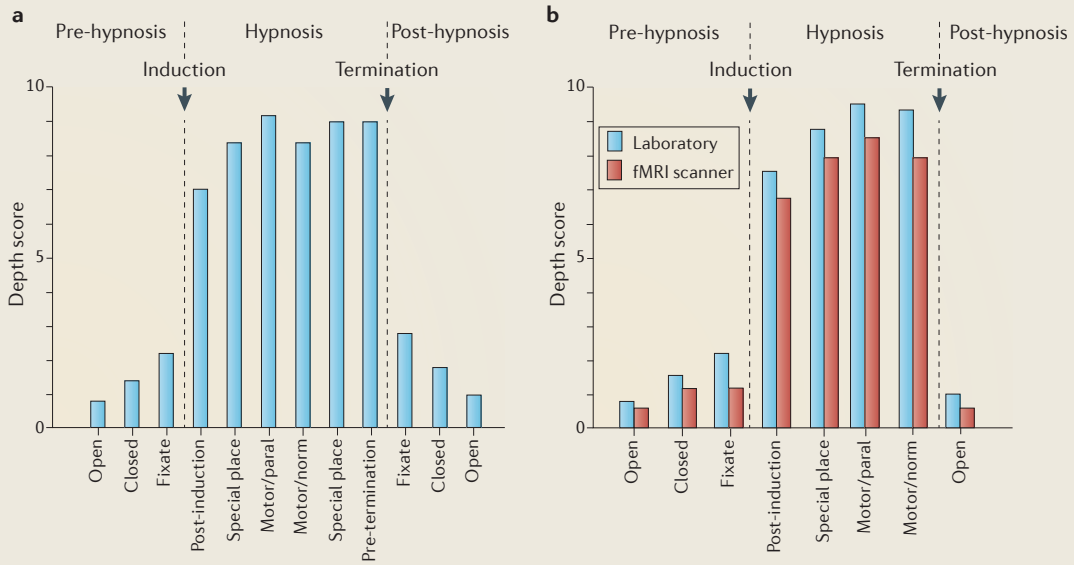
One controversy that has long exercised the hypnosis community is whether the hypnotic trance involves a special or unique state of consciousness[22,31]. This particular issue has been investigated using brain imaging — a method that does not affect a participant's perceived hypnotic depth or responsiveness to suggestion (BOX 2). In highly hypnotically suggestible individuals, hypnotic depth, increased imagery and exceptional experiences in neutral hypnosis were related to power in the fast (beta2, beta3 and gamma) frequencies on the electroencephalogram (EEG) and to reduced global functional connectivity[32], suggesting that hypnotic induction engages a range of related cognitive

Box 2 | **Effect of the fMRI environment on hypnosis and responsiveness to suggestion**

A practical and important methodological question for cognitive neuroscience is whether the experience of hypnosis and the ability to respond to suggestion are affected by the neuroimaging environment. In particular, the functional MRI (fMRI) procedure, with its noise, long duration and claustrophobic surroundings, could be expected to adversely affect an individual's ability to enter a hypnotic state or to respond adequately to targeted suggestions. One study explored this question in a group of 18 volunteers with previous experience of hypnosis[119]. In the first part of the study, all 18 subjects underwent hypnosis in a normal laboratory environment and received the suggestion that one of their limbs was paralysed. Eight of these subjects went on to experience an identical hypnotic procedure, including the paralysis suggestion, in an fMRI scanner. In both parts of the study, participants rated their depth of hypnosis at various stages before, during and after a standardized hypnotic induction procedure on a scale of 0–10 (0 representing 'not hypnotized at all' and 10 representing 'as deeply hypnotized as you have ever been before'). (See the figure, part **a** for depth scores for the first part of the study (all 18 subjects) and part **b** for depth scores of the 8 subjects who participated in both parts of the study.) They also rated their sense of involuntariness and the difficulty in attempting to move their 'paralysed' limb after receiving the suggestion.

In the laboratory (non-fMRI) setting, the expected large increase in subjective depth of hypnosis occurred after the induction procedure, with a further small increase after the introduction of suggested limb paralysis. Depth of hypnosis then remained stable until the termination of hypnosis, followed by an immediate return to pre-hypnosis levels (see the figure, part **a**).

The pattern of change in subjective hypnotic depth was similar under the laboratory and the fMRI conditions (see the figure, part **b**). Also, no differences were found between the two conditions in the difficulty and involuntariness associated with attempted movement of the 'paralysed' limb following the paralysis suggestion. These findings are consistent with a rapid creation of a hypnotic state that remains stable over time, is not disturbed by the introduction of targeted suggestions and can be equally rapidly removed without lingering after-effects, irrespective of whether participants are tested in or outside the scanning environment. Importantly for neuroscience research using hypnosis as an investigative tool, the depth of hypnosis achieved and the ability to respond to suggestions was not affected by the concurrent presence of the neuroimaging procedures. Figure is reproduced, with permission, from REF. 119 © (2007) Taylor & Francis.



Open, eyes open; closed, eyes closed; fixate, fixation of gaze on a target; post-induction, immediately following the induction procedure; special place, a hypnotic 'deepening' procedure involving personalized safe and relaxing imagery; motor/paral, hypnotically suggested limb paralysis; motor/norm, hypnotically suggested paralysis ended; pre-termination, immediately before hypnosis was terminated.

processes. Two studies compared brain activity in the same individuals during 'neutral' (resting) hypnosis with the 'normal' resting state (or 'default mode') outside hypnosis[33,34] (FIG. 1). The induction of hypnosis was associated with reduced activity in anterior parts of the default-mode system[33,34] and with increased activity in prefrontal attentional systems[34]. Consistent with these changes, participants reported not only being more relaxed during hypnosis but also more absorbed, less distracted by outside stimuli and less likely to engage in analytical thinking, with their minds being 'less crowded' with thoughts and associations[34]. A recent review of findings from neuroimaging studies using 'neutral' hypnosis concluded that such studies "support the hypothesis that hypnotic inductions produce changes in brain activity" (REF. 22), although it remains to be seen if these particular changes are unique to hypnosis or to the type of hypnotic induction procedure used. It also remains unclear whether these brain changes are causally related to the increase in responsiveness to suggestions seen after a hypnotic induction procedure in highly suggestible individuals compared with their responsiveness to the same suggestions without an induction procedure[22,35].

Intrinsic hypnosis studies

Hypnotizability and suggestibility. Although 'trance' and 'suggestion' can be distinguished as two components of hypnosis, there has been a tendency to confound the terms. For example, the classic measures of hypnotic susceptibility (or 'hypnotizability') do not refer to an individual's ability to enter a hypnotic state (to be 'hypnotized') but reflect the number of suggestions that an individual successfully experiences and reports after a hypnotic induction procedure[30]. Accordingly, these measures could arguably be referred to as 'hypnotic suggestibility' scales. Two of the oldest of these scales are the Harvard Group Scale of Hypnotic Susceptibility and the Stanford Scale of Hypnotic Susceptibility, but there are several more recent ones[36]. Measuring suggestibility using these scales typically involves delivering a hypnotic induction procedure and then presenting a series of suggestions. The scales themselves are robust, produce normally distributed patterns of responsiveness across groups of individuals, have good test–retest reliability and are frequently used in neuroscience research to select highly responsive individuals. Individuals scoring between 9 and 12 out of a possible 12 on the Harvard scale are often considered to be 'highly hypnotizable', but as we have indicated above, a more appropriate label might be 'highly suggestible'.

Responding to hypnotic suggestions. Scales that measure hypnotic suggestibility typically include a range of suggestions. These are usually classified into three broad categories (but see REF. 37), ranked in terms of perceived difficulty (as reflected by the number of individuals who are typically able to respond effectively to them). The three categories are: 'ideomotor–ideosensory direct' suggestions, which produce experiences such as heaviness or involuntary arm levitation in most participants; 'ideomotor challenge' suggestions, which are effective in just over half of those tested and consist of ideomotor suggestions that the individual is then 'challenged' to overcome (resulting in, for example, an inability to raise one's hand against feelings of heaviness or to open tightly closed eyelids); and 'cognitive' suggestions, which affect high-level psychological processes involving memory and perception (resulting in hallucinations or selective amnesia) and tend to be less commonly experienced. People who are highly suggestible can experience all of these effects, whereas low-suggestible individuals tend to respond primarily to ideomotor–ideosensory suggestions. The three categories probably represent different points on a continuum of difficulty (as determined by the specific scoring criteria used in the scales), but it is also possible that they tap into different underlying neurocognitive processes. Irrespective of the difficulty of a specific suggestion, an effect is considered a 'classical suggestion-effect' only if it is experienced as involuntary; as 'happening all by itself' (REF. 38).

Not everyone responds in the same way to suggestions. Participants describe adopting different cognitive strategies once a suggestion has been presented[39]. Some subjects appear to simply focus their attention on the content of suggestions and then disattend to extraneous stimuli, whereas others report actively 'thinking with' the suggestion or engaging in goal-directed imagery and may report being more involved in the process[40,41]. Irrespective of the different cognitive styles adopted following suggestion, the suggested effect itself is characteristically experienced as being involuntary and effortless[42]. These two response styles are not mutually exclusive, and some individuals report engagement in one or the other at different times. Important questions remain, such as whether highly hypnotically suggestible subjects

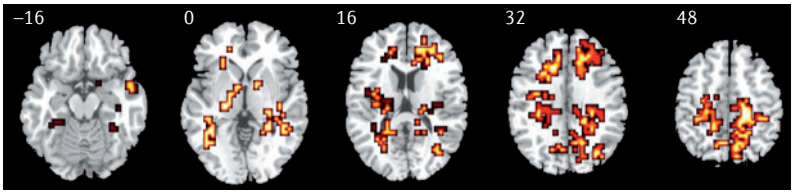


Figure 1 | **Modulating the default-mode and attentional networks using hypnosis.** The 'default-mode' network comprises brain regions that are more active under a low-demand condition (for example, lying quietly in an alert state or when passively viewing a stimulus such as a fixation cross) compared with high-demand task conditions. Hypnosis has been used to vary the resting ('default') state of cognition and brain function; a recent study assessed subjective measures of hypnotic depth and brain activation (using functional MRI) in subjects during hypnosis[34]. The figure shows that the brain regions in which activity decreased with increasing depth of hypnosis included established 'default network' areas, including cortical midline structures of the left medial frontal gyrus, right anterior cingulate gyrus and bilateral posterior cingulate gyrus, and bilateral parahippocampal gyri. Brain regions that showed increased activation with increasing depth of hypnosis included the right middle frontal gyrus, bilateral interior frontal gyrus and bilateral precentral gyrus (not shown). Thus, hypnotic trance was associated with reduced default network activity and increased activity in prefrontal attentional systems. These data are consistent with the view that hypnosis involves a 'special' cognitive state in the sense that it is associated with an altered pattern of brain activity. Figure is reproduced, with permission, from REF. 34 © (2012) Taylor & Francis.

predominantly adopt one or the other of these response styles or whether individuals use different response styles for different types of suggestion.

Individual differences in hypnotic responsiveness. Despite impressive efforts since the 1930s, the search for distinctive psychological correlates of hypnotizability, measured predominantly by the classic hypnotic suggestibility scales described above, has yielded few positive results[43–45]. None of the major personality variables correlate with hypnotic suggestibility. It has also been difficult to find consistent correlations between formal measures of dissociation and hypnotic suggestibility[46], perhaps surprisingly, given the prevalence of compartmentalization — a form of dissociation — in hypnotic phenomena[47]. By contrast, mental absorption does show an association with hypnotic suggestibility when the scales used to measure it are administered in a hypnotic context, and fantasy proneness predicts an individual's subjective experience of their response to hypnotic suggestions (but not their behavioural responses). There is also evidence for a link between creativity and hypnotic suggestibility and for a relationship between empathy and responsiveness to hypnotic suggestion[48]. Furthermore, there is good evidence that expectancy, particularly as reflected by an individual's own estimation of their probable responsiveness to hypnotic procedures, influences subsequent behavioural responses to suggestion. This effect is increased if the expectancy measure is taken after the individual has undergone a hypnotic induction procedure[46].

Importantly, hypnotic suggestibility does not correlate with interrogative suggestibility or placebo suggestibility[24,49]. It does, however, correlate with other measures of suggestibility, such as the Chevreul pendulum effect[49] and, as we discuss later, with the ability to respond to suggestions (such as those included in hypnotic suggestibility tests) without a hypnotic induction procedure.

Neural basis of hypnotic responsiveness. There is a long tradition linking the experience of hypnosis to right hemisphere functioning based on the apparent association of hypnotic phenomena with more-intuitive, holistic and non-analytical processes (see REF. 20). Indeed, a three-stage model of a typical hypnotic induction procedure, which is based primarily on EEG data, proposes a shift from left to right hemisphere processing as induction proceeds[50,51]. A similar pattern emerged in a study using left and right hemifield stimulus presentations in a temporal order judgement task in which participants were presented with two lights in rapid succession, one to each visual field, and were asked to detect which light flashed first[52]. Highly hypnotically suggestible participants could detect the order of stimuli at shorter inter-stimulus intervals if the first light was presented to the right visual field (indicative of faster processing in the left hemisphere) in the absence of hypnosis, and this shifted to faster processing in the right hemisphere after a hypnotic induction procedure. This reversal was not seen in low-suggestible participants, who showed slower processing times in response to both left and right visual field presentations under hypnosis compared with the no hypnosis condition[52]. These results support the view that highly hypnotically suggestible individuals in particular are characterized by a shift towards right hemisphere processing in hypnosis. However, recent evidence suggests that right hemisphere damage resulting from stroke does not necessarily affect hypnotic suggestibility[53].

More recently, interest has focused on the involvement of frontal cortical systems in mediating responsiveness to suggestion and the accompanying experience of involuntariness[9,20]. This involvement is thought to reflect the top-down regulation of attentional shifts and dissociations that are presumed to underpin hypnotic responsiveness[9,27,28,54]. High hypnotic suggestibility in general, and the ability to develop hypnotically suggested analgesia in particular, correlate with the size of the anterior part of the corpus callosum[55], an area that mediates changes in attention[56] and the transfer of information between prefrontal cortices[57]. In addition, disrupting activity in the left dorsolateral prefrontal cortex with repetitive transcranial magnetic stimulation selectively increases subjective responses to suggestions independently of changes in expectancy[58], possibly reflecting a disruption of higher-order processes that mediate awareness of action intentions[59]. In addition, a functional MRI (fMRI) study found higher levels of functional connectivity between the left dorsolateral prefrontal cortex and the dorsal anterior cingulate cortex (ACC) — which form part of a network of areas involved in evaluating the salience of somatic, autonomic and emotional information[60] — under normal resting state conditions in high hypnotically suggestible individuals compared with a low-suggestible control group[9]. Taken together, these studies are consistent with a leading role for frontal executive systems in hypnotic responsiveness.

Genetic and developmental factors in hypnotic suggestibility. Hypnotic suggestibility is normally distributed in human populations and remains a stable individual trait. Test–retest reliability for standard measures of hypnotic suggestibility is high over a period of 25 years[61]. A classic twin study provided evidence that hypnotic suggestibility is heritable[62]. Consistent with this, the Val/Met variant of the catechol-*O*-methyltransferase (*COMT*) gene is more frequent in individuals with high hypnotic suggestibility, whereas the Val/Val and Met/Met genotypes are more common in people with medium and low suggestibility[44,63,64]. Interestingly, the *COMT* genotype is associated with prefrontal executive functions and working memory[65]. In view of the association between hypnotic suggestibility and prefrontal attentional capacities, it is also interesting that the efficiency of executive attentional networks is highly heritable[66].

Despite uncertainties about the comparability of suggestibility scales for adults and children, there is a general consensus that children are more hypnotically

Interrogative suggestibility
The tendency, during cross-examination, to yield to leading questions and to shift replies once interpersonal pressure has been applied.

Placebo suggestibility
An expectancy-based tendency to experience a positive outcome after the administration of an inert substance or ineffective treatment.

Chevreul pendulum effect
A pendulum held by an individual is experienced as moving 'all by itself' in response to expectation or suggestion (see 'ideomotor movement').

Hypnotic analogues
Reversible simulations of clinical conditions produced by tailored hypnotic suggestions informed by clinical phenomenology.

suggestible than adults, with a peak of responsiveness occurring between the ages of 8 and 12 years[67] but that the underlying cognitive processes are the same in both age groups[54,68].

The 'reality' of hypnotically suggested effects. Participants in hypnosis studies typically describe the perceptual and behavioural changes experienced in response to suggestion as 'real' (that is, indistinguishable from other everyday experiences) and beyond voluntary control. They also report that these experiences are not imaginary and not the result of simple compliance with what they think the experimenter wants to hear or had suggested. According to Woody and Bowers[69], hypnosis produces 'genuine like changes' in the control of experience and behaviour. They proposed that specific suggestions bypass executive system processes that normally control our behaviour and that the experience of involuntariness is an accurate reflection of an alteration in control. Such an account assumes that hypnotic analogues not only simulate the surface features or presenting symptoms of many clinical conditions but also produce the physiological and neural changes that accompany them.

Understandably, scepticism remains regarding the credibility of these first-person reports. However, recent neuroscience studies provide compelling evidence that hypnosis is a physiologically based experience and that the use of targeted suggestions disrupts well-established automatic, unconscious processes over which participants are thought to have little or no volitional control. For example, one study provided evidence that first-person reports of hypnotic suggestion-induced alterations in colour perception were associated with changes in blood flow in colour-processing regions of the brain[11]. Similarly, hypnotized subjects who received a post-hypnotic suggestion to forget episodic autobiographical memories and then underwent fMRI during a recognition memory test showed alterations in occipital, temporal and frontal brain areas involved in memory retrieval[70]. Another study showed that different cognitive states induced by hypnosis can promote or inhibit gastric acid production[71]. Further evidence that hypnotically suggested alterations in perception or behaviour are associated with congruent brain activity patterns associated with such experiences in non-hypnotized individuals is discussed below. Importantly, in a positron emission tomography (PET) study, participants asked to simulate ('malinger') limb paralysis during hypnosis showed different brain activity compared with when they were experiencing a hypnotically suggested limb paralysis, even though no behavioural difference between the two conditions was detectable on clinical neurological examination[72].

a

b

Post-hypnotic suggestion	Reaction time in congruent condition (ms)	Reaction time in neutral condition (ms)	Reaction time in incongruent condition (ms)
Absent	703	748	860
Present	664	671	669

Figure 2 | **Using hypnotic suggestion to abolish the Stroop effect. a** | In the classic Stroop task, subjects are asked to name aloud the ink colour of printed words. The colours might be incongruent with the word (for example, the word RED printed in green ink) or congruent with the word (for example, the word ORANGE printed in orange ink). Individuals are typically slower at naming the ink colour of incongruent colour words owing to an automatic tendency to prioritize the reading of words over naming the ink colour, a phenomenon known as the Stroop interference. **b** | A study using highly hypnotizable individuals showed that a specific hypnotic suggestion — namely, that words would appear meaningless — could eliminate this classic Stroop interference effect[17]. Without hypnotic suggestion, reaction times are longer in the incongruent condition than in the congruent or neutral conditions, but this Stroop effect disappears under hypnotic suggestion. These findings — recently confirmed[19] — showed that hypnotic suggestion (when it is effective) is capable of eliminating the deeply entrenched involuntariness and largely automatic process of reading. Part **b** is reproduced, with permission, from REF. 17 © (2002) American Medical Association.

Responding to suggestion without hypnosis. Thus far, this Review has focused on the ability to respond to a particular type of suggestion during hypnosis after undergoing a hypnotic induction procedure. However, individuals can also respond when the suggestion is made during hypnosis but is subsequently tested once hypnosis has been terminated — this is known as post-hypnotic suggestion[73] — or even if the suggestion is presented without any hypnotic induction[30,74].

Several studies have used post-hypnotic suggestions. For example, in a study that tested whether suggestions can modulate the Stroop effect (which takes advantage of our ability to read words faster than we can name colours), hypnotized subjects received the suggestion that when the experimenter clapped his or her hands, the subject would see words (presented in a coloured font on a screen) as meaningless symbols. Subsequently, after hypnosis had been terminated, a hand-clap signal was given, and the Stroop effect was temporarily eliminated[17]. Some researchers have argued that post-hypnotic suggestion offers the prospect of a 'cleaner' experimental manipulation[54] based on the assumption that the resultant change occurs in the context of a more 'normal' non-hypnotic mental state, even though the target suggestion itself was previously given under hypnosis[75] (FIG. 2).

It has long been recognized that in highly hypnotically suggestible individuals, suggestions can be effective without a hypnotic induction procedure[76]. This phenomenon has been termed 'imaginative suggestibility' (REF. 30) to distinguish it from 'hypnotic suggestibility' and has, until recently, received little attention. An individual's responsiveness to suggestions measured by traditional

hypnotic susceptibility scales, in which the suggestions are preceded by a hypnotic induction procedure, strongly correlates with their responsiveness to the same suggestions given without a hypnotic induction procedure[30,74]. Indeed, an individual's responsiveness to suggestions without hypnosis is one of the best predictors of responsiveness to hypnotic suggestions — the other being response expectancy[30]. This implies that hypnotic and imaginative suggestibility involve a common process and raises the question of whether experiencing a hypnotic induction procedure actually influences an individual's responsiveness to suggestion. It is important to note that the label 'imaginative' does not imply that the effects produced by suggestion made outside hypnosis are 'imaginary' — they are seen as experiential changes with a similar quality of involuntariness to those produced when the suggestion is given and acted on in hypnosis. Hypnotic suggestibility is in effect a measure of imaginative suggestibility administered after a hypnotic induction procedure[30].

Suggestibility, of course, is not the unique preserve of hypnosis. Examples of human experience and behaviour influenced by suggestion outside the domain of hypnosis include ideomotor movements[77], psychosomatic interactions[21], choice blindness[78], postural sway, placebo effects, implicit learning and decision-making[79]. Suggestion provides for and shapes response expectancies, which in turn remain a crucial aspect of suggestibility[80]. Although suggestibility takes many forms[79], it is arguably observed most clearly in social settings, in which the suggestion is embedded in the interaction with another person.

Trance and suggestibility. It has been widely assumed that administering a hypnotic induction procedure creates a special mental state that increases suggestibility[22]. Consistent with this, in one study in which it was suggested that subjects would 'see' colour while looking at a grey image and 'see' shades of grey while looking at a coloured image, highly suggestible subjects reported a greater ability to add or drain colour from the visual stimulus as a result of the targeted suggestion when they were hypnotized compared with when they were not, although the difference was small[35]. Data from fMRI studies showed that there were higher levels of activation bilaterally in the cuneus during hypnosis (compared with a no-hypnosis condition) in highly suggestible individuals when 'adding' colour to a grey image, and higher activation in the left inferior occipital gyrus and the middle occiptal gyrus bilaterally when 'draining' colour from a coloured image[35]. These effects were associated with activity changes in anterior parts of the default-mode network that in a related study have been interpreted as indicating a hypnotic state change[33]. The observation that a suggestion delivered after a hypnotic induction procedure produces more profound brain changes than the same suggestion without a hypnotic induction procedure has also been reported for hypnotically modulated pain[81]. These studies suggest that for prospective neuroscience research, carefully selecting experimental participants for 'high hypnotic suggestibility' remains a useful strategy. Interestingly, the sedative gas nitrous oxide can also increase suggestibility (measured using hypnotic suggestibility scales) independently of the participant's expectancy, suggesting a possible common neural mechanism that may underlie both types of suggestibility[82].

Instrumental hypnosis studies

There has been a growing increase in the use of hypnotic suggestion as a technique for exploring cognitive and neurocognitive mechanisms underlying normal and abnormal psychological conditions[6,8]. Below, we discuss several studies that challenge classic examples of 'automaticity' in cognitive processing, explore the cognitive and neurocognitive processes mediating perceptual and motor abilities and provide insights into the aetiology and symptomatology and treatment of a number of clinical conditions.

'Automatic processes'. In cognitive psychology, a number of cognitive processes are regarded as being 'automatic', meaning 'not requiring control or influence by the individual' (REF. 83). Several recent studies involving hypnosis have modified this automaticity such as Flanker, Stroop and McGurk effects[17–19], demonstrating the power and potential that hypnotic suggestion offers for probing theories of cognitive functioning in the laboratory.

For example, studies that used the Stroop task showed that hypnotic suggestions could 'turn off' the prepotent tendency to read printed words[17,84]. In one study, hypnotized subjects were given a suggestion that they would see words as meaningless symbols. Subsequently, on the Stroop task, when instructed to name the ink colour that the words were printed in, the same subjects showed little of the interference effect when the word and ink colour were incongruent[17] (FIG. 2). Similarly, a post-hypnotic suggestion for amnesia improved performance in subsequent trials of a random number generation task by suppressing the normal, involuntary tendency for repetition avoidance[85].

Hypnotic suggestion has also been used to study automaticity in synaesthesia, in which a stimulus in one sensory modality reliably evokes an experience in the same or a different modality. Synaesthesia is commonly regarded as an automatic response: that is, outside the individual's control. A recent EEG study challenged this assumption[12]. Here, a person with face-colour synaesthesia received a post-hypnotic suggestion to temporarily lose her synaesthesia, and the participant completed a colour-naming task in which faces presented in colours were either congruent or incongruent with her usual synaesthetic associations. The suggestions were effective in abolishing both the previously demonstrated response interference caused by incongruent face colours and conflict-related N400-evoked responses recorded over frontal midline electrodes. These findings demonstrate that the conscious and apparently automatic experience of synaesthesia can be temporarily abolished by using the cognitive control of selective suggestion.

Perceptual and motor processes. Hypnotic suggestions have been used to explore the neurocognitive processes that underlie perceptual and motor abilities. One study

Ideomotor movements
Apparently involuntary or spontaneous movements of the body or held objects corresponding to an individual's thoughts or beliefs but produced by unconscious motor activity.

Psychosomatic interactions
When an individual's erroneous belief (for example, "I touched a poisonous leaf") results in a bodily reaction (for example, inflammation of the skin).

Choice blindness
The failure to notice that the consequences of a previous freely made choice have changed.

Postural sway
The tendency of the body to sway from side to side or front to back when standing still.

involved participants who were given the hypnotic suggestion that they could change their perception of a grey-scale Mondrian image into a coloured one, or vice versa[11]. Participants not only verbally reported that they experienced the change, but brain imaging results showed corresponding changes in brain activation bilaterally in fusiform cortical areas associated with colour perception. This finding was subsequently replicated in an fMRI study using an experimental design that included the same suggestions but this time given under a no-hypnosis condition[22,35,86]. Interestingly, in a control condition in which participants were asked to imagine the colour changes, activation was only found in in right fusiform areas[11], not inconsistent with findings from other studies[87].

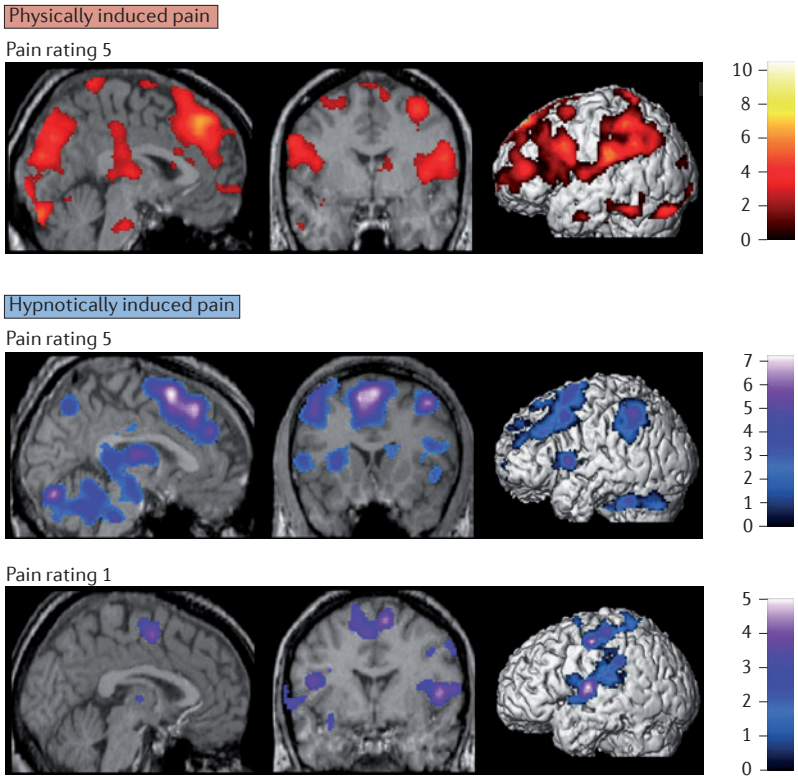


Figure 3 | **fMRI images of hypnotic pain and physical pain.** In this functional MRI (fMRI) study, eight highly hypnotically suggestible participants, who were hypnotized throughout the session, received painful (48.5 °C) heat stimuli from a thermal probe placed on the palm of their right hand (the physically induced pain condition)[16]. On some trials they were given the suggestion that the probe would be activated to the same painful level (the hypnotically induced pain condition) when in fact it remained at a comfortable setting (37.0 °C). Participants reported experiencing pain, and fMRI scans showed similar activation in brain areas associated with painful stimulation in both conditions. The figure shows brain activations for physically induced pain rated 5 on a 1–10 scale (top panel); for hypnotically induced pain (middle panel) rated 5 on a 0–10 scale; and for hypnotically induced pain rated 1 on a 0–10 scale (bottom panel). The activations are shown in red–yellow for physically induced pain and in blue–purple for the hypnotically induced pain. Importantly, for both physically induced and hypnotically induced pain, the amount of brain activation was proportional to the degree of pain reported. The bottom two rows in the figure show this for hypnotically induced pain: a hypnotically suggested pain experience rated at 1 (bottom panel) is accompanied by less brain activity than hypnotically induced pain rated at 5 (middle panel). Figure is reproduced, with permission, from REF. 16 © (2004) Elsevier.

Motor involuntariness is a particularly effective and powerful hypnotic suggestion. In a study exploring the experience of volition through an individual's own subjective estimation of the time at which the finger movement occurred, hypnotized participants received the suggestion that a finger movement could occur 'all by itself' (REF. 88). Participants' estimates of the time of this 'anarchic' movement were similar to estimates of the time of a truly passive movement created mechanically by the experimenter. Both of these estimates were closer to the actual time of the movement than the estimated time of an intentional movement (which revealed the well-known anticipatory bias). As the hypnotic suggestion for an involuntary motor response selectively eliminates the subjective experience of volition but not the unconscious preparatory motor processes leading up the execution of the movement, this finding suggests that it is the former and not the latter that underlies the tendency to underestimate the time of execution of one's intentional actions. In another study of motor control, the hypnotic suggestion that arm movements were being produced by the action of a pulley system was given[13]. This resulted in the appropriate limb actions but was accompanied by the experience of 'passivity' and a pattern of brain activity involving the parietal cortex and cerebellum that is normally associated with passively, but not voluntarily, generated movements. This result was taken to indicate that a psychogenic delusion of passive movement was associated with the failure to cancel predictable movement-related neural feedback[13].

Similarly, hypnotically suggested heat pain in the absence of a noxious stimulus is associated with activation in brain areas that normally mediate the experience of pain, including the thalamus and ACC, secondary somatosensory cortex (S2), insula and prefrontal and parietal cortices[16] (FIG. 3). If participants simply imagined the same pain experience, however, there was only minimal activation in the ACC, S2 and insula[16]. Hypnotic suggestion has also been shown to increase and decrease the subjective experience of fibromyalgia-associated pain with corresponding modulation of activity in the neural pain matrix[81]. Moreover, hypnotic suggestion can differentially modulate the sensory and affective (emotional) components of heat pain experiences. Here, a suggestion that increased or decreased the perceived unpleasantness of peripherally administered heat pain resulted in corresponding selective modulation of activation in the ACC, and suggestions of increased or decreased perceived pain intensity resulted in modulation of activity in the primary somatosensory cortex. In other words, the suggestions selectively modulated the brain areas that, under no-hypnosis conditions, mediate the sensory and affective components of pain[14,89]. These effects have been further explored in an EEG study[15]. This study showed that hypnotic suggestion has a stronger effect on the affective component than on the sensory component of laser-induced pain. The authors of this study concluded that suggestions probably exert their influence through top-down effects on pain processing[15]. Collectively,

these findings confirm that hypnotic suggestion can be used to develop and test models of perceptual and motor processes.

Clinical analogues. At an experimental and clinical level, hypnotic suggestion has shown some success in the treatment of several neurological conditions, such as contralateral tactile extinction[90], phantom limb pain[91] and the after-effects of stroke[92], and in the modulation of fibromyalgia pain[81]. Furthermore, meta-analyses and randomized clinical trials have provided evidence for the clinical efficacy of hypnosis procedures as an adjunct to several established therapies, such as cognitive behavioural therapy, over a broad spectrum of conditions but particularly in relation to chronic and acute pain, immune functioning and irritable bowel syndrome[93–95]. These findings indicate the relevance and importance of hypnosis as an effective clinical technique.

A fascinating and informative application of hypnotic suggestion for the cognitive neurosciences is the ability to experimentally simulate different clinically relevant features involving cognition and perception[2,6]. Hypnotic suggestion has been used in a small number of preselected participants to develop and test models involving several specific psychopathologies. This include psychodynamic conflict[96], delusions[97,98], functional memory disorders[99], auditory hallucinations[10], functional paralysis[100] and obsessive-compulsive disorder[101] (BOX 3).

These applications provide a credible methodological approach from which to explore the causal involvement of specific brain areas and putative cognitive subsystems responsible for specific clinical symptoms. The ability to turn 'on' and turn 'off' such symptoms in the same subjects has the merit of being able to use within-group designs[8].

Although this instrumental approach does not depend on the structural or functional pathologies seen in patients with neuropsychological conditions, the use of hypnotic clinical analogues is theoretically and clinically relevant, given the growing number of patient symptoms seen by many different medical specialties for which biomedical science currently has yet to provide an adequate biomedical cause[102,103]. Significant numbers of newly referred neurology out-patients are considered to be unexplained by 'organic disease' (REF. 104). Moreover, there is a now a growing literature that shows how hypnosis can be used to induce temporary functional changes in behaviour and/or subjective experience and associated brain activity that is qualitatively similar to symptoms observed in some neurological and psychiatric conditions. Such studies not only provide experimental models for understanding these conditions but could help to inform and revise current ideas about the aetiology and treatment of some of these disorders[101]. Examples of such 'clinical hypnotic analogues' include the paralyses seen in conversion disorder[100,105–107], symptoms of contralateral visual neglect seen after brain injury[6], medically unexplained (or 'functional') pain[16], involuntary movements seen in schizophrenia and other clinical states[13,88] and alexia[108] (BOX 4).

Conclusions and future directions

Hypnosis will no doubt continue to attract its share of detractors, motivated in part by the fact that until recently, 'hypnotic' phenomena remained largely subjective and unverifiable. However, the growing acceptance of the role of the 'cognitive unconscious' (REFS 109–111) in shaping conscious experience and behaviour and the advent of increasing sophisticated experimental designs

Box 3 | **Hypnotic analogues of clinical delusions**

Delusions are false beliefs that people hold with conviction and despite evidence to the contrary. They are commonly seen in patients with dementia, stroke, Alzheimer's disease, traumatic brain injury and psychiatric conditions such as schizophrenia. Hypnotic suggestion has been used to study delusions and test cognitive theories[98]. One of the first studies to use hypnosis instrumentally to study paranoia was reported in 1981 (REF. 120).

Hypnotic suggestions can generate anomalous experiences and also false beliefs about the world. Like delusions, many (although not all) hypnotic experiences are believed with conviction, are maintained regardless of contrary evidence and are experienced as involuntary and real. Indeed, it has been argued that hypnotized individuals are essentially deluded about the real state of the world and that hypnosis is a good technique for modelling delusions[121]. Studies of hypnotic delusions include gender change[122], intermetamorphosis[123], somatoparaphrenia[124] and mirrored-self-misidentification[125,126].

In 2000, Langdon and Coltheart[127] proposed the influential two-factor model to explain delusions. Factor 1 generates the delusion's content and involves a neuropsychological anomaly affecting perceptual and/or emotional processing. Factor 2 explains why the belief is not rejected as untrue. According to this account[128], different types of delusion may results from different factor 1 deficits, whereas factor 2 remains common across all delusions.

For example, in the mirrored-self-misidentification delusion, factor 1 is either a deficit in recognizing faces (leading the patient to not recognize their own face in the mirror) or a deficit in understanding mirrors (leading the patient to think that mirrors are windows). As a consequence of either deficit, a patient may think that there is a stranger in the mirror. The additional, second factor explains why the delusion is maintained.

In a study into mirrored-self-misidentification, highly hypnotizable individuals received the suggestion that they would see a stranger when they looked into a mirror[126]. Participants showed striking similarities to clinical patients with mirrored-self-misidentification. Not only did subjects report seeing a stranger in the mirror, but they described physical differences between the stranger and themselves, were amused and sometimes disturbed that the stranger copied their actions, and even looked around the room to find the stranger. These examples illustrate the versatility and usefulness of hypnotic suggestion in understanding clinical conditions while not ignoring important differences between hypnotic models and clinical disorders in terms of affect, duration and severity.

Alexia
An acquired inability to read.

Gender change
The creation (for example, by hypnotic suggestion) of a subjectively compelling belief in an individual that their sexual identity has been reassigned.

Intermetamorphosis
The belief that one has physically and psychologically become another person.

Somatoparaphrenia
A delusional belief that one's own limb belongs to someone else.

Mirrored-self-misidentification
The belief that one's reflection in the mirror is a stranger.

Associative prosopagnosia
The loss, or significant impairment, of the ability to recognize familiar people by their face.

Box 4 | **Neuropsychological case study: prosopagnosia**

Hypnotic suggestion has been used to study the neuropsychological condition of associative prosopagnosia[6]. Although traditionally associated with acquired brain injury, there are many cases of 'developmental prosopagnosia' or 'congenital prosopagnosia' (REF. 129). The subject of this study was a highly hypnotically suggestible student with no history of acquired brain injury. Following a standardized hypnotic induction procedure, the subject received suggestions to induce a clinical analogue of prosopagnosia. No information about test performance or assessments was provided to the subject, who was largely naive with respect to any knowledge of the clinical condition.

Specifically, the subject received the suggestion that he would be able to see faces but that he would be incapable of recognizing familiar faces and that such faces would lose their sense of familiarity. Stimuli comprised 10 famous people, 10 family members and 20 unknown people matched for photographic quality, and each photograph was presented twice in a pseudo-random order. The results were consistent with those seen in clinical cases of prosopagnosia. For example, the subject recognized 3 out of 20 famous faces, despite showing normal (20 out of 20) recognition outside hypnosis. The subject also only recognized 10 out of 20 family members' faces after two consecutive presentations. With the exception of his mother, father and grandfather, he often used relationships (for example, 'my cousin') to help identify family members during hypnotic prosopagnosia, whereas he always used first names outside hypnosis.

Following several sessions, the subject gave a detailed phenomenological report of the effects of the targeted suggestion. This provided several interesting observations, including a first-hand account of losing a sense of "meaningful recognition" for family members' faces well known to him. He described how he saw faces "in a very different way", that faces lacked global integration ("not seeing the whole face") and that he often perceived faces in terms of their local 'patchy' details (for example, eyebrow, nose, and so on). In the case of well-known politicians and family members, he described how initially there was a "flash of recognition" followed by a focus on local features. With more extended exposure times, he described how the same faces became fractionated and distorted, with the result that he grew uncertain about faces that he initially felt he had recognized.

and functional imaging techniques has provided opportunities for cognitive neuroscience to make significant inroads into the neurocognitive correlates of both hypnosis and — perhaps more importantly — the nature of suggestion and expectation itself[112]. The psychological disposition to modify and generate experiences following targeted suggestion remains one of the most remarkable but under-researched human cognitive abilities given its striking causal influence on behaviour and consciousness.

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