

Review

Hypnotizability-Related Asymmetries: A Review

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Abstract: Hypnotizability is a dispositional trait reflecting the individual ability to modify perception, memory and behavior according to imaginative suggestions. It is measured by validated scales that classify the general population in high (highs), medium (mediums) and low (lows) hypnotizable persons, predicts the individual proneness to respond to suggestions, and is particularly popular in the field of the cognitive control of pain and anxiety. Different hypnotizability levels, however, have been associated with specific brain morpho-functional characteristics and with peculiarities in the cognitive, sensorimotor and cardiovascular domains also in the ordinary state of consciousness and in the absence of specific suggestions. The present scoping review was undertaken to summarize the asymmetries observed in the phenomenology and physiological correlates of hypnosis and hypnotizability as possible indices of related hemispheric prevalence. It presents the findings of 137 papers published between 1974 and 2019. In summary, in the ordinary state of consciousness, behavioral, neurophysiological and neuroimaging investigations have revealed hypnotizability related asymmetries mainly consisting of pre-eminent left hemisphere information processing/activation in highs, and no asymmetries or opposite directions of them in lows. The described asymmetries are discussed in relation to the current theories of hypnotizability and hypnosis.

Keywords: hypnotic susceptibility; neutral hypnosis; EEG spectral analysis; EEG nonlinear analysis; brain activations; functional connectivity; psychophysiology

1. Introduction

The story of medical hypnosis started long ago, in Switzerland, with Paracelsus and tells of various definitions and interpretations of this phenomenon, from mesmerism to psychoanalysis [1]. In the 20th century, two different approaches to it—clinical and experimental—were proposed. Clinical hypnosis, named also Ericksonian owing to the great work performed by Milton Erickson [2] in the clinical field, is based on psychoanalytic assumptions, considers hypnosis as a tool to access the unconscious mind and states that any person can be hypnotized [3]. Experimental hypnosis leaves any personality theory out of consideration. It conceptualizes the individual susceptibility to experience hypnosis as a measurable personality trait that has a high test-retest reliability [4,5] and has been found to be associated with a number of cognitive-emotional characteristics such as sustained attentional abilities, vividness of imagery, fantasy proneness, creativity and emotionality [6–10]. Hypnotizability predicts the proneness to modify perception, memory and behavior according to specific instructions named suggestions in both the awake and hypnotic state [11].

In recent decades, experimental findings related to the physiological mechanisms sustaining hypnotic phenomenology have made the edge between the clinical and experimental approach less clear-cut [12,13]. In fact, on one hand hypnotizability does predict the response to suggestions [11],

and the effects of suggestions administered in the ordinary state of consciousness are not predicted, or are slightly different from those observed under hypnosis [13,14]. On the other hand, the theoretical assumption that only the persons scoring high on hypnotizability scales (*highs*) can accept suggestions has been challenged by studies reporting that also medium (*mediums*) and low hypnotizable individuals (*lows*) can respond to a few suggestions such as analgesia, although through different mechanisms [15,16].

Within the experimental reference frame, two major theoretical approaches have been proposed, namely neo-dissociative and socio-cognitive. The former assumes that hypnotic behavior, that is responding to suggestions and reporting involuntariness in action, depends on the hierarchical organization of cognitive activities which can be disrupted by hypnosis. This would allow lower cognitive modules to accept suggestions in the absence of conscious higher controls [15,16]. In contrast, the socio-cognitive approach states that the response to suggestions is a function of several individual and environmental factors allowing certain persons to behave according to suggestions independent from the induction of the hypnotic state. In brief, each individual responds through her/his specific cognitive-emotional characteristics and the experimental condition. In fact, it has been shown that targeting a relation as “hypnosis” and enhancing the expectation of hypnosis facilitates the response to suggestions more than actual hypnotic induction [12]. Experimental support has been provided to both theories, although recent research indicates the socio-cognitive reference frame as the most appropriate to account for most experimental findings.

Although the most popular aspect of hypnotizability is the proneness of the individuals with high hypnotizability to respond to suggestions, a renewed interest into this individual characteristic has come from the observation that it is much more than a cognitive disposition enabling individuals to enter the hypnotic state and accept suggestions, as it is associated with psychophysiological characteristics observable out of hypnosis and in the absence of suggestions. Indeed, different hypnotizability scores are associated with specific brain morpho-functional characteristics [17,18] and with sensorimotor, cardiovascular and cognitive-emotional correlates (Table 1), which makes hypnotizability relevant to the individual psycho-physiological identity and, thus, to the everyday life [19–23].

Table 1. Hypnotizability-related behavioral differences observed out of hypnosis.

Highs with Respect to Lows		
spinal reflexes	H reflex habituation during long lasting relaxation F wave reduced frequency of occurrence (right hand)	Santarcangelo et al., 1989 Santarcangelo et al., 2003
postural and locomotor control	less accurate during sensory alteration	Santarcangelo et al., 2008; Menzocchi et al., 2010a Menzocchi et al., 2010b; Solari et al., 2015 Menzocchi et al., 2015
visuomotor control	less accurate	
haptics	better performance in the visual recognition of bimanually explored nonmeaningful objects better performance in the blindfolded reproduction of haptically explored angles	Castellani et al., 2011 Menzocchi et al., 2012
autonomic control	preeminent parasympathetic control during long-lasting relaxation sympathetic control in standing position less engaged	Santarcangelo et al., 2012 Santarcangelo et al., 2007
flow-mediated artery dilation	not reduced by stress and nociceptive stimulation not reduced by stress and nociceptive stimulation	Jambrik et al., 2004a Jambrik et al., 2004b; Jambrik et al., 2005a Jambrik et al., 2005b
functional equivalence between imagery and perception	stronger	Papalia et al., 2014; Santarcangelo, 2014; Ibanez-Marcelo et al., 2019 Bocci et al., 2017 Spina et al., 2020
cerebellar control of pain motor cortex excitability μ 1 polymorphism	paradoxical after anodal cerebellar stimulation higher in basal and imagery conditions higher frequency of the polymorphism less responsive to opiates	Presciuttini et al., 2018 Facco et al., 2016 Kirenskaia et al., 2011 De Pascalis et al., 1989
emotional reactivity	greater	Diolaiuti et al. 2019
interoceptive sensitivity	greater	

The aim of the present scoping review was to summarize the asymmetries observed in the phenomenology and the physiological correlates of hypnosis and hypnotizability as possible indices of related hemispheric prevalence. In fact, a debate about the pre-eminent role of the right or left hemisphere in hypnotizability-related psychophysiological features and in the shift from wakefulness to hypnosis has engaged hypnosis scholars for several decades. The review is based on all the research/review papers providing reliable statistical information derived from PsycINFO, PsycARTICLES and published in PubMed (years 1974–2019; key words: “hypnotic susceptibility and asymmetry”, “hypnotizability and asymmetry”, “hypnosis and asymmetry”, “hypnosis and laterality”, “hypnotizability and laterality”). The review led to the selection of one hundred and thirty-seven studies. The results were reported considering separately individual differences in cognitive domains: fantasy proneness, cognitive and physiological flexibility, focused attention, divided attention, executive functions, memory, and visuospatial abilities. The main goals of this review were to (1) sum up the current state of the knowledge regarding the associations between hypnotizability and brain-related asymmetry patterns and (2) discuss the implications of this knowledge and summarize the most reliable view on hypnotizability-related physiological asymmetries. Then, we briefly report the most relevant behavioral findings. In the Section 3, we report the neurophysiological studies on the EEG hemispheric asymmetry of conventional alpha, theta, beta and gamma frequency bands and findings of nonlinear dynamical analyses of EEG as correlates of hypnotizability. In the Section 4 we describe the most relevant neuroimaging findings and in the Section 5 we summarize the described findings and indicate the questions deserving further investigation.

Since the nature of tasks influences the lateralization of brain activity, we predominantly limit our description of hypnotizability-related EEG asymmetries to resting conditions, in both the awake and hypnotic state. What can be said, in general, is that, during tasks, EEG hemispheric asymmetries occur more frequently in *highs* and are larger in *highs* than in *lows*. This has been observed, for instance, (i) for the recall of emotional events, which has been found to be associated, in *highs*, with an increase

of 40-Hz EEG density in the right hemisphere during positive experience and with a density reduction in the left hemisphere during negative emotions [24]; (ii) for self-generated happy and sad emotions, during which *highs* showed significantly greater hemispheric asymmetries (right greater than left) in the parietal region in high theta, high alpha, and beta activity [25], (iii) for beta activity in eyes-open rest during both waking and hypnosis, which was larger in the *highs'* left than right hemisphere [26].

2. Behavior Studies

Several cognitive characteristics of *highs*—greater creativity, fantasy proneness, absorption in mental images [27–31]—have been long considered the effect of strategies engaging the right hemisphere preferentially. In line with this hypothesis, a progressively reduced frequency of the F wave, which measures the motoneurons postsynaptic excitability [32,33], was observed in the right-hand *abductor digiti minimi* during long-lasting relaxation [34]. This finding, which was found to occur faster during hypnosis than during simple relaxation, was interpreted as being due to self-hypnosis. Thus, it would not contrast with the proposed inhibition of the left hemisphere during hypnotic induction [35,36].

A number of behavioral studies, indeed, have suggested a functional left rather than right directed hemispheric asymmetry in *highs* in the ordinary state of consciousness. In particular, the *highs'* electrodermal responses are larger and haptic processing is faster for the left than for the right hand [35,37]; word fluency, a left prefrontal function [38], is greater in *highs* than in *lows* [39,40]; the *highs'* processing of temporal judgments is faster in the left than in the right hemisphere, which was reversed by hypnotic induction [41] in a line bisection test [42]; the *highs'* error is directed toward the right side at any distance of the line presentation [43], in contrast to the general population and to *lows* who exhibit left directed error for shorter distances and right directed error for larger distances [44,45]. In addition, the analysis of the *highs'* written language indicates a larger use of abstract nouns, which is preeminently sustained by the left hemisphere activity [46], ideomotor responses are found more frequently on the left side, although not consistently reported [47,48] and during, suggestions of arms heaviness, the *highs'* left arm lowers more than the right one [49] which could be accounted for by lower activation of the right hemisphere. Finally, only for *highs*, angry emotional valence is identified faster when presented to the right hemisphere [6]. To explain task-related asymmetry findings in term of hypnotic susceptibility [10], a greater overall cognitive and physiological flexibility can be advocated in *highs*, as they have more effective and flexible frontoparietal systems for both attention and inhibition of irrelevant stimuli [8,50–53].

In this research line, the inconsistency of the Right Hemisphere (RH)-activation hypothesis of hypnosis has been demonstrated by Kihlstrom and colleagues [54]. These authors assessed the hypnotizability of patients with either left- or right-hemisphere lesions and showed that brain-injured individuals can experience hypnosis and that their responses can be assessed using slightly modified versions of hypnotizability scales. Additionally, their results showed that unilateral damage of the right hemisphere following stroke does not impair hypnotic responding and that people with brain damage can be as hypnotically responsive as controls. Further, Dienes and Hutton [55], assuming that the dorsolateral prefrontal cortex (DLPFC) is a key region involved in higher-order processes related to performing actions, used repetitive transcranial magnetic stimulation (rTMS) under the hypothesis that a selective blocking of DLPFC by rTMS should make it harder for participants receiving a motor suggestion to be aware of the intention to perform the suggested action. If one is unaware of the intention, the arm will appear to lift by itself, producing the classic suggestion effect. In fact, the subjective rating of hypnotic suggestibility was higher after stimulation of the left-sided DLPFC. These findings support the theories postulating that diminished function in the frontal cortex is related to hypnotic response. Among these, the main is the cold control theory (see e.g., [56,57]), some forms of dissociated control theory (e.g., [58]) and left-frontal lobe inhibition neurophysiological approaches [36,39].

3. Neurophysiological Studies

3.1. EEG Alpha, Hypnotizability and the Right Hemisphere

A prevalent hypothesis on the hypnotizability-related asymmetries concerns differences in hemisphere functioning between resting-relaxation in waking and the so-called “neutral hypnosis” (i.e., resting hypnosis in the absence of targeted suggestions). This view suggests that the relative activation of the RH is characteristic of the high hypnotizable individuals during hypnosis (for reviews, see [59–61]). Bakan [62] was the first to suggest that hypnosis involves the RH activation owing to the association of hypnotic behavior with the creative, intuitive, nonanalytic, and holistic processing style assumed to reflect RH function. This hypothesis was proven as indefensible given that several general aspects of hypnosis, including the required attentional focus and the role of language in the establishment of hypnotic rapport, might be more appropriately seen as left hemisphere (LH) rather than RH brain functions [63,64], although the hypothesis of hypnosis as an RH task was seductive for many researchers (for reviews see [36,60,65]). Earlier research evidenced that the task-dependence of EEG alpha asymmetry, measured as the attenuation of the alpha rhythm in the activated hemisphere, reflects lateral specialization of the cerebral hemispheres. It was assumed that analytic tasks involving verbal or arithmetic manipulations yield relatively less alpha activity in the LH (LH tasks) than the musical and spatial (imagery, RH tasks) [66–68]. The ratio between left- and right-hemisphere alpha amplitude (LH / RH) was suggested as a reliable measure of task-related EEG asymmetry in a conducted follow-up study using essentially the same analytic and spatial tasks, but adding two so-called right-hemisphere tasks. These authors, using a slightly modified alpha laterality index $((RH - LH)/(RH + LH))$ replicated their earlier findings, i.e., slightly more pronounced RH alpha was generated on analytic rather than on spatial tasks. Alpha during the hypnotic task resembled that of the spatial task and, contrary to expectations, alpha during the musical task resembled the alpha measured during the analytic (LH) tasks. These authors also found no alpha differences between high and low hypnotizable groups on any of the experimental tasks. In a subsequent study, MacLeod-Morgan and colleagues [69,70] followed the Morgan, McDonald and MacDonald [66] strategy. Subjects received all tasks under eyes-open and eyes-closed conditions, with three potential LH-tasks (random number generation, verbal categories, and mental arithmetic) and three potential RH tasks (spatial orientation, listening to music, and tonal memory). The authors found that the alpha laterality score computed for each of the LH and RH tasks did not reflect the predominance of right-hemisphere activity. Thus, the hypothesis that highly hypnotizable subjects would show greater laterality differences than *lows* on those tasks which favor their natural predisposition (i.e., RH tasks) was not confirmed. Interestingly, it was with the analytic or LH tasks that a significant relation was found between hypnotizability and lateralized alpha activity. These findings suggest that low hypnotizable people processed analytic information more asymmetrically than high hypnotizable people, and directly contradict the earlier findings of no laterality differences between high and low hypnotizable persons on analytic LH tasks. MacLeod-Morgan [71,72] failed to provide any cogent explanation for her findings. According to Perlini and Spanos [73], the findings regarding alpha rhythm may be difficult to interpret because MacLeod-Morgan’s sample was heterogeneous, as it included hypnosis-practitioners and naïve subjects, and their laterality index was questionable. In fact, it did not provide reliable, similar alpha laterality values on each of the three LH and RH tasks. Subsequently, De Pascalis and Palumbo [74] conducted an exact replication with 40 naïve-volunteers of the Macleod-Morgan and Lack study [72], but the findings obtained by these authors were the opposite to those reported in the referenced study. During the difficult tasks, in fact, *highs* and *lows* produced similar alpha laterality ratios, whereas in minimally demanding tasks *highs* showed a drop in negative alpha ratio reflecting greater relative LH activation (i.e., more relative left-hemisphere alpha attenuation). Further, *lows* had relatively higher RH activation during easy tasks. It is difficult to reconcile the disparate findings of these two studies. Rather, these discrepant findings suggest that there is no compelling evidence for hypnotizability differences in performance on reliable task-related hemispheric asymmetries. Additionally, De Pascalis,

Silveri and Palumbo [75] investigated the relationship between alpha laterality and hypnotizability by employing covert mental activity tasks resembling natural thinking. Participants were required to perform covert verbal-numeric and imaginative-visual tasks, all under eyes-closed conditions. For imaginative-visual tasks (RH tasks) and a verbal task (LH task), there were no hypnotizability differences in alpha asymmetry; however, during a mental arithmetic task, *lows* produced a greater relative proportion of right-hemisphere alpha than highly hypnotizable individuals (i.e., LH activation). It is important to remark that this arithmetic task was the one considered by Macleod-Morgan and Lack [72] as attentionally demanding and hence one in which *highs* should lateralize more than *lows*. Rather, *lows* showed the shift in lateralization. In sum, findings from these studies suggest that the MacLeod-Morgan [70] and Macleod-Morgan and Lack [72] hypothesis of RH activation in *highs* did not hold to empirical testing. In addition, it is in contrast to the observation that the induction of hypnosis, necessary for the measure of hypnotizability, is obtained through verbal suggestion, and therefore requires the language-processing ability typically associated with the left hemisphere [54]. Therefore, the right-hemisphere hypothesis of hypnotizability and hypnosis has been abandoned.

3.2. Alpha Asymmetry, Hypnotizability and Cognitive Flexibility

Although attempts to replicate MacLeod-Morgan and Lack's findings have produced heterogeneous results; these author's findings led to the hypothesis that *highs* had a flexible cognitive style which allowed them to shift easily between analytic (LH) and holistic (RH) style of processing according to task requirement. This flexibility is amplified by the induction of hypnosis [10]. In her seminal review, Crawford [10] examined anterior versus posterior alpha hemispheric asymmetry during eyes-closed resting-baseline, imagery and arithmetic conditions in high and low hypnotizable people. Low hypnotizable persons showed a greater relative proportion of right-hemisphere alpha in the anterior regions. Additionally, during each of these three conditions, *highs* showed a greater relative proportion of right-hemisphere alpha in the posterior regions than *lows*. Crawford suggested that the posterior right-hemisphere differences reflect a differential preference for imaginative processing of *highs* versus *lows* and that the anterior right-hemisphere differences reflect a more focused attention (relative to global attention) strategy preferred by *lows* in comparison to *highs*. This conclusion is rather strange since, in all previous reports, hypnotizability differences in alpha activity at posterior scalp sites were explained in terms of the greater capacity of *highs* for focused attention than *lows* (for a critical analysis see [73]). Later, Crawford and Gruzelier [65] pointed out that the choice of slow alpha (7–10 Hz) or fast alpha bands (10–13 Hz) across studies may have affected hypnotizability versus hemispheric asymmetry findings since research has shown that slow and high alpha frequency bands are functionally different [76,77]. The slow alpha activity is related to relative cognitive inactivity or low alertness [6,78] and the fast alpha activity to mental workload (see e.g., [79,80]) and memory performance [81]. More recently, Gruzelier [8] substantially abandoned any explicit reference to hemispheric asymmetry versus analytic and holistic tasks and proposed that *highs* are skilled for tasks involving either analytic or holistic processing, and for tasks involving either focused/sustained attention or disattention and that this ability is better evidenced when they are hypnotized. He suggested that, more than changes in laterality, hypnosis involves the inhibition of frontal-lobe functioning, particularly affecting the prefrontal cortex. Support and extension to this hypothesis were provided in a later study from this group showing that hypnosis reduces conflict-related activity in the anterior cingulate cortex (ACC) during the performance of a Stroop task [53].

3.3. EEG Theta

According to Crawford and Gruzelier [65], the most consistent relationship between EEG activity and hypnotizability exists in the 4–8 Hz theta band and more recently this hypothesis has been confirmed [60,82]. The evidence shows that *highs* tend to evidence more baseline theta activity than *lows* [26,83–88], although there are also inconsistent findings [89,90], suggesting that this relationship is not 100% consistent across all samples and all hypnotic procedures. Galbraith and collaborators [85]

found the highest significant positive correlations between hypnotizability and EEG activity for the high-frequency theta band (5–7 Hz) in the eyes-open resting condition and was seen to reflect the ability of these subjects to focus attention on relevant stimuli and to shut off the irrelevant ones. However, research has devoted little attention to the relationship between theta hemispheric asymmetry and hypnotizability. Crawford, Clarke and Kitner-Triolo [25] reported that *highs* show a significantly greater activity in the right relative to the left hemisphere at parietal scalp region for the high theta, high alpha (11.5–13.45 Hz), and beta bands (16.5–25 Hz). Barabasz [91] reported that *highs*, but not *lows* generated more right-sided theta power just after a condition of restricted environmental stimulation. More recently, Lipari and coll. [92], using quantitative functional MRI and EEG neuroimaging changes (Low Resolution Brain Electromagnetic Tomography (sLORETA) method) in cortical activity during hypnosis induction and deep “pure hypnosis” in a hypnotic “virtuoso” subject, reported a reduced activity within a low theta and alpha band (4.5–10.5 Hz) reduced over left Brodmann areas BA17 and 19 for an eyes-closed resting in waking condition versus a late hypnotic induction stage comparison. Considering that in other studies conducted outside of the hypnotic context, high-theta has been associated with a continuous concentration of attention and selective attention [93–96], we think that this finding is in line with those reported by Galbraith and coll. [85] and by Sabourin and coll. [26], suggestive of greater absorptive attention in high hypnotizable people on hypnotic induction sustained by the occipital right hemisphere activation during neutral hypnosis. However, some findings show a tendency for all individuals to respond to hypnotic inductions and suggestions with increases in theta activity in both hemispheres [26,82,97–99]. Among these the most reliable findings were reported by Ray and collaborators [96,97]. These authors compared the EEG activity during an initial baseline period: baselines preceding and following a standard hypnotic induction and during the induction. In terms of theta activity, they found that *highs*, compared to the *lows*, had greater theta power in the more frontal areas of the cortex. Additionally, in the period preceding and following a standardized hypnotic induction, *lows* displayed an increase in theta activity, whereas *highs* displayed a decrease.

Considering that in these studies significant theta effects were also seen in low susceptibles from the pre- to post-hypnosis baseline, in agreement with Graffin, Ray and Lundy [97], we think that theta may also be related to some other factor such as relaxation and not hypnosis per se. More recently, Jamieson and Burgess [100] measured functional connectivity across conventional EEG bands during pre-hypnosis and hypnosis eyes-closed conditions. They found a relative increase in theta (4–7.9 Hz) coherence during hypnosis conditions in *highs* but not *lows* with a large proportion of significant links being focused on a central-parietal hub. Interestingly, this study seems to support the hypothesis of enhanced inter-hemispheric theta symmetry during hypnosis rather than the prevalence of hemispheric asymmetry in functional theta connectivity in high hypnotizable participants.

According to Jensen and collaborators [101], the EEG theta activity has yielded the more consistent findings between hypnotizability or hypnotic responding and theta band measures of structural connectivity, hemisphere asymmetry, and theta power. These findings are consistent with the possibility that, on the whole, they may reflect factors facilitating the response to hypnotic suggestions. This conclusion is derived from findings about hypnotizability/hypnosis and EEG oscillation measures showing that (i) *highs* display a rather robust trend of higher theta activity compared to *lows* and this effect has been proved to be the strongest one; (ii) with the exception of the theta band, studies have shown directions of changes different between *highs* and *lows* (i.e., increases in *highs* and decreases in *lows*, or vice-versa), and (iii) these changes with respect to basal conditions are greater in *highs* than in *lows*. This view is in line with previous findings disclosing differences between *highs* and *lows* in the brain areas (sLORETA) associated with theta and beta activity [102], and in subjects’ phenomenological experience of hypnosis and the associated frequency activity patterns [102].

3.4. EEG Beta and Gamma

Considering the hypothesized capacity of high hypnotizable people to focus attention out and within the hypnosis condition, it is surprising that little research has been devoted to the study of the

relationship between EEG-beta asymmetry and hypnotizability in waking and hypnosis conditions. This may be due to the fact that both beta and gamma activities measured from the scalp are more prone to noise contamination from extracranial sources such as myogenic (muscle) activity and electrical background noise. The scalp EEG measures of faster wave frequencies are therefore less reliable than measures of slower wave frequencies. This may have produced less reliable findings of correlates of beta and gamma activity in EEG research, making tests of hypotheses related to these frequencies challenging and, thus, evoking less consideration for these fast-frequency oscillations.

De Pascalis and Imperiali [89] found no relationships between beta and hypnotizability at temporal and parietal derivations, bipolarly referenced to central vertex during eyes-open and eyes-closed waking rest. About 10 years earlier, Akpinar, Ulett and Itil [102,103] and Ulett and colleagues [103–105] showed that high hypnotizable subjects had greater beta EEG activity at the right occipital recording site during a resting non-hypnotic condition. Additionally, Sabourin and collaborators [26] found hemispheric asymmetry in the beta band (13–28 Hz) for high hypnotizable participants. In particular, *highs*, in the eyes-open rest condition but not in the eyes open condition, had substantially more mean beta power in the left hemisphere across frontal, central and occipital locations than did *lows*, while they did not differ significantly in the right hemisphere. In contrast, *lows* did not show significant differences in beta power between hemispheres. These findings are supportive of the hypothesis of higher focused arousal involving the left-hemisphere activation, expressed in beta hemispheric asymmetry across the entire scalp in high hypnotizable individuals. Recently, Fingelkurts and coll. [106], in a single case study of a virtuoso subject, found an enhanced left- rather than right-hemisphere activity at the frontal pole (Fp1 versus Fp2 scalp sites) for the low-frequency beta (18.5–21 Hz) during hypnosis as compared to non-hypnosis and baseline conditions. A number of further studies have been based on the assumption that neural synchrony in humans reflects the phenomenal unity of consciousness [107] that implies a lower functional neural connectivity in *highs* as compared with *lows* to spontaneous phenomenological changes during hypnosis.

Following this perspective, White and colleagues [108] employed a virtual reality hypnotic induction and found that *highs* had decreased connectivity in the beta band (13–30 Hz) between medial frontal and left prefrontal sites, whereas *lows* exhibited the opposite pattern. Finally, Isotani and coll. [102] found that, before hypnotic induction, *highs* show higher dimensional complexity (higher arousal) than *lows* at baseline. Additionally, *highs* and *lows* were in different brain electric states, with beta-1 (12.5–18 Hz) and beta-2 (18.5–21 Hz) activities both more posterior and rightsided for *highs* than for *lows*.

More recently, Jamieson and Burgess [100] found a decrease in low-frequency (13–19.9 Hz) beta connectivity from a pre-hypnosis to hypnosis condition with a focus on a frontocentral and an occipital hub that was greater in high compared to low hypnotizable subjects. These authors interpreted their findings as indicating that the hypnotic induction elicited a qualitative change in the organization of specific control systems within the brain for high as compared to low susceptible participants and suggest this qualitative change as a potential indicator of the originally theorized hypnotic-state.

A high-frequency EEG activity centered at 40-Hz (36–44 Hz) has been found to co-vary with focused arousal, a functional component of the multi-dimensional attentional process [109–114]. Focused arousal, its brain circuitry, and direct electrical measurement procedure, and its relationship with an EEG activity within a 36–44 Hz frequency band, centering at 40-Hz has been described by Sheer [115,116]. This EEG activity is part of a currently labeled “gamma” band that is usually divided into two sub-bands, one narrow low gamma (30–80 Hz), including the classic labeled ‘40-Hz EEG’, and a broad high gamma band (80–200 Hz). Task-specific increased gamma activities have been observed in a number of recent studies, suggesting a functional role of gamma oscillations in humans (e.g., [117,118]). However, because of regional differences in the brain across tasks, and even inconsistencies in the frequency bands involved, the functional role of gamma oscillations is still not known [119]. Yet, gamma activity has been shown associated with brain activation and functional

magnetic resonance imaging (fMRI) both in primary sensory-motor cortices and in the associative cortex, see review by [120].

Original studies linking hemispheric asymmetry and hypnotizability were conducted by De Pascalis and colleagues. In their first study, they evaluated the relationship between hypnotizability and hemispheric asymmetry during the recollection, in a waking state, of three positively and three negatively valenced personal life events [121]. These authors found a significantly lower time density of 40-Hz EEG production (second per minute of 40-Hz activity production) in *highs* than *lows* in a few waking conditions. In addition, *highs*, but not *lows*, exhibited increased density over both left and right hemispheres during two of three positive emotional tasks, while they showed a depressed activity over the left and an increased activity over the right hemisphere during negative emotional tasks. Thus, in comparison with *lows*, the *highs* showed greater absorptive ability in recollecting emotional events and emotional feelings and this ability was also paralleled by more consistent task-related 40-Hz EEG hemispheric shifts. The greater hemispheric specificity of high hypnotizable participants was later confirmed in hypnosis condition wherein *highs* accessed affects more easily than *lows* [24]. In another study [122] De Pascalis and colleagues examined the changes in 40-Hz EEG production in *highs* and *lows* during the hypnotic induction and during hypnotic susceptibility testing (12-items) of the Stanford Hypnotic susceptibility Scale (Form C). With respect to resting period, *highs* showed increased time density of 40-Hz EEG activity over both hemispheres in the early hypnotic induction, and showed decreased activity in the left and an increased activity in the right hemisphere in the late hypnotic induction. A reduction of 40-Hz EEG time density in both hemispheres characterized the *lows*. These differences in hemispheric asymmetry between hypnotizability groups were confirmed by a later study [123] examining the spectral amplitude changes across conventional EEG frequency bands and 40-Hz band (36–44 Hz) in high and low hypnotizable participants during the hypnotic induction and the hypnotic dream and age-regression tests of the Stanford Hypnotic Clinical Scale (SHCS). In eyes-open and -closed conditions, in waking and hypnosis, *highs* produced a greater 40-Hz EEG spectral amplitude than *lows* across frontal, central and posterior scalp sites. In the early and middle hypnotic induction *highs* displayed a greater amount of beta3 (20–36 Hz) than *lows* and this difference was even more pronounced in the left hemisphere. *Highs*, during the hypnotic dream, also displayed in the right hemisphere a greater 40-Hz EEG amplitude relative to the left hemisphere. This difference was even more evident for posterior recording sites. These results appear to be in agreement with Gruzelier's [36] view of the hypnotic condition, where the inhibition of the initially dominant left hemisphere activity and the release of right-hemisphere processes characterize the hypnotic condition. Using an electrophysiological measure of phase synchrony, Terhune, Cardeña and Lindgren [124] examined frontal-parietal EEG functional connectivity in *highs* and *lows* in control and hypnosis conditions. *Highs* reliably displayed lower frontal-parietal alpha2 (10.5–12 Hz) synchronization in the left hemisphere during hypnosis than *lows*, but the two groups did not differ in the control conditions. The authors interpreted these results as suggesting that *highs* have a more labile left-sided frontal-parietal network than *lows* and are thereby more responsive to hypnotic inductions and related procedures. In another study Cardeña and coll. [125] focused on the neurophysiological correlates of hypnosis itself, i.e., in the absence of explicit suggestions, also referred to as 'neutral' hypnosis wherein participants usually report spontaneous alterations in various aspects of consciousness. These authors adopted a neuro-phenomenological approach consisting on analyzing participants' (*highs*, *mediums*, *lows*) reports of perceived depth and spontaneous experience during rest following a hypnotic induction. Multiple rest periods of perceived hypnotic depth were analyzed and related to EEG frequency band power and global functional connectivity. Perceived depth increased substantially after the induction especially among *highs* and then *mediums*, but remained almost unchanged among *lows*. In the sample as a whole, depth correlated moderately to strongly with power and/or topographic heterogeneity in EEG power (measured using the Global Field Power (GFP) curve) for the fast EEG frequencies of beta2 (18.5–21.0 Hz), beta3 (21.5–30 Hz), and gamma (35–44 Hz). Although this study was designed assuming our brain as a single symmetrical rather than an asymmetrical entity, it provides a valid

demonstration of how the experiential and overall-EEG data time-series analyses provide new data in terms of spontaneous temporal state fluctuations that occur in neutral hypnosis over time and across hypnotizability levels.

Using Low Resolution Brain Electromagnetic Tomography (sLORETA) method, Cardeña and colleagues [126] evaluated hypnosis depth reports and EEG activity in *highs*, *mediums* and *lows* during both voluntary and hypnotically induced left-arm lifting. In this study hypnotizability did not disclose a significant effect on EEG activity, but hypnotic depth correlated with left hemisphere increased anterior slow EEG and decreased central fast EEG activity. These authors also found that the hypnotic condition was associated with stronger activity in fast EEG frequencies (i.e., beta2: 18.5–21.0 Hz, beta3: 21.5–30 Hz, and gamma: 35–44 Hz) in left-anterior regions and slow EEG frequencies in left-centroparietal regions. On the whole, the hypnotic condition excitation was more anterior, the inhibition more posterior, and the opposite was found in the voluntary condition, and these anterior-posterior differences reached significance only among *mediums* and *highs*.

In sum, the above-mentioned findings support the importance of anterior-posterior differences in brain activity in hypnosis [97,127]. However, according to Jensen and colleagues [82], the relationship between gamma activity (as measured by scalp EEG) and hypnotizability/hypnosis is inconsistent across studies. These authors suggest that the relative unreliability of faster oscillations EEG activities measured from the scalp is due to contamination from the electric myogenic activity and background electrical noise. In addition, it has been postulated that when EEG theta oscillatory activity is present, it could inhibit recipient downstream neuron assemblies so that mostly phase-locked gamma frequencies occur [128]. In this way, slower frequencies such as hippocampal theta and/or theta from other structures such as basal ganglia might modulate the firing of faster cortical gamma frequencies [128–131]. Although some research in humans suggests that theta-gamma coupling might occur and be related to attention and memory functions, it is not entirely clear whether theta-gamma coupling always happens and whether both the phase and amplitude of gamma co-vary with the phase and amplitude of theta. If research will provide further support to the above-mentioned theta-gamma mechanism, this may also help explain the findings regarding the links between theta and gamma power, hemispheric gamma asymmetry and hypnotic responding (see review by [82]).

3.5. Nonlinear Dynamical Analysis of the EEG

Nonlinear dynamics or chaos has been applied to a variety of physiological processes, including EEG in hypnosis, but the implications and understanding of dimensionality are yet to be fully articulated. In contrast to the traditional techniques that decompose the component frequencies in the EEG and thus reflect one-dimensional information, nonlinear dynamic techniques, popularly known as “chaos,” suggest that a time series may be analyzed to reflect all other variables participating in the dynamics of the system. This approach can give important insight into the interpretation of EEG dynamics of a variety of cognitive-emotional processes including hypnosis [132,133].

Baghdadi and Nasrabadi analyzed the EEG during the hypnotic induction of the Waterloo-Stanford Group Scale (WSGS) to extract different features consisting mainly of fractal analysis and phase coherence and time-amplitude spectrum measures [134]. These different features were found to be a good index on the hypnotizability level. In particular, the feature based on the linear combination of the scaling exponent in theta band in channel C4 (right central site) was related to the hypnotizability level more than the other frequency bands. At the end of hypnotic induction scaling exponents decreased in all groups. In a later study, Yargholi and Nasrabadi used the recurrence quantification (RQ) analysis of the EEG recording data of the above-mentioned study obtained during the 12 suggestibility tests of the WSGS and showed that left hemisphere recordings were more efficient in distinguishing subjects with different hypnotic susceptibility than those of the right hemisphere [135].

4. Neuroimaging

Crawford and her colleagues [136] conducted a pioneering neuroimaging study measuring regional cerebral blood flow (rCBF) with the 133-xenon inhalation method, while *highs* and *lows*, in waking and after hypnotic inductions, experienced ischemic pain to both arms under two conditions: attend to pain and suggested analgesia. They found that *highs*, but not *lows*, showed a significant increase in overall CBF, suggesting that hypnosis requires cognitive effort. Mainly, these authors observed during hypnotic analgesia a highly-significant bilateral CBF activation of the orbito-frontal cortex and CBF increase over the somatosensory in *highs* while low-hypnotizable persons showed decreases. Later studies using positron-emission tomography (PET) and statistical parametric mapping disclosed extensive distribution of activation amid both cerebral hemispheres and showed that right hemisphere injured patients exhibit normal hypnotic responsiveness [137,138]. Another original PET study by Szechtman and collaborators [139] employed PET to study positive auditory hallucinations under hypnosis in *highs* compared to *lows*. Activation in the right ACC i.e., Brodman's area 32, was greater in hearing and hallucinating than in imagining or baseline in a group of *highs* under hypnosis when they heard an auditory stimulus and when they hallucinated hearing it, but not when they simply imagined hearing it. The same tasks did not yield this activation in the group of *lows* who were not able to hallucinate the auditory stimulus.

More recent functional magnetic resonance imaging (fMRI) findings disclosed asymmetries in grey matter volumes (GMV) and functional connectivity in *highs*. In particular, fMRI studies described larger GMV in the left superior and medial frontal gyri, middle occipital cortex, superior temporal gyrus and insula, right inferior parietal lobule [140], smaller GMV in the left superior temporal gyrus and posterior insula [141], in the right inferior temporal gyrus and in the left cerebellar lobules IV-VI [18]. An anteroposterior gradient was observed for the *corpus callosum* [142].

In resting conditions asymmetric activations were observed in the left inferior temporal gyrus, postcentral gyrus, left superior frontal and medial gyrus, precentral and inferior occipital gyrus [143]. In the comparison between hypnotic state and non-hypnotic rest, anterior-posterior asymmetries appear, as *highs* decrease brain activity in the anterior parts of the default mode circuit, whereas *lows* deactivate areas involved in alertness [144]. In addition, higher functional connectivity was observed in *highs* than in *lows* between the Dorsal Anterior Cingulate Cortex (DACC) and the left dorsolateral prefrontal cortex (DLPFC) and anterior insula [145] as well as between the posterior cingulate cortex/precuneus and the left frontoparietal network including the dorsolateral prefrontal cortex (DLPFC), whereas lower functional connectivity was found between the right frontoparietal network and the right lateral thalamus/caudate [141].

Hypnotic induction modulates the described patterns of activation, although the different types of induction and the suggestions eventually administered beyond that of relaxation make the comparison between the reported findings very difficult. In the hypnotic condition [143] observed a reduced number of left activations with respect to wakefulness.

In this research line, De Pascalis and Scacchia (2016) conducted an ischemic pain study during waking and hypnosis conditions using LORETA analysis of the event-related potentials (ERPs) elicited by binaural auditory startle stimuli. This study aimed to identify cortical regions sensitive to temporal processing of pain reduction through placebo (analgesic cream) in waking and hypnosis on cold pain relief in the right-hand. Differences in cortical regional activity between waking and hypnosis placebo were found in an early processing stage (about 110 ms from auditory tone onset). That is, placebo in waking conditions showed an earlier inhibition in the right temporal lobe (or relative higher activation in the left temporal lobe), while the hypnotic placebo showed such an inhibition in both left and right frontal and ACC regions. Besides, in a late processing stage (about 175 ms from auditory tone onset) common to both waking placebo and hypnotic placebo analgesia was the enhanced activity in the ACC. These results in the whole were seen as indicating that placebo analgesia modulated pain-responsive areas known to reflect the ongoing pain experience.

Thus, generally speaking, we may assume that neuroimaging findings are in line with the results of EEG studies as they indicate major left activations and greater functional connectivity for the *highs*' left hemisphere during wakefulness, but not in the hypnotic condition [54].

Cojan, Piguet and Vuilleumier [146] used the fMRI to investigate the recruitment of attentional networks during a modified flanker task in *highs* and *lows* in a normal waking state. They demonstrated that the right inferior frontal gyrus (IFG) was more recruited in *highs* during selective attention conditions, suggesting better control of conflict in these individuals. In addition, this region was more connected with activity in ventromedial prefrontal cortex (PFC) and precuneus (which are involved in the default mode network, DMN) in *highs*, suggesting a tight dialogue between internally and externally driven processes that may permit higher flexibility in attention and underlie a greater ability of *highs* to dissociate. In contrast, low hypnotizable subjects recruited more parietal cortex and anterior cingulate regions during selective attention conditions (which are involved in the salience network), suggesting a better detection and implementation of conflict. This study demonstrated that the greater ability displayed by the *highs* in focalizing attention, while simultaneously engaging more introspective self-monitoring processes, may be a consequence of the enhanced modulation of connectivity between the selective attention and default-mode networks. Thus, this was one of the first neuroimaging studies to provide a shred of clear experimental evidence in support of Hilgard's neo-dissociative theory accounting for hypnotic susceptibility and hypnotic phenomena [147] by suggesting a new neuroimaging evidence of the subjective experience of dissociation that characterizes the subjective experience during hypnosis. In a later study, [148] used fMRI to investigate activity and functional connectivity among the Default Mode Network (DMN), the executive control network (ECN), and the salience network (SN) during hypnosis for four conditions (rest, memory retrieval, and two different hypnosis experiences). In terms of brain asymmetry findings, these authors found a clear reduced connectivity between ECN (left DLPFC) and the DMN (i.e., PCC) in *highs* alone during hypnosis. These DMN regions are involved in self-referential processing and episodic memory [149], while the ECN is involved in cognitive control [150], and the two networks become anti-correlated during working memory tasks [151]. This finding is contrary to observations previously reported by McGeown and coll. [127]. Dissociation between ECN and DMN in response to hypnotic induction is likely to reflect the engagement in the hypnotic state and the associated detachment from internal mental processes such as mind-wandering and self-reflection. According to Jang and colleagues [148], their findings strongly support the hypothesis of hypnosis as a different state of consciousness, rather than a reduced level of arousal. Interestingly, this finding is related to the previous and more recent report by McGeown and coll. [140] wherein self-reported deeper levels of hypnosis were associated with decreased functional connectivity within the anterior DMN, also suggesting reduced awareness. Hypnotic depth ratings were positively correlated with GMV in the frontal cortex and the ACC, and hypnotic suggestibility was positively correlated with GMV in the left temporal-occipital cortex. Both the observations of greater GMV volume in the medial frontal cortex and ACC, and lower connectivity in the DMN during hypnosis were interpreted by these authors as findings indicating the individual proneness to experience a greater hypnotic depth. Significantly, these patterns of results suggest that hypnotic depth and hypnotic suggestibility should not be considered as synonyms.

5. Conclusions

In terms of the relationship between hemispheric asymmetry and hypnotic susceptibility, the earliest EEG studies did not provide consistent information in that, in the ordinary state of consciousness, few authors reported the prevalence of left-hemisphere activation (i.e., higher alpha activity in the right relative to the left hemisphere) in *highs* and this effect was not confirmed by other reports [98]. Consistently, De Pascalis [123] at the very beginning of hypnotic induction showed a greater amount of left-hemisphere beta3 amplitude (20–36 Hz) in *highs* than in *lows*, whereas other studies reported an anteroposterior gradient for theta [26,97] and gamma activity [152] as a function of hypnotizability. Additionally, review studies [54] have indicated no difference in hypnotizability

between individuals with left versus right hemisphere lesions. Moreover, even though some above mentioned studies have reported a greater right hemisphere activity positively associated with hypnotizability, other studies have found a greater left hemisphere activity associated with higher hypnotizability [26] and other reports did not describe any difference between the right and left hemisphere activity [70,97]. Thus, the right-hemisphere activation hypothesis of hypnotizability and hypnosis was bound to fail. On the whole, research findings seem to be more consistent with a model of hypnosis hypothesizing, for highly hypnotizable individuals, more effective and flexible frontoparietal systems for both attention and inhibition rather than a general tendency to simply shift from left to right hemisphere processing with hypnosis [10]. In addition, from a dissociated control perspective, Woody and colleagues suggest that hypnotized subjects are similar to patients with lesions in the prefrontal cortex, whereas Gruzelier model views hypnosis as a consequence of the activation of anterior frontal-inhibitory processes involving the left hemisphere inhibition. Therefore, as suggested by Kihlstrom [60], we have three good reasons for thinking that investigations of the role of the frontal lobes and their functional relationship with the posterior regions in terms of individual differences on hypnotizability and hypnosis will be more productive than studies devoted to testing the sole right hemisphere activation hypothesis.

Brain morphofunctional asymmetries are present in *highs* in the ordinary state of consciousness and the functional features are modified by hypnotic induction. This is relevant to the definition of hypnosis as a mental state of reduced connectivity between left DLPFC and PCC [149] despite the absence of a discriminant index. Many questions, however, remain without an answer. For instance, is the left cerebellar reduced GMV sufficient to account for the *highs'* postural, locomotor and visuomotor less strict control [19]. Are the asymmetric morphofunctional difference in limbic structures involved in the *highs'* greater interoceptive sensibility and different interactions between interoception and emotion [42]. Is the functional connectivity between the precuneus and the left fronto-parietal [17] uniquely involved in the *highs'* ability to easily change their state of consciousness and bodily condition? In addition, most of the reported studies did not enroll *mediums*, who represent the large majority of the population, and this reduces their impact by preventing a reliable interpretation of findings. Finally, the most interesting and fascinating aspect of hypnotic phenomenology is the *highs'* greater proneness to respond to suggestions. In this respect, it is unlikely that, beyond attentional aspects [60,101], brain morphofunctional asymmetry may play a role. For instance, it has been shown for sensorimotor suggestions that *highs* display a largely distributed, bilateral mode of information processing for both the sensory and cognitive tasks [21,153], and suggestions displaying deeper relational aspects could be sustained by hormonal factors not easily referable to lateralized mechanisms [16].

The strength of the present review is its psychophysiological perspective, which has taken into account both behavioral and neurophysiological findings and the observation that, although a few experimental findings may support both neo-dissociative and socio-cognitive theories of hypnosis, the latter are the most appropriate to account for current experimental evidence. A weakness of the study consists of the heterogeneity in the methodology of the reported studies, which sometimes prevented a direct comparison between findings. In addition, not all the reported studies were conducted according to recent recommendations [153], thus disentangling the role of hypnotizability, hypnotic state and suggestions may have been difficult and may have limited the relevance of the reported findings.

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