

## ATTENTION AND HYPNOSIS: *Neural Substrates and Genetic Associations of Two Converging Processes*

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**Abstract:** Although attention is a central theme in psychological science, hypnosis researchers rarely incorporate attentional findings into their work. As with other biological systems, attention has a distinct anatomy that carries out basic psychological functions. Specific brain injuries, states, and drugs can all influence attentional networks. Investigation into these networks using modern neuroimaging techniques has revealed important mechanisms involved in attention. In this age of genomics, genetic approaches can supplement these neuroimaging techniques. As genotyping becomes an affordable and technologically viable complement to phenotyping, exploratory genetic assays offer insights into the genetic bases of both attention and hypnotizability. This paper discusses relevant aspects of attentional mechanisms and their underlying neuroanatomy as they relate to hypnosis. Underlining data from attentional networks, neuroimaging, and genetics, these findings should help to explain individual differences in hypnotizability and the neural systems subserving hypnosis.

The notion of attention is an integral, defining aspect of hypnosis. Despite the important role attention plays in the hypnotic process, hypnosis practitioners and researchers tend to overlook attentional processes. However, psychological and neurobiological investigations have revealed important empirical information about the anatomy and mechanisms of attentional processing. In this paper, we will reexamine these existing data in the context of our novel findings to reveal even closer connections between attention and hypnosis.

One of the oldest and most central issues in psychological science, attention is the process of selecting for active processing certain aspects

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of our physical environment (e.g., objects) or ideas stored in our memories. Throughout history, many great minds have wrestled with the definition of attention. Aristotle regarded attention as a narrowing and focusing of the senses. Years later, William James (1890, p. ) wrote, "Everyone knows what attention is. It is the taking possession of the mind in clear and vivid form of one out of what seem several simultaneous objects or trains of thought." James's mention of attention toward either objects or thoughts relates to today's approaches to "sensory orienting" and "executive control."

Following a lull in the field during the early 1900s, after World War II Donald Broadbent resumed the quest to discover attentional mechanisms. Applying formal information theory, Broadbent likened attention to a filter. He proposed that attention was bounded by the amount of information located between parallel sensory systems and a limited capacity perceptual system (1958). This view facilitated objective studies of the limitations of the human ability to deal with multiple signals at one time in a variety of practical tasks.

As psychology moved toward the study of cognitive mechanisms, new objective methods allowed for investigation into attentional selection. For example, studies showed that words could activate their semantic associates without awareness to the word's identity (i.e., priming). The parallel organization of sensory information was also extended to semantic processing. In this case, selecting a word meaning for active attention actually suppresses the availability of alternative word meanings. These data revised the notion of attention as a filter, instead describing it as a mechanism for assigning priority to motor acts, consciousness, and memory.

Psychological studies have furnished interesting results about the limits of performance and unconscious processing. Supplementing these findings with neurological data has provided a more complete picture of the neural mechanisms of attention. Cognitive neuroscientists have suggested that the human brain concurrently entertains several attentional systems, or networks, consisting of separate interrelated functions (Posner & Petersen, 1990). Brain networks that subservise attention are now well described and serve as model systems for exploring symptoms that arise from various forms of pathology (Berger & Posner, 2000). Recent data break down the whole process of attention into distinct brain areas that mediate different processes. We can thus construct attention as an organ system with its own functional anatomy, circuitry, and cellular structure (Posner & Fan, 2004).

This information about attentional processing raises important questions in cognitive science (e.g., what is the relationship between attention and consciousness?) and provides insights into neurological and psychiatric disorders. Furthermore, the data establish that attention permits voluntary control over thoughts, feelings, and actions as a

means of self-regulation in adulthood and across development (Bronson, 2000; Posner & Rothbart, 1998, 2000; Rothbart, Ellis, & Posner, in press). Variations in the operational efficiency of these attentional systems serve as a basis for individual differences in self-regulation and emotional control. Careful study of these individual differences should help illuminate mechanisms of volition and sustained effort as well as the influence of suggestion on brain function (Raz, in press-b). These aspects of attention are compatible with recent data regarding hypnotic phenomena (Raz & Shapiro, 2002).

## GROSS CHARACTERISTICS OF ATTENTION

To study the neurological characteristics of attention, an experimental system must be employed. Visual attention often serves in this capacity, because it is the most widely studied perceptual system. Researchers and clinicians have investigated the optics, anatomy, development, pathology, and underlying neural processes of the visual system. More recently, Raz et al. documented the effects of attention on visual acuity in hypnotic contexts (Raz et al., in press).

In practice, visual attention allows us to explore how we redirect our attentional “beam” to various areas of the visual field and change the detail with which we look at a particular area. For example, a reader can look at this page and focus on its setup as a whole, or he or she can zoom in on specific words and certain letters therein. Paying attention to single characters permits us to examine punctuation marks, catch typos, or even spot minute imperfections on the physical paper. However, at this level of detail, we may miss the bigger idea conveyed in a paragraph. As we shift our focus, we can change the target location of our attention or the size of our attentional field. Metaphors that describe visual attention, such as *spotlight*, *zoom lens*, *gating*, and *gradient*, attest to the fundamentally spatial nature of attention. The term *spotlight* exemplifies our common knowledge of the different types of attention needed for reading versus proofreading.

When presented with a large visual array of targets for our attention, we can choose to examine our environment globally, or we can focus on specific features. Damage to components of the neuronal network impairs this ability to shift between attentional targets. Patients with difficulty examining local features usually have a damaged left temporo-parietal lobe. Other patients may do well with local features but fail to absorb the overall contour; they usually have a damaged right temporo-parietal lobe. Indeed, the parietal lobe tends to emphasize the shifting between local and global attention, whereas the temporal lobe determines whether one can actually examine a local or global feature of a stimulus.

In the process of visual attention, we usually foveate, or look at, our exact item of interest. Although our attention generally relates to where we fixate, it is easy to dissociate the two processes. If we cue someone to focus their attention on a location in space other than the center of gaze, they become sensitive to information occurring at the cued location and insensitive to information at the fovea. The attentional focus rather than the visual focus maintains a low threshold and fast response time. We use these covert attentional shifts to determine where in the visual field we will target our gaze.

Attention to visual elements can also apply to other modalities, such as the auditory system. When multiple people talk simultaneously, we may select one stream of conversation to follow in detail. To direct our attention, we often visually orient toward the person speaking and hone in on the frequency of their voice or the content of the information relayed. When we attend to one stream, the other auditory stimuli fade into the background. The information is present but does not reach focal analysis. Data indicate that we process much of this unattended information in subtle and complicated ways. We can suddenly gain interest in unattended information (e.g., because our name is mentioned) whereby we quickly shift attention to the new information. Researchers have studied these attentional phenomena experimentally in some detail.

## COMPONENTS OF ATTENTION

There is an emerging consensus that attention does not constitute a singular mechanism but is instead a complex system presiding over a number of distinct neuronal circuits. Michael I. Posner and his colleagues, whose experimental paradigm considerably advanced contemporary understanding of attention, initially proposed this theory (Posner, 2004). Inspired by the notion of anteriorly and posteriorly located attentional networks, their model comprises three distinct attentional control systems: *select*, *orient*, and *alert*. These operations form three functionally and anatomically unique control systems. *Alerting* refers to a change in a person's internal state in preparation for perceiving a stimulus. *Orienting* directs the person's point of reference to sensory objects, and the process of *selection* involves choosing among conflicting actions. In the field of attention research, focusing on these components reduces the complex process of attention into measurable units.

It is now possible to use this model clinically, with the help of noninvasive neuroimaging techniques such as electrophysiological measurements from scalp event-related potentials (ERP), functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), near infrared spectroscopy (NIRS), positron emission tomography (PET),

and single photon emission computed tomography (SPECT). These tools allow the examination of anatomical and functional changes in brain activity while a subject performs a task. Their development has forged an impressive link between psychology and neuroscience over the past 2 decades (Posner, *in press*).

Applications of neuroimaging to the field of attention have provided much information on how the brain houses attentional processes. Initial efforts to study hypnotic phenomena and attention with neuroimaging used cerebral blood flow, SPECT, PET, and occasionally fMRI (Baer et al., 1990; Crawford et al., 1998; Crawford et al., 2000; Halligan, Athwal, Oakley, & Frackowiak, 2000; Kosslyn, Thompson, Costantini-Ferrando, Alpert, & Spiegel, 2000; Maquet et al., 1999; Rainville, 2002; Rainville, Duncan, Price, Carrier, & Bushnell, 1997; Rainville, Hofbauer, Bushnell, Duncan, & Price, 2000; Rainville, Hofbauer, Bushnell, Duncan, & Price, 2002; Rainville et al., 1999; Szechtman, Woody, Bowers, & Nahmias, 1998). Although not widely used in the field, neuroimaging studies of hypnotic processes have produced intriguing results. For example, researchers have used the orienting network as defined by Posner and colleagues to understand the effects of lesions that produce neglect of sensory information either by brain damage or by restricting transmitter input. Studies of frontal attention networks have provided similar understanding of pathologies at higher levels of cognition.

In the clinical arena, research using neuroimaging has even related attentional networks to attention deficit hyperactivity disorder (ADHD). Bush et al. used a conflict task to compare adults diagnosed with ADHD to healthy controls (1999). The healthy subjects showed more anterior cingulate cortex (ACC) activation than did those diagnosed with ADHD, probably due to higher attentional efficiency. Although the ADHD group experienced only a slight decrease in performance, their brains activated an entirely different network. Whereas healthy controls activated the ACC, persons diagnosed with ADHD relied on the anterior insula—a brain region typically associated with responses in routine tasks not involving conflict. Recent findings from a follow-up study indicate that when adults diagnosed with ADHD are medicated with methylphenidate (e.g., Ritalin), their ACC activation increases toward normal levels (Bush, Spencer, Holmes, Surman, & Biederman, 2003). Recent neuroimaging data collected from children diagnosed with ADHD reveals similar trends (Raz, 2004).

## ATTENTIONAL NETWORKS

To further investigate attentional networks, we recently devised a simple Attention Network Test (ANT) that can be performed by adults, children, and even nonhuman primates (Barnea, Rassis, Raz, Othmer, & Zaidel, 2004; Fan, McCandliss, Sommer, Raz, & Posner,

2002; Raz, in press-a; Raz, Fan, et al., in press; Raz, Fossella, et al., in press; Raz & Shapiro, 2002). The ANT takes about half an hour to administer and provides three numbers that indicate the efficiency of the networks that perform the alert, orient, and conflict-resolution functions. Previously published results prove its reliability, its heritability, and the independence of results for the three different attentional functions (Fan, McCandliss, Flombaum, & Posner, 2001; Fan, Wu, Fossella, & Posner, 2001; Fossella, Posner, Fan, Swanson, & Pfaff, 2002; Fossella, Sommer, et al., 2002).

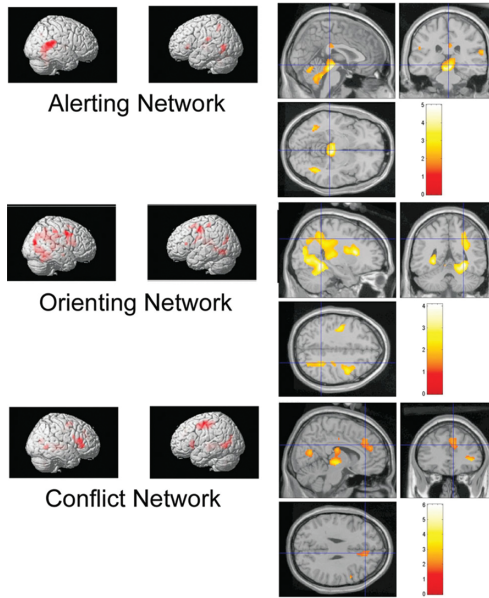
Whereas earlier studies examined areas involved in the individual components of the ANT (Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000; Hopfinger, Buonocore, & Mangun, 2000), recent reports address the brain areas involved in carrying out the ANT as a whole (Fan, McCandliss, et al., 2001). These fMRI data suggest that the test activates three largely orthogonal networks related to components of attention (see Figure 1). Supporting these findings, Raz and Shapiro (2002) reported that the pulvinar, superior colliculus, superior parietal lobe, and frontal eye fields were often active in studies of the orienting network. The anterior cingulate gyrus is an important part of the executive network, as it is involved in selective attention and conflict resolution. The right frontal and parietal areas are active when people maintain the alert state (Fan, Raz, & Posner, 2003).

Pharmacological studies (e.g., Marrocco & Davidson, 1998) have related each of the networks with specific chemical neuromodulators. For example, cholinergic systems arising in the basal forebrain play an important role in orienting, whereas the norepinephrine system rooted in the locus coeruleus of the midbrain is involved in alerting. Lastly, the ACC and lateral prefrontal cortex are target areas of the mesocortical dopamine system, which is involved in executive attention.

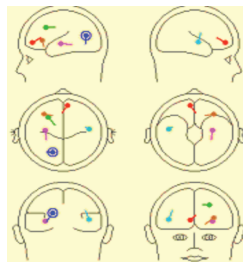
## ATTENTIONAL AND HYPNOTIC PHENOMENA

Hypnosis is often labeled as attentive receptive concentration (H. Spiegel & Spiegel, 1987). Indeed, evidence relating hypnotic phenomena to attentional mechanisms is mounting (Raz, Shapiro, Fan, & Posner, 2002b), and there is general agreement that hypnotic phenomena involve attention (Karlin, 1979) and relate to self-regulation (Posner & Rothbart, 1998). Although several investigators have hypothesized that hypnotic suggestibility correlates with underlying differences in individual patterns of waking attention (Tellegen & Atkinson, 1974), theories of hypnotic response regarding attentional processes differ (Kirsch, Burgess, & Braffman, 1999).

The marriage of attention and hypnosis led us to use hypnosis, particularly the Stroop task, to examine disparate attentional networks. In



**Figure 1.** Functional anatomy of attentional networks. Cross-sectional views from aggregate fMRI activations acquired from sixteen individuals performing the ANT in a 3 Tesla magnet (Fan, McCandliss, Flombaum, & Posner, 2001). These activation patterns outline some of the functional anatomy subserving the three attentional networks. The alerting effect occurs via thalamic activations, orienting effects occur via parietal activations, and conflict effects occur via ACC activations.



**Figure 2.** Spatial locations of significant fMRI activations in Stroop conflict comparing posthypnotic suggestion with no suggestion in highly hypnotizable individuals. To relate the fMRI with the ERP data (reported elsewhere), brain electrical source analyses (BESA) explored the time course of the fMRI generators. Six fixed dipoles were placed at locations suggested by the fMRI data. The BESA algorithm provided evidence consistent with independent generators at both the anterior cingulate cortex (shown in green) and cuneus (shown in blue).

the classic Stroop task, experienced readers are asked to name the ink color of a displayed word (Stroop, 1935). Responding to the ink color of an incompatible color word (e.g., the word *red* displayed in blue ink), subjects are usually slower and less accurate than when identifying the ink color of a control item (e.g., “\*\*\*\*” or *lot* inked in red). This difference in performance is called the Stroop Interference Effect (SIE) and is one of the most robust and well-studied phenomena in attentional research (MacLeod, 1992; MacLeod & MacDonald, 2000). There has been a gradual appreciation that attention can mediate word reading. However, attention remains largely an automatic task, because a proficient reader cannot withhold accessing the word’s meaning despite explicit instructions to attend only to the ink color. The standard beliefs in both the word recognition and Stroop fields maintain that words are automatically processed to the semantic level (MacLeod, 1991; Neely, 1991), thereby making SIE the “gold standard” for studying attentional measures (MacLeod, 1992; Raz & Shapiro, 2002).

Drawing on behavioral (Raz, Shapiro, Fan, & Posner, 2002a), optical (Raz, Landzberg, et al., 2003), and neuroimaging assays (Raz, Fan, Shapiro, & Posner, 2002; Raz et al., 2002a; Raz, Shapiro, Fan, & Posner, 2002c), we recently reported that effective posthypnotic suggestion consistently cancelled the SIE in highly hypnotizable subjects (Raz et al., 2002b). This effect was not a result of optical degradation of the input stimuli (Raz, Landzberg, et al.). Nonetheless, our results indicate that the effect must operate via a top-down cognitive mechanism that modifies the processing of input words. Because the SIE typically activates the dorsal part of the ACC, these data support the view that monitoring conflict among potential responses also involves the dorsal ACC (Botvinick, Braver, Barch, Carter, & Cohen, 2001).

Neuroimaging studies of executive attention conducted using Stroop or Stroop-like tasks have shown activation of midline frontal areas (e.g., ACC) and the lateral prefrontal cortex (Bush, Luu, & Posner, 2000). Overall, these tools provide a method of teasing out the functional contributions of different areas within the executive attention network. Most evidence indicates that lateral prefrontal areas are involved in representing specific information over time (working memory), while medial ACC areas are implicated in the detection, resolution, or monitoring of conflict (Kerns et al., 2004).

#### *Using Posthypnotic Suggestion to Reduce Conflict in the Human Brain*

Other researchers have attempted to explore the Stroop effect under hypnosis (Blum & Graef, 1971; Blum & Wiess, 1986; Dixon, Brunet, & Laurence, 1990a; Dixon & Laurence, 1992; MacLeod & Sheehan, 2003; Nordby, Hugdahl, Jasiukaitis, & Spiegel, 1999; Sheehan, Donovan, & MacLeod, 1988; D. Spiegel, Cutcomb, Ren, & Pribram, 1985; Sun, 1994; Szechtman et al., 1998). However, these assays have largely concen-



trated on the effect of hypnosis without suggestion and often used nonclassic Stroop paradigms (Sheehan et al., 1988). Historical single-case reports (MacLeod & Sheehan, 2003; Schatzman, 1980), obscure publications (Sun, 1994), and informal personal communications (Wheatley, personal communication, May 7, 2003) proposing hypnotic removal of Stroop conflict had not been rigorously studied prior to our efforts to study conflict removal.

Multiple neuroimaging methods using variations of conventional Stroop tasks have shown activation of a network of brain areas, including the dorsal ACC. These studies required participants to respond to one dimension of a stimulus rather than a strong conflicting dimension (Botvinick et al., 2001; Bush et al., 2000; MacDonald, Cohen, Stenger, & Carter, 2000). Their results introduced a popular theory of cognitive control proposing that the ACC is part of a network involved in handling conflict between neural areas (Botvinick, Braver, et al., 2001; Bush et al., 2000). Whereas some researchers view the ACC through the lens of a conflict monitoring model (Botvinick et al., 2001; Cohen, Botvinick, & Carter, 2000; Kerns et al., 2004), others construe it as a regulation model engulfing broader processes of consciousness and self-regulation, including executive attention and mentation (Bush et al., 2000).

To unravel the brain mechanism by which the posthypnotic suggestion affects visual processing in the Stroop conflict, we studied highly hypnotizable and less hypnotizable participants both with and without a suggestion to construe the input words as nonsense strings. We complemented the high spatial resolution of fMRI by event-related scalp electrical potentials (ERPs), which afford high temporal resolution. We acquired the fMRI and ERP data separately while the same participants performed similar Stroop tasks. Elimination of the Stroop conflict resulted in an attenuation of fMRI signal at the ACC and extrastriate areas (Raz et al., 2002; Raz et al., 2002a; Raz et al., 2002c). Posthypnotic suggestion caused highly hypnotizable subjects to view Stroop words as nonsense foreign signs. This finding illuminated the mechanism by which the posthypnotic suggestion operated in highly hypnotizable subjects.

These data are consistent with reports that both attention and suggestion can modulate neural activity for visual stimuli (Kosslyn et al., 2000; Mack, 2002; Martinez et al., 1999; Rees, Russell, Frith, & Driver, 1999). One such study created a situation in which subjects could look directly at a five-letter word without attending to it, as they had to concurrently respond to a superimposed stream of pictures shown in different orientations. As shown by fMRI, the subjects failed to perceive words placed at the center of gaze even for decidedly familiar and meaningful stimuli (Rees et al., 1999). In another study, PET data showed that highly hypnotizable individuals neither perceive color nor activate extrastriate areas related to color after receiving instruc-

tion to see a color pattern in gray-scale (Kosslyn et al., 2000). Finally, research involving PET assays of pain showed that specific modulatory hypnotic suggestions could affect activation of different brain structures. Whereas soothing the conflict by suggesting a drop in pain unpleasantness reduced specific activity in the ACC (Rainville et al., 1997; Wager et al., 2004), suggesting a decrease in pain intensity reduced the activity in the somatosensory cortex (Hofbauer, Rainville, Duncan, & Bushnell, 2001). These accounts underline the influence that attention and suggestion can impart to conflict situations and top-down cognitive control (Posner & Rothbart, 1998; Rainville, 2002; Rainville et al., 2002; Raz & Shapiro, 2002).

Using scalp ERPs offers a higher temporal resolution for investigating hypnosis. We investigated the effects of suggestion on brain activity and found an early reduction in brain waves under experimental suggestion. Electrophysiological activity differed as early as 150 ms following word presentation. Under suggestion, the N1, an early ERP component believed to be influenced by attention to a channel of information, was absent. We did not observe posterior activity in the group that received suggestion until after 250 ms. These findings indicate that a change in visual input processing caused the absence of conflict. To relate the fMRI with the ERP data, brain electrical source analyses (Scherg & Berg, 1990) explored the time course of the fMRI generators (see Figure 2). These analyses provided evidence consistent with independent generators at both the ACC and cuneus (Raz, *in press-b*).

In addition to providing the conflict resolution data, this experimental design demonstrates the possibility of dissociating attention based either on input processing from sensory activity or on the input stream. Although this outcome leaves unclear how posthypnotic suggestion reduced visual input, two potential mechanisms exist. Either all input decreased, or the reduction was word-specific. Our ERP data support the former interpretation.

Other relevant ERP data were obtained using the error-related negativity (ERN), an electrophysiological index closely associated with commission of errors in cognitive tasks involving response conflict (Carter et al., 1998; Falkenstein, Hohnsbein, Hoormann, & Blanke, 1991; Gehring & Fencsik, 2001). Results showed that although the posthypnotic suggestion reduced conflict, it did not decrease conflict monitoring (Raz, Fan, & Posner, 2004). In the group that received posthypnotic suggestion, ACC activation decreased prior to the subjects' responses. However, ACC activation increased upon incorrect responses on incongruent trials regardless of suggestion. Thus, it was possible to eliminate conflict resolution (early ACC diminution) yet maintain conflict monitoring (ACC activation following incorrect responses).

Finally, recent behavioral data comparing hypnotic and nonhypnotic suggestions using a similar experimental protocol at the Univer-

sity of Connecticut also showed significant reduction, but not elimination, of Stroop conflict under both hypnotic and nonhypnotic suggestions (Pollard, Raz, & Kirsch, 2003). Although susceptibility to suggestion, not explicit hypnotic procedures, may be the critical factor underlying Stroop conflict reduction (Braffman & Kirsch, 1999; Kirsch & Braffman, 2001; Pollard, Raz, & Kirsch, 2003), this model suggests that individual differences in sensitivity to suggestion and hypnosis may play an important role in attentional processes.

### GENETICS OF HYPNOTIZABILITY

Most evidence concerning the genetic bases of hypnotizability dates back 20 to 30 years ago and centers on twin data reported by Morgan and colleagues (Morgan, 1973; Morgan, Hilgard, & Davert, 1970). The first study reported a correlation of .63 for monozygotic (MZ) twins and .08 for dizygotic (DZ) twins, whereas the second study reported .52 for MZ twins and .18 for DZ twins. Rawlings (1978) and Bauman and Bul' (1981) echoed similar findings in subsequent reports. Other than these general findings, researchers did not pursue the linking of genetics with hypnotizability until the recent genomics revolution.

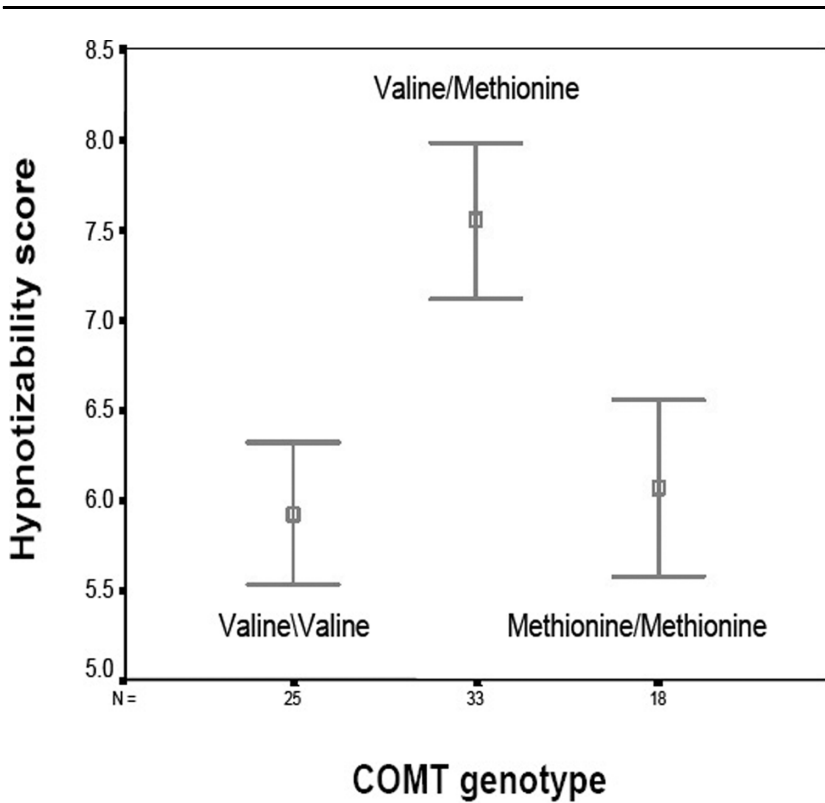
Over the past decade, the Human Genome Project has made great progress in identifying the protean 30,000 genes in the human genome as well as the approximately 1.7 million polymorphic sites scattered across the 6 billion base-pair length of the human genome (Wolfsberg, Wetterstrand, Guyer, Collins, & Baxevanis, 2002). These findings have illuminated how genes can influence disease development. They have also aided scientists in the search for genes associated with particular diseases. In addition, genomics has promoted the discovery of new treatments and afforded insights into behavioral genetics, such as the relationship between certain genetic configurations and manifest behavior.

In the field of hypnotizability, a team led by geneticist Richard Ebstein has pioneered recent efforts to establish viable correlations relating phenotype and genotype (Bachner-Melman, Ebstein, & Lichtenberg, 2002; Benjamin et al., 2000; Ebstein, Bachner-Melman, & Lichtenberg, 1999; Lichtenberg, Bachner-Melman, Ebstein, & Crawford, 2003; Lichtenberg, Bachner-Melman, Ebstein, & Crawford, 2004; Lichtenberg, Bachner-Melman, Gritsenko, & Ebstein, 2000). Using the Stanford Hypnotic Susceptibility Scale, Form C (SHSS:C) and primarily administering the test in Hebrew, they have examined a number of such correlations. One gene they investigated, catechol-O-methioninehyltransferase (COMT), influences performance on prefrontal executive cognition and working memory tasks (Weinberger et al., 2001) and is associated with pain regulation (Wager et al., 2004; Zubieta et al., 2003). Their results reveal an association between COMT high/low enzyme activity

polymorphism and hypnotizability (Ebstein et al., 1999; Lichtenberg et al., 2000). A significant difference in hypnotizability exists between individuals who carry the valine/methionine and valine/valine COMT genotypes (Lichtenberg et al., 2003; Lichtenberg et al., 2004; Lichtenberg et al., 2000).

Given this correlation between COMT and hypnotizability, we set out to investigate further potential connections. Our previous fMRI data had identified the ACC as a key node in both the conflict network and the dopaminergic system (Raz, *in press-b*; Raz et al., 2002c). Also, involvement of dopamine in the function of executive attention is well documented (Marrocco & Davidson, 1998). Furthermore, drugs known to affect the dopaminergic system while altering consciousness (e.g., propofol) induce hypnosis-like experiences (DiFlorio, 1993; Fiset et al., 1999; Rainville et al., 2002; Xie et al., 2004). Accordingly, we wanted to reexamine the COMT results reported by Lichtenberg et al. (2000).

Our initial study involved 80 healthy volunteers who provided DNA samples via sterile cheek swab. We genotyped the DNA samples for a few well-known genetic polymorphisms involving dopamine, including DRD3, DRD4, MAOA, DAT, and COMT, as previously described (Fossella, Posner, et al., 2002; Fossella, Sommer, et al., 2002). We then compared individual genetic differences with variations in hypnotic susceptibility, as measured using the SHSS:C without the anosmia to ammonia item (Raz et al., 2002b). In line with Ebstein's data (Ebstein et al., 1999; Lichtenberg et al., 2003; Lichtenberg et al., 2004; Lichtenberg et al., 2000), we found a polymorphism in the COMT gene that related to hypnotizability (see Figure 3). Specifically, valine/methionine heterozygous subjects were more highly suggestible than either valine/valine or methionine/methionine homozygous subjects. The inverted U-shaped trend of valine/methionine COMT heterozygotes towards higher hypnotizability is congruent with data reported by other researchers. However, the data differ from our previous studies examining the role of COMT in executive attention as measured by the ANT as well as by the Stroop task (Sommer, Fossella, Fan, & Posner, *in press*). The ANT studies found that subjects with the valine/valine genotype showed somewhat more efficient conflict resolution (measured by a lower Stroop interference effect) than do subjects with the valine/methionine genotype (Fossella, Posner, et al., 2002; Fossella, Sommer, et al., 2002). This trend was also seen in subjects who performed the Stroop task (Sommer, Fossella, Fan, & Posner, *in press*). The valine allele of COMT, which confers relatively higher levels of enzyme activity and thus lower amounts of extrasynaptic dopamine, has been examined in the context of neuroimaging studies, where it correlated with lower activity of the dorsolateral prefrontal cortex (Egan et al., 2001). Results from other genetic polymorphisms,



**Figure 3.** COMT and hypnotizability. Distributions of COMT genotypes vs. SSHS:C hypnotizability score. The Y-axis shows hypnotizability scores (mean  $\pm$  Standard Error). The X-axis shows the distribution for each genotypic class at the COMT Valine 108/158 Methionine polymorphism.

including DRD3, DRD4, MAOA and DAT, showed no significant associations with hypnotizability (Raz, Fossella, et al., 2003).

#### INDIVIDUAL DIFFERENCES IN ATTENTION AND HYPNOTIZABILITY

Healthy individuals exhibit differences in the efficiencies of each of the attentional networks. We can examine this phenomenon by evaluating alerting, orienting, and executive attention using the ANT. Self-report scales can also reveal individual differences in attentional components. One higher-level factor called *effortful control* involves the ability to voluntarily shift and focus attention and inhibit certain

information. Effortful control as reported by the subject seems to relate most closely to the executive attention network. Twin studies have proposed that individual differences in effortful control are highly heritable, in agreement with the hypnosis data (Morgan, 1973; Morgan et al., 1970). Furthermore, individuals high in effortful control also report themselves as relatively low in negative emotion. These data suggest that executive attention is important for control of both cognition and emotion.

Using modified Stroop procedures, researchers have examined highly hypnotizable versus less hypnotizable subjects outside of hypnosis and report reliable differences in attentional processing between the two groups (Dixon, Brunet, & Laurence, 1990b; Dixon & Laurence, 1992). Stroop interference is significantly larger for the highly hypnotizable individuals compared to the less hypnotizable persons (Raz et al., 2002a). This finding suggests that outside of the hypnotic context, highly hypnotizable people process words more automatically than do their less hypnotizable counterparts. However, it also implies a significant deviation in baseline efficiency of the executive attention network in highly hypnotizable people. In this regard, the nascent COMT findings may herald a genetic approach (H. Spiegel & Spiegel, 1987) whereby a genotype may suggest a "biological propensity" to complement an attentional phenotype such as hypnotizability.

## CONCLUSION

This paper has outlined close links between attentional and hypnotic mechanisms while providing preliminary data supporting a candidate gene approach to attention and hypnotizability. Neuroimaging assays and exploratory genetic associations from the domain of attentional research will continue to illuminate hypnotic phenomena into the future. Hypnosis is a complex phenomenon that is likely associated with many genetic polymorphisms. Although COMT is not the "hypnotizability gene," as data accumulate from multiple laboratories, meta-analyses across these findings will likely increase our appreciation of genotyping as an important supplement to phenotyping (Ebstein et al., 1999; Egan et al., 2001; Lichtenberg et al., 2003; Lichtenberg et al., 2000; Lichtenberg et al., 2004; Rawlings, 1978; Raz, 2003a, 2003b; Raz, Fan, et al., in press; Raz, Fossella, et al., in press; Raz, Fossella, et al., 2003; Zubieta et al., 2003). Indeed, genomics is sure to supplement attentional assays and increase our knowledge base (Fan, Fossella, Sommer, Wu, & Posner, 2003; Fan, Wu, et al., 2001; Fossella, Posner, et al., 2002; Fossella, Sommer, et al., 2002).

The possibility of illuminating hypnotic phenomena with attentional paradigms from cognitive neuroscience has become a reality. Compelling cumulative data demonstrate that hypnosis can significantly alter performance for highly suggestible individuals on attentional tasks such as the Stroop and ANT (Fan et al., 2002; Raz, 2003a, 2003b, in press-a, in press-b; Raz, Fan, et al., in press; Raz et al., 2004; Raz, Fan, et al., 2002; Raz, Fossella, McGuiness, Zephrani, & Posner, in press; Raz, Fossella, et al., 2003; Raz, Landzberg, et al., 2003; Raz & Michels, 2004; Raz & Shapiro, 2002; Raz et al., 2002a, 2002b, 2002c). Results from neuroimaging and genetics studies support a potential common mechanism of dopaminergic modulation affecting both attentional and hypnotic performance. Such a mechanism may, however, overlap with different aspects of executive attention. These findings may reveal a significant disparity between the mechanisms subserving the cognitive capacities of highly suggestible and less-suggestible individuals (Dixon et al., 1990a, 1990b; Dixon, Labelle, & Laurence, 1996; Dixon & Laurence, 1992) and are likely to impact future research in the field.

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## Aufmerksamkeit und Hypnose: Neuronale Substrate und genetische Zusammenhänge von zwei zusammenlaufenden Prozessen

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**Zusammenfassung:** Obwohl Aufmerksamkeit ein zentrales Thema in der Psychologie darstellt, beziehen Hypnoseforscher nur selten Befunde aus der Aufmerksamkeitsforschung in ihre Arbeiten ein. Wie auch andere biologische Systeme, verfügt auch Aufmerksamkeit über distinkte physiologische Grundlagen, auf deren Basis psychologische Prozesse ablaufen. Spezifische Gehirnverletzungen, Bewusstseinszustände und Drogen können allesamt Aufmerksamkeitsnetzwerke beeinflussen. Die Untersuchung dieser Netzwerke unter Verwendung moderner bildgebender Verfahren hat wichtige aufmerksamkeitsbezogene Mechanismen aufgedeckt. Im Zeitalter der Genforschung könnten genetische Ansätze zusätzlich zu den Befunden aus bildgebenden Untersuchungen herangezogen werden. Genetische Untersuchungen stellen ein zunehmend billigeres und praktikableres Komplement zu phänotypischen Untersuchungen dar. Exploratorische genetische Untersuchungen ermöglichen Einblicke in die genetischen Grundlagen von Aufmerksamkeit und Hypnotisierbarkeit. Dieser Artikel erörtert relevante Aspekte von Aufmerksamkeitsmechanismen und ihrer zugrundeliegenden Neuroanatomie im Bezug zur Hypnoseforschung. Befunde aus Studien zu Aufmerksamkeitsnetzwerken, bildgebenden und genetischen Untersuchungen können dazu beitragen, interindividuelle Unterschiede der Hypnotisierbarkeit und die mit Hypnose befassten neuronalen Subsysteme besser zu verstehen.

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## Attention et Hypnose : substrats neuronal et association génétiques de deux processus convergeants

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**Résumé :** bien que l'attention soit un thème central en science psychologique, les chercheurs en hypnose intègrent rarement des découvertes sur l'attention dans leur travail. De même que pour d'autres systèmes biologiques, l'attention a une anatomie distinctive qui accomplit des fonctions psychologiques de base. Des états, des drogues, des blessures cérébrales particuliers peuvent influencer les réseaux de l'attention. Des investigations de ces réseaux, utilisant les techniques modernes de neuro-imagerie ont révélé d'importants mécanismes impliqués dans l'attention. Dans cet ère génomique, l'approche génétique peut compléter ces techniques de neuro-imagerie. Technologie de plus en plus viable et peu coûteuse, la recherche de génotype vient en complément du phénotype : les essais exploratoires génétiques offrent un insight des bases génétiques à la fois de l'attention et de l'hypnotisabilité. Cet article parle des différents aspect des mécanismes de l'attention et de leur neuro-anatomie sous-jacente lorsqu'ils sont liés à l'hypnose. Basée sur des données des réseaux de l'attention, la neuro-imagerie et la génétique, ces résultats devrait aider à

expliquer les différences individuelles d'hypnotasibilité et des systèmes neuronaux favorisant l'hypnose.

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**La atención y la hipnosis: Sustratos neurológicos y asociaciones genéticas de dos procesos convergentes**

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**Resumen:** Aunque la atención es un tema central en la psicología, los investigadores de la hipnosis rara vez incorporan los hallazgos sobre la atención en su trabajo. Al igual que con otros sistemas biológicos, la atención tiene una anatomía clara que lleva a cabo funciones psicológicas básicas. Lesiones específicas en el cerebro, estados, y drogas pueden influir las redes de atención. La investigación de estas redes que utilizan las técnicas modernas de imágenes cerebrales han revelado mecanismos importantes implicados en la atención. En esta era de la genética, los enfoques genéticos pueden complementar estas técnicas de imágenes. Conforme la tipología genética llegue a ser un complemento económico y tecnológicamente viable a la tipología fenotípica, los ensayos genéticos exploratorios ofrecen una visión sobre las bases genéticas tanto de la atención como de la hipnotizabilidad. Este trabajo discute aspectos pertinentes de los mecanismos de atención y su neuroanatomía fundamental en relación a la hipnosis. Enfatizando la información de las redes de atención, imágenes cerebrales y la genética, estos resultados ayudan a explicar las diferencias individuales en la hipnotizabilidad y los sistemas neurológicos subyacentes a la hipnosis.

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