entailed in developing more complex and sophisticated experimental tasks that need to be specially tailored to hysterical symptoms.

Such challenges notwithstanding, the potential role of emotions in the formation and maintenance of hysterical symptoms appears to be a topic of increasing interest in the current hysteria research. It is, therefore, safe to assume that the development towards designing more complex and symptom-specific fMRI studies will continue in the near future. Yet, one thing with which, in my opinion, future studies will have to deal with more systematically is clarifying if the distinct experimental interventions they are deploying are capable of inducing sufficiently clear-cut and controllable emotional and affective responses. To achieve this goal, however, researchers will perhaps first need to more clearly delineate the concepts of 'emotion' and 'affect' with which they operate. As highlighted by my analysis, these two concepts have so far remained vaguely defined in fMRI-based hysteria research. Sometimes they are used interchangeably as mere synonyms,[552] whereas at other times, their deployment implies mutually opposing theoretical frameworks. Such conceptual inconsistencies lead to the production of results that are difficult to compare across studies and impossible to unify into an overarching interpretation regarding hysteria patients' potential deficit in emotion processing. It appears to me that as long as such conceptual inconsistencies remain unaddressed, they will continue to impede future research.

4.4 Identifying Symptom-Related Alterations in the Intrinsic Dynamic Organisation of Hysteria Patients' Brains

Apart from the emotion processing analysed in the section above, two other action-guiding concepts have attained increasing epistemic importance in the fMRI hysteria research in the second decade of the twenty-first century. These two concepts are resting-state functional connectivity and functional neuroplasticity.[553] Both concepts

researchers did not use affective visual stimuli but instead chose to investigate how patients with non-epileptic seizures "respond to acute emotional and psychological stress." Allendorfer et al., "Psychological Stress," 2, article 101967. To experimentally induce acute emotional stress in their study participants, the researchers used negative verbal feedback. The participants were asked to perform a so-called 'stress math task' inside the scanner. Regardless of their actual math performance, during the task, the participants were exposed to pre-recorded auditory feedback repeatedly telling them that they were too slow and thus failing the task. Allendorfer et al., 3, article 101967. Finally, an additional study worth mentioning is Luo et al., "Pain Processing." In this fMRI study, published in 2016, the researchers examined "the association between emotion and pain-related brain activities" in patients with chronic somatoform pain disorder. Luo et al., 969. To do so, Luo et al. scanned their patients' brain activity while exposing them to painful pinprick stimuli and simultaneously asking them to view a series of pleasant, unpleasant and neutral pictures from the IAPS. In short, Luo et al. investigated how changing affective context modulates the patients' perception of pain at the neural level.

552 See, e.g., Aybek et al., "Emotion-Motion Interactions," 3–4, e0123273.

553 See, e.g., Diez et al., "Fast-Tracking"; LaFaver et al., "Before and After"; Otti et al., "Chronic Pain"; Wegrzyk et al., "Functional Connectivity"; Wei et al., "Default-Mode Network"; and Roy et al., "Dysphonia."

were developed in cognitive neuroscience to designate two different kinds of intrinsic dynamic properties of the human brain. In the following two sections, I will argue that fMRI research on hysteria has significantly broadened its epistemic scope by adopting these two concepts. Instead of being limited to mapping spatial aspects of patients' underlying brain dysfunctions, hysteria researchers are now paying increasing attention to the aberrant temporal dynamics in the patients' brain activity.

The concept of resting-state functional connectivity is rooted in the fMRI-based discovery made in 1995. Biswal et al. established that even when subjects are at 'rest'—i.e., not exposed to external stimuli or asked to perform a task—their brains exhibit spontaneous BOLD signal fluctuations that appear to be synchronised across multiple neuroanatomical regions.[554] Put differently, low-frequency changes of the BOLD signal acquired at rest, which had previously been discarded as noise, turned out to contain salient information about the intrinsic activity of the human brain. Subsequent neuroimaging studies have shown that the brain's intrinsic activity is organised into what is referred to as resting-state connectivity networks. Such resting-state networks comprise sets of widespread anatomical regions that exhibit patterns of temporally coherent spontaneous BOLD fluctuations.[555]

These findings have given rise to a new strand of neuroimaging research that has moved beyond the task-based approach. This new research focuses instead on investigating the network structure of the brain's intrinsic activity during the resting state.[556] Significantly, the concept of resting-state functional connectivity has not only been used to characterise patterns of intrinsic synchronous activity across multiple brain areas in healthy individuals. The same concept has also been used to analyse how the patterns of the brain's intrinsic synchronous activity are altered in patients with various neurological and psychiatric diseases.[557] This second approach has recently also found application in fMRI hysteria research.[558]

An equally dynamic view of the brain's intrinsic properties is embodied in the concept of neuroplasticity. One crucial difference between the concepts of resting-state connectivity and neuroplasticity pertains to their mutually distinct underlying temporal perspectives. Contrary to resting-state connectivity, the temporal perspective that informs the concept of neuroplasticity is not synchronous but instead decidedly diachronic. Generally speaking, neuroplasticity refers to the inherent ability of the brain to keep reorganising itself throughout the subject's life span. This reorganisation happens in response to changing experiences, such as "maturation, adaptation to a mutable environment, specific and unspecific kinds of learning, and compensatory adjustments in response to functional losses from aging or brain damage."[559]

554 See Biswal et al., "Functional Connectivity."

555 See, e.g., Smith et al., "Functional Architecture," 13040–45.

556 For a historical overview of the resting-state fMRI research, see, e.g., Snyder and Raichle, "History of the Resting State."

557 See, e.g., Greicius et al., "Alzheimer's Disease."

558 See, e.g., Diez et al., "Fast-Tracking"; Ding et al., "Connectivity Networks"; Li et al., "Insular Subregions"; and van der Kruijs et al., "Resting-State Networks."

559 Berlucchi and Buchtel, "Neuronal Plasticity," 307.

An admittedly broad concept, neuroplasticity can encompass a wide spectrum of brain modifications. On the one hand, neuroplastic reorganisation can affect various structural properties of the brain, thus resulting in molecular and cellular alterations of white and grey matter. On the other hand, neuroplastic changes can occur at any level of the brain's functional organisation, producing modulations in functional connectivity or activation patterns.[560] By implicitly relying on the concept of functional neuroplasticity, multiple recent fMRI studies have attempted to link hysteria patients' externally observable clinical improvements to distinct changes in the patterns of their brain activity and connectivity.[561]

In the following two sections, I will trace how, in the second decade of the twenty-first century, authors of multiple fMRI studies deployed the action-guiding concepts of resting-state functional connectivity and functional neuroplasticity to investigate the neural basis of diverse hysterical symptoms.[562] These two strands of fMRI hysteria

560 For detailed accounts, see von Bernhardi, von Bernhardi, and Eugenín, "Neural Plasticity"; and Sharma, Classen, and Cohen, "Neural Plasticity."

561 See, e.g., Bryant and Das, "Neural Circuitry"; Dogonowski et al., "Recovery"; Espay et al., "Neural Responses"; LaFaver et al., "Before and After"; and Yoshino et al., "Therapy." Admittedly, most of these fMRI studies did not explicitly invoke the concept of functional neuroplasticity. Yet, it is evident that they were informed by this concept since all these studies examined how the patterns of hysteria patients' brain activity and connectivity changed as a direct consequence of a targeted therapeutic intervention.

562 Notably, the related concepts of structural connectivity (i.e., the existence of white matter tracts that physically connect various brain regions), as well as structural neuroplasticity (the brain's ability to alter its physical structure in response to changing experience) have also begun to play an increasing role in a strand of neuroimaging research on hysteria that has emerged in the 2010s. This new strand of structural neuroimaging research runs parallel to fMRI studies and focuses on identifying microscopic anatomical alterations in the hysteria patients' brains. These include aberrant structural connectivity patterns, as well as abnormal, purportedly stress-related neuroplastic changes in the regional grey matter volumes, surface areas, and cortical thickness of various neuroanatomical structures. For a succinct overview, see Bègue et al., "Structural Alterations." To make such potential microscopic abnormalities visible, researchers utilise state-of-the-art techniques of the so-called quantitative anatomical imaging. For example, to study structural connectivity, researchers have used a particular MRI technique called diffusion tensor imaging (DTI). For details, see, e.g., Lee et al., "White Matter." Conversely, to examine regional microscopic anatomical changes, researchers have collected standard structural T1-weighted images (see section 3.2.1) for patients, as well as healthy controls. They then submitted the resulting structural images to statistical analyses that entailed a computerised voxel-wise comparison of the datasets between patients and controls. For such purposes, researchers have typically used either voxel-based morphometry (VBM) or voxel-based cortical thickness (VBCT) analyses. For details, see Bègue et al., "Structural Alterations," 3–12, article 101798. The preliminary findings suggest that although, as stated repeatedly, hysteria patients' brains lack gross anatomical lesions, they nevertheless may exhibit microstructural abnormalities in multiple cerebral structures. In addition to the functional disturbances that are in the focus of the fMRI research, the patients' potential microstructural brain abnormalities might play a causal role in this disorder. However, the findings from structural neuroimaging studies have so far been highly inconsistent, ambiguous, and difficult to interpret. See Bègue et al., 14–15, article 101798. Even more to the point, what remains far from clear is the potential relation of the suggested microstructural abnormalities to the fMRI findings of functional disturbances in hysteria, which are at the centre of our enquiry. Hence, such structural neuroimaging studies are tangential to our

research are currently at an early stage and thus still unable to offer any definitive answers. Nevertheless, I will argue that the deployment of the concepts of resting-state connectivity and functional neuroplasticity has already contributed to the emergence of an increasingly complex picture of the potential neurophysiological disturbances underpinning hysteria. As my analysis will show, the primary contribution of these two action-guiding concepts has been to foreground the highly dynamic nature of the neural disturbances that are implicated in heterogeneous hysterical symptoms.

4.4.1 Characterising the Loss of Temporal Coherence in Hysteria Patients' Intrinsic Brain Activity

The first resting-state fMRI study of a hysterical symptom was published in 2011.[563] In it, van der Kruijs et al. aimed to delineate potential disturbances of functional brain connectivity in patients with psychogenic non-epileptic seizures, whose brain activity was measured while they were not engaged in any explicit task. Interestingly, this was also the first fMRI study to investigate the neural basis of this common yet, until that point, under-researched hysterical symptom, which Charcot called the hysterical attack.[564] By the end of the decade, more than thirty additional resting-state fMRI

discussion. Moreover, to examine the potential validity and epistemic implications of the structural neuroimaging findings for hysteria research, we would have to discuss the imaging techniques and statistical analyses such studies have employed, which is beyond the scope of this book.

563 The full study was published online on November 5, 2011. See van der Kruijs et al., "Dissociation in Patients." The summary of the findings was published in the form of conference proceedings a few months earlier. See van der Kruijs et al., "Executive Control."

564 For the current definition and epidemiology of psychogenic/functional non-epileptic seizures, see Reuber and Brown, "Understanding," 199; and Hubsch et al., "Clinical Classification," 955. It is interesting to note that reliable diagnostic differentiation between non-epileptic and epileptic seizures remains a major concern, as in Charcot's time. And similarly to Charcot's time, images, although of a different kind, facilitate such differential diagnosis in the present-day clinical context. Specifically, the current gold standard for differential diagnosis is video–electroencephalographic monitoring (vEEG). This test combines EEG recordings of the patient's brain activity with a simultaneous video recording of the seizure. The visual data obtained by EEG and video recordings are then jointly analysed to determine if the patient had an epileptic or a non-epileptic attack. In effect, "[p]attern recognition of events forms the cornerstone of interpreting video-EEG findings." Seneviratne, Reutens, and D'Souza, "Stereotypy," 1159. Aside from a particular pattern of the EEG rhythm that characterises the wakeful state, clinicians also pay particular attention to various semiological features of the seizures as captured by the video recording. The currently accepted differential clinical signs of non-epileptic seizures that inform the vEEG analysis include: "long duration, occurrence from apparent sleep with EEG-verified wakefulness, fluctuating course, asynchronous movements, pelvic thrusting, side-to-side head or body movement, closed eyes during the episode, ictal crying, memory recall and absence of postictal confusion." Reuber and Brown, "Understanding," 200. Moreover, based on the analysis of vEEG recordings of multiple patients, several present-day researchers have posited that the clinical manifestation of non-epileptic seizures "is stereotypical and can be objectively classified" for diagnostic purposes. Hubsch et al., "Clinical Classification," 959. The latter claim is curiously reminiscent of Charcot's approach to the hysterical attack. However, it should be emphasised that, unlike fMRI, vEEG cannot provide insights into the neural basis of non-epileptic seizures.

studies followed.[565] At first, most of the studies investigated non-epileptic seizures. But gradually, the scope of resting-state studies expanded to include the multisymptomatic form of hysteria (i.e., somatisation) and functional pain, two other manifestations of hysteria that had thus far only rarely been the topic of task-based fMRI research.[566] By the late 2010s, the resting-state fMRI research into hysteria also began to address various motor symptoms, which until then had been at the centre of task-based fMRI studies.[567]

At a closer look, this initial focus of resting-state studies on the under-researched hysterical symptoms appears almost self-explanatory. Compared to task-based studies, the process of fMRI data acquisition in the resting-state paradigm is considerably simpler and shorter. In the latter case, there is no need to design multi-component tasks whose potential adequacy hinges on the prior assumptions about the cognitive and neural processes associated with the symptom of interest.[568] Instead, in resting-state studies, researchers simply ask their subjects to lie passively in the scanner for about five to fifteen minutes. Typically, subjects are instructed to merely relax and let their minds wander without thinking about anything in particular.[569] Hence, by freeing researchers from having to design adequate experimental tasks, resting-state fMRI has opened up the possibility of studying particularly those manifestations of hysteria that had proven

565 See Dienstag et al., "Motor Control"; Diez et al., "Fast-Tracking"; Ding et al., "Connectivity Density"; Ding et al., "Connectivity Networks"; Guo et al., "Anatomical Distance"; Huang et al. "Spontaneous Activity"; Kim et al., "Functional Connectivity"; Li et al., "Causal Connectivity"; Li et al., "Insular Subregions"; Li et al., "Regional Activity"; Li et al., "Regional Brain Function"; Liu et al., "Functional Hubs"; Luo et al., "Pain Processing"; Maurer et al., "Impaired Self-Agency"; Monsa, Peer, and Arzy, "Self-Reference"; Otti et al., "Chronic Pain"; Otti et al., "Somatoform Pain"; Ou et al., "Nucleus Accumbens"; Ou et al., "Regional Homogeneity"; Pan et al., "Functional Connectivity"; Song et al., "Regional Homogeneity"; Stankewitz et al., "Fronto-Insular Connectivity"; Su et al., "Connectivity Strength"; Su et al., "Interhemispheric Connectivity"; Su et al., "Regional Activity"; Szaflarski et al., "Facial Emotion Processing"; van der Kruijs et al., "Resting-State Networks"; Wang et al., "Clinical Significance"; Wegrzyk et al., "Functional Connectivity"; Wei et al., "Default-Mode Network"; Yoshino et al., "Regional Neural Responses"; Yoshino et al., "Therapy"; and Zhao et al., "Functional Connectivity."

566 The defining characteristic of functional pain is the absence of detectable physical pathology. Consequently, the presence and intensity of functional pain are assessed solely based on the patients' self-reports. See, e.g., Otti et al., "Chronic Pain," 57, 61. The few task-based fMRI studies that predated the emergence of the resting-state research into this elusive symptom include Gündel et al., "Somatoform Pain"; Noll-Hussong et al., "Sexual Abuse"; and Stoeter et al., "Somatoform Pain." Moreover, as discussed in section 3.1.3, most task-based fMRI studies until the late 2010s focused on a single symptom or a single type of symptoms, thus neglecting the multisymptomatic forms of hysteria.

567 See Diez et al., "Fast-Tracking"; Maurer et al., "Impaired Self-Agency"; and Wegrzyk et al., "Functional Connectivity."

568 The challenges entailed in task design were discussed in section 3.1.1.

569 In some studies, the subjects were told to keep their eyes open. In other studies, the subjects were instructed to close their eyes but to avoid falling asleep. Compare, e.g., Otti et al., "Chronic Pain," 59; and Szaflarski et al., "Facial Emotion Processing," 195. See also Raichle, "Two Views," 181, box 1. However, according to recent research, even this apparently minimal difference between keeping the eyes open or closed might be of physiological importance and thus modulate the imaging result. See, e.g., Yuan et al., "Eyes Open."

difficult to address through the task-based approach.[570] These manifestations included messy hysterical attacks (i.e., non-epileptic seizures), elusive functional pain, as well as multisymptomatic forms of hysteria with their complex and highly variable mixture of concurrent somatic symptoms. Even patients with such difficult to control or elusive symptoms could lie motionless in the scanner for a few minutes while the spontaneous fluctuations in their brain activities were being measured.[571]

However, contrary to the simplicity with which resting-state fMRI data are acquired, the subsequent stages of data processing represent a major challenge for researchers. First, the preprocessing stage is considerably more elaborate as it entails additional steps that are not required in task-based studies.[572] Second, unlike the task-based approach that, as discussed previously, mainly utilises the general linear model, resting-state fMRI does not rely on a single analysis method. Instead, the same resting-state fMRI dataset can be analysed in a variety of ways, several of which we will address shortly.[573] Moreover, not only is there no consensus as to which of the available methods is the most adequate for the analysis of resting-state fMRI data but also new methods continue to be developed.[574] As I will show, choosing which method of analysis to apply to the data is the crucial interpretational decision researchers make in a resting-state study since each method approaches the concept of functional connectivity from a different perspective.[575]

For this reason, my discussion will only fleetingly address the often mutually inconsistent results that individual resting-state studies of hysterical symptoms have generated. Rather, I will focus on examining the epistemic implications of various analysis methods through which the authors of representative studies of hysterical symptoms have differently framed the concept of functional connectivity of the brain

---

570 Significantly, task-based and resting-state approaches are not mutually exclusive. As we will discuss shortly, these two approaches can be combined within the same study but necessitate the acquisition of two separate fMRI datasets, one using an experimental task and another without. See, e.g., Szaflarski et al., "Facial Emotion Processing"; and Baek et al., "Motor Intention."

571 Notably, there is one key limitation to resting-state fMRI investigation of patients with convulsive non-epileptic seizures. These patients can only be measured in the interictal state, i.e., the period between the actual seizures. Otherwise, their uncontrolled movements within the scanner would render the fMRI data uninterpretable or even lead to possible injuries. See Reuber and Brown, "Understanding," 201. Hence, resting-state fMRI studies cannot provide insights into the potential changes in the patients' brain activity during a convulsive non-epileptic seizure.

572 Since researchers look for patterns of synchronous activity in the spontaneous fluctuation of the BOLD signal, any form of systematic noise, including normal physiological processes such as breathing or heartbeat, can skew the results. In other words, systematic noise represents a much more insidious problem for the resting-state than for the task-based fMRI analysis. For a detailed overview of the preprocessing steps in the resting-state data analysis, see Bijsterbosch, Smith, and Beckmann, *Resting State*, 25–50.

573 For example, in each of the following four studies, the same resting-state fMRI dataset was submitted to four different analysis methods: Ding et al., "Connectivity Density"; Ding et al., "Connectivity Networks"; Li et al., "Insular Subregions"; and Li et al., "Regional Activity."

574 Poldrack, Mumford, and Nichols, *Handbook*, 130.

575 By contrast, in the previous chapter, I argued that in task-based studies, the initial interpretation decision already entails the choice of the experimental tasks and, therefore, takes place long before the data acquisition has even started. See section 3.1.1.

at rest. This section will examine four types of methods that have been deployed in the resting-state hysteria research during the 2010s. These include: first, seed-based functional connectivity; second, independent component analysis (ICA); third, multiple approaches to measuring regional signal characteristics; and, finally, different graph theory (node-based) analyses.[576]

In their pioneering resting-state fMRI study of a hysterical symptom, van der Kruijs et al. applied seed-based connectivity analysis to their fMRI dataset. Despite being the oldest resting-state analysis method, seed-based connectivity continues to be widely used even in more recent hysteria studies, probably due to its simplicity.[577] It is often referred to as a hypothesis-driven method. To perform this type of analysis, researchers first have to define an a priori region of interest, or in specialist terms, a seed. They do so by selecting a particular brain area and specifying its standard space coordinates, size, and shape.[578] As we will see shortly, the selection of the seed is typically grounded in some hypothesis about the potential functional relevance of the chosen region to the hysterical symptom being studied, hence the designation of seed-based analysis as a hypothesis-driven method. After researchers have chosen the seed, automated algorithms extract its BOLD signal time course and compare it to the time course from every other voxel in the brain in a voxel-by-voxel procedure. During this process, the algorithms compute the temporal correlation between the seed region and all the other voxels by quantifying the similarity in the spontaneous fluctuation of their signals over time. Various mathematical methods are available, each of which quantifies a different aspect of the temporal correlation between the seed region and the rest of the brain.[579]

The brain areas whose correlation coefficients exceed some a priori defined threshold are deemed to be functionally connected with the seed region. The brain areas thus identified are then visualised in the form of a spatial connectivity map that displays their anatomical locations. The assumption is that the resulting connectivity map shows

576 Resting-state analysis methods can be grouped in different ways, contingent on the chosen criteria of classification. For example, some authors differentiate between voxel- and node-based methods, depending on the smallest spatial unit each method uses. See Bijsterbosch, Smith, and Beckmann, *Resting State*, 51–107. As will become apparent by the end of the section, my classification foregrounds different approaches to defining functional connectivity that underpins each analysis method.

577 The seed-based analysis was used in the first resting-state fMRI study. See Biswal et al., "Functional Connectivity." Although my discussion here starts with the first resting-state fMRI study of hysteria, the rest of this section will not follow a chronological order. My departure from chronology is due to my focus on delineating the four different types of resting-state analyses I listed above. All these methods are used in parallel in the current hysteria research. Hence, analysing the individual resting-state studies in the chronological order of their publication would only muddle the differences among the four types of methods that informed these studies without bringing any additional insights.

578 Bijsterbosch, Smith, and Beckmann, *Resting State*, 54. Conceptually, resting-state seed-based analysis is similar to the PPI analysis. As discussed previously, the PPI analysis is used in task-based fMRI studies to assess how functional connectivity between a pre-defined seed region and the rest of the brain is modulated by some aspect of the experimental task. For details, see section 3.4.4.

579 For an overview of different mathematical methods, see Fiecas et al., "Temporal Correlations."

those brain areas that "are involved in the same underlying functional process" as the seed region, even if they are not "directly connected by neural fibers."[580] After obtaining connectivity maps for each subject separately, researchers then submit them to group-level analysis. Importantly, not only seed-based but also all resting-state fMRI studies in the context of fMRI hysteria research aim to isolate potentially abnormal patterns of functional connectivity associated with the hysterical symptom of interest. Therefore, in most studies, researchers typically produce maps that compare resting-state connectivity patterns between hysteria patients and healthy control subjects.[581] Those aspects of resting-state functional connectivity that differ between patients and healthy subjects are declared aberrant and attributed to the hysterical symptom under study.

As my description above demonstrates, the seed-based analysis identifies all brain regions whose spontaneous resting-state activity temporally correlates with the activity of the a priori defined seed region. Therefore, the critical decision in performing this analysis is which seed region to choose and how. In this respect, several resting-state fMRI studies of hysteria have taken different approaches. For example, in the initial resting-state study that focused on non-epileptic seizures, van der Kruijs et al. first asked their subjects—both patients and healthy controls—to perform two different tasks.[582] Van der Kruijs et al. chose to use the experiential tasks that specifically addressed the patients' clinical features of emotional suggestibility and a hypnosis-like tendency to dissociate.[583] Hence, the two tasks served to isolate the brain regions that, according to the researchers' a priori hypothesis, were implicated in the development of non-epileptic seizures. The fact that van der Kruijs et al. chose this approach meant that they had to acquire both task-based and resting-state fMRI datasets separately. Interestingly, the activation maps computed for the task-induced brain activations did not reveal any statistically significant differences between patients and controls.[584] Nevertheless, both tasks fulfilled their intended purpose since the researchers used the nine brain areas that showed the strongest task-induced activations in both patients and control as seed regions for the subsequent analysis of the resting-state fMRI dataset.[585] In short, the results of the task-based analysis provided the conceptual basis for the subsequent resting-state analysis by informing the selection of the seed regions.

580 Lv et al., "Nonexperts," 1393.

581 See, e.g., Otti et al., "Chronic Pain"; and van der Kruijs et al., "Dissociation in Patients."

582 Van der Kruijs et al. used a picture-encoding task and the Stroop task. In the picture-encoding task, the subjects were required to differentiate between familiar and novel images "with a high positive sentimental value." Van der Kruijs et al., "Dissociation in Patients," 241. In the Stroop task, a word stimulus was presented in green, blue, yellow or red on a black background. Subjects were instructed to think of the colour in which the word was displayed. For example, if the word 'blue' was written in red letters, the subject had to think 'red.' Ibid.

583 Echoing Janet's theories of hysteria, van der Kruijs et al. defined psychological dissociation as "a disruption of the integration of a person's conscious functioning by severing the connections to thoughts, memories, feelings and sense of identity." Moreover, in another parallel to Janet, they postulated that dissociation was "closely related to the process of hypnosis." Van der Kruijs et al., 239.

584 Van der Kruijs et al., 242.

585 Van der Kruijs et al., 242.

Contrary to the lack of differences in the task-based activation patterns, the seed-based analysis revealed widespread alterations in functional connectivity in patients relative to controls. In patients, van der Kruijs et al. identified "stronger connectivity values between areas involved in emotion (insula), executive control (inferior frontal gyrus and parietal cortex), and movement (precentral sulcus)."[586] The researchers conjectured that these aberrant patterns of increased connectivity pointed to a possible neural mechanism through which "emotion can bypass executive control and cause involuntary movement" in patients with non-epileptic seizures.[587] Although this conjecture referred to a different hysterical symptom and entailed a far more precise mapping of the implicated neuroanatomical regions and their pairwise functional connections, its basic tenet was curiously reminiscent of the mechanism Charcot had postulated as the neural basis of traumatic hysterical paralysis more than a century earlier.[588]

But before we proceed to analyse how other researchers chose to define seed regions in subsequent fMRI resting-state studies of hysteria, one other aspect of the van der Kruijs et al. study deserves our attention. For a while, the parallel acquisition of a task-based and a resting-state fMRI dataset, as performed by van der Kruijs et al., remained somewhat of an anomaly in hysteria research. Throughout the 2010s, the authors of most fMRI studies of hysteria opted to use either the task-based or the resting-state approach,[589] although, as we have seen, these two approaches are not mutually exclusive. Only a few more recent task-based fMRI studies of hysteria, some of which we analysed earlier (i.e., Baek et al., Morris et al., and Szaflarski et al.), have revived the strategy of acquiring both a task-based and a resting-state fMRI dataset.[590]

Similarly to van der Kruijs et al., in these recent studies, the anatomical regions with aberrant task-induced responses served as seeds for the subsequent seed-based analyses of the resting-state data. Contrary to van der Kruijs et al., the main focus of the recent studies was on their task-based findings, which were expanded through the inclusion of complementary seed-based resting-state results. I will not go into details of the resting-state findings concerning each of these studies. Yet, what matters to our discussions is the following. Through the combined use of the two approaches, the authors of the recent studies have, in each case, determined that the regions with an aberrant task-induced activation also tended to exhibit disturbed resting-state connectivity with other, anatomically distant areas of the brain.[591] In

586 Van der Kruijs et al., 239.

587 Van der Kruijs et al., 245.

588 As previously discussed, Charcot conjectured that strong emotions could bypass voluntary control and trigger the inhibition of voluntary movement, thus giving rise to hysterical paralysis. For details on Charcot's conjecture, see section 1.3.2.

589 See, e.g., Li et al., "Insular Subregions"; Maurer et al., "Impaired Self-Agency"; Otti et al., "Chronic Pain"; and Wegrzyk et al., "Functional Connectivity."

590 See Allendorfer et al., "Psychological Stress"; Baek et al., "Motor Intention"; Dogonowski et al., "Recovery"; Morris et al., "Avoidance"; and Szaflarski et al., "Facial Emotion Processing."

591 Allendorfer et al., "Psychological Stress," 8, article 101967; Baek et al., "Motor Intention," 1629–30; Dogonowski et al., "Recovery," 273; Morris et al., "Avoidance," 291; and Szaflarski et al., "Facial Emotion Processing," 200–1.

other words, the broader insight emerging from these studies is that local task-induced anomalous neural responses appear to be associated with global disturbances in resting-state functional connectivity. However, what is unresolved is how these different disturbances influence each other. Moreover, it has not always been clear how to interpret the complementary findings of task-based and resting-state approaches in terms of correlated cognitive processes.[592]

Since these open questions remain to be addressed by future studies, let us return to the segment of fMRI hysteria research that has relied exclusively on the resting-state approach. Following the pioneering example set by van der Kruijs et al., several subsequent resting-state studies applied seed-based analysis not just to non-epileptic seizures but also to motor symptoms and somatisation (i.e., the multisymptomatic form of hysteria).[593] But unlike van der Kruijs et al., subsequent resting-state studies tended to deploy somewhat less elaborate approaches to defining the seed regions. In most cases, the choice of seeds was derived from the results of previous task-based or resting-state fMRI studies that had investigated the respective hysterical symptoms.

For example, in a resting-state study of non-epileptic seizures published in 2014, Li et al. searched for the brain areas that exhibited abnormal functional connectivity with the insula.[594] The insula is part of the brain's limbic system and is thought to be involved in "multimodal functions, including emotion regulation, visceral sensory perception, self-awareness, and sensorimotor processing."[595] Importantly, van der Kruijs et al. identified the insula as one of the seeds that exhibited abnormal functional connectivity to the motor cortex in their patient sample.[596] Li et al. explicitly drew on this finding but went a step further. They parcellated the insula into three distinct functional subregions and then calculated the connectivity patterns for each of these segments.[597] Hence, whereas van der Kruijs et al. treated the insula as a single seed, Li et al. divided this anatomical region into three separate seeds. In patients, Li et al. found abnormal patterns of functional connectivity for each of the insular subregions, particularly to multiple areas within the motor system. Deploying reverse inference, Li et al. conjectured that the altered functional connectivity of the insular subregions could mean that, in hysteria patients, stressful emotions have an aberrantly enhanced "direct influence on their motor functions."[598]

---

592 See Dogonowski et al., "Recovery,"273; and Morris et al., "Avoidance," 291. In the next section, I will address this point when discussing the Dogonowski et al. study.

593 See, e.g., Li et al., "Insular Subregions"; Maurer et al., "Impaired Self-Agency"; and Wang et al., "Clinical Significance."

594 Li et al., "Insular Subregions."

595 Li et al., 637.

596 Van der Kruijs et al., "Dissociation in Patients," 242–45.

597 Li et al., "Insular Subregions," 637. Based on previous studies that had employed "a diverse range of methodological approaches," Li et al. argued that the insula comprised three subregions, each of which had a distinct functional specialisation. Ibid. "These include a ventral anterior region related to chemosensory and socio-emotional processing, a dorsal anterior region related to higher cognitive processing, and a posterior region associated with pain and sensorimotor processing." Ibid.

598 Li et al., 644. On the reverse inference, see section 3.5.3 and Poldrack, "Cognitive Processes."

By contrast, in a study focusing on patients with multiple somatic symptoms, Wang et al. decided to investigate altered resting-state functional connectivity patterns of the cerebellum. Wang et al. chose this particular region due to its apparent functional involvement "in emotion and cognition," although they admitted that the exact role of the cerebellum in these processes remains debated.[599] Similarly, in another study that focused on patients with multiple somatic symptoms, Ou et al. deployed the seed-based method to examine alterations in the connectivity between the region called nucleus accumbens and the rest of the brain. They chose this particular region as their seed because previous studies have shown that it plays an important function in the so-called reward circuit, "a group of neural structures related to associative learning, incentive salience, and positive emotions."[600] Finally, Maurer et al. opted to use the temporoparietal junction (TPJ) as the seed in their resting-state study that investigated the impaired sense of agency in hysteria patients with mixed motor symptoms.[601] Maurer et al. justified their decision by referencing the findings by Voon et al. on the reduced activity in the TPJ during hysterical as opposed to mimicked tremor.[602]

All these studies detected abnormal patterns of resting-state functional connectivity in patients relative to healthy controls. However, due to the differently defined seed regions, which, in turn, were informed by diverse assumptions about the symptoms' potential neural bases, the spatial distributions of the resulting aberrant connectivity patterns varied across the studies. In the end, such disparate findings were difficult to reconcile, let alone unify into a single, overarching interpretation.

Drawing on the discussion above, it can be said that the main advantage of the seed-based analyses is that it allows researchers to focus on the neuroanatomical regions they presume to be implicated in the hysterical symptom of interest. Using this type of analysis, researchers can investigate "the strength and significance of pairwise relationships" between the seed thus chosen and all other areas across the brain.[603] In effect, the potential epistemic gain of this type of analysis hinges on two conditions. First, what matters is the hypothesised cognitive and functional relevance of the chosen seed region to the symptom of interest, i.e., whether or not that region has contributed to the formation or maintenance of the hysterical symptom. Second, the validity of the analysis is necessarily contingent on the anatomical precision with which the chosen seed region was defined. If these conditions are fulfilled, seed-based analysis provides an effective method for exploring salient patterns of connectivity in a highly focused manner. Moreover, the interpretation of the results is less challenging compared to other resting-state methods because, in this case, it is typically informed by the hypothesis that guided the choice of the seed region.[604]

However, the unavoidable downside of this selective focus is that, by its very definition, seed-based analysis disregards all other potentially interesting functional

599 Wang et al., "Clinical Significance," 2, e4043.

600 Ou et al., "Nucleus Accumbens," 2, article 585.

601 Maurer et al., "Impaired Self-Agency," 564–65.

602 We have discussed this particular Voon et al. study in section 4.2.1.

603 Su et al., "Increased Functional Connectivity," 2.

604 See, e.g., van der Kruijs et al., "Dissociation in Patients," 244–45.

connectivity patterns in which the seed region does not partake. To offset this limitation, several fMRI hysteria studies have used an alternative connectivity method called independent component analysis (ICA).[605] The major advantage of ICA is that it allows researchers to analyse a resting-state fMRI dataset without having to define an a priori seed.

Referred to as a multivariate method because all the voxels in the brain volume are analysed simultaneously, ICA separates the resting-state BOLD signal into a set of its underlying structured components.[606] Each resulting component entails voxels whose BOLD time courses exhibit statistically significant temporal synchrony and are, therefore, considered to comprise a resting-state functional network. In other words, a resting-state network obtained through ICA consists of a set of neuroanatomical regions "that show a similarity" in the time courses of their spontaneous BOLD fluctuations.[607] Following the analysis, each component (i.e., the network) is visualised in the form of a separate spatial map. Importantly, each such map "reflects where in the brain a certain signal portion" has been detected.[608] It should be noted that each component thus extracted is described not only by a spatial map but also by an accompanying time course. The time course shows how the intensity of the extracted portion of the signal—i.e. the component—changed over time.[609]

In effect, ICA enables researchers to estimate "the full spatial structure of all of the [functional] networks" that simultaneously constitute the resting-state signal.[610] However, these components are necessarily unknown before the analysis because they are not directly observable.[611] To identify them, sophisticated automated algorithms deploy black-boxed mathematical operations to estimate the optimal mixture of underlying components that make up the original resting-state BOLD signal.[612] Hence, unlike seed-based analysis that requires a hypothesis-driven a priori definition of the seed and is limited to assessing pairwise connections with this single region, ICA is

605 See, e.g., Otti et al., "Chronic Pain"; and van der Kruijs et al., "Resting-State Networks."

606 Bijsterbosch, Smith, and Beckmann, *Resting State*, 55. By contrast, all other methods we discussed previously—the task-based analysis using the GLM, the PPI, and the seed-based resting-state connectivity—deploy the univariate approach in which the fMRI dataset is analysed one voxel at a time. See sections 3.4.2 and 3.4.4.

607 Bijsterbosch, Smith, and Beckmann, *Resting State*, 61. Significantly, one influential study has empirically demonstrated that the "sets of major brain networks, and their decompositions into subnetworks, show close correspondence between the independent analyses of resting and activation brain dynamics." Smith et al., "Correspondence," 13040. In short, it appears that the same sets of functional networks are active both during explicit tasks and in their absence, i.e., at 'rest.'

608 Bijsterbosch, Smith, and Beckmann, *Resting State*, 55.

609 Bijsterbosch, Smith, and Beckmann, 55–56.

610 Bijsterbosch, Smith, and Beckmann, 61.

611 The situation is similar to "being in a room listening to a lecture; you can hear the lecturer's voice, but you might also hear birds singing outside, repetitive banging from the construction noises at the building next door," and perhaps the nearby traffic. Bijsterbosch, Smith, and Beckmann, 61. "Therefore, the signal that your ears pick up is a mixture of all these sources, but your brain is able to separate them and pay attention to the lecturer's voice. ICA takes the same approach" to resting-state fMRI dataset. Ibid.

612 For details, see Bijsterbosch, Smith, and Beckmann, 55–57.

a data-driven method that allows the simultaneous extraction of multiple large-scale resting-state networks. However, as my analysis will show, this neither means that ICA is devoid of implicit assumptions about the brain's functional organisation nor that human judgment plays no role in this process.

First, to enable the algorithms to separate the original BOLD signal into its unknown components, it is necessary to make an assumption about the nature of the relationships among these components. The underlying assumption in ICA is that all structured components are statistically independent or, in other words, generated by mutually unrelated neural processes.[613] As a result of this assumption, ICA extracts only spatially non-overlapping components, thus disregarding the likely possibility "that some regions might be part of multiple networks."[614] Another direct consequence of the assumption of statistical independence is that ICA disregards any patterns of connectivity among the extracted networks, thus treating them as noise.[615]

Second, the crucial decision that researchers have to make, and on which the potential interpretability of the resulting maps hinges, is specifying how many components the algorithms should extract from the data. This step is necessary because the algorithms cannot differentiate between components whose identified temporal synchrony was caused by structured noise of non-neural origins (such as breathing) and those components that reflect the synchronised neural activity of spatially distributed brain regions.[616] Therefore, unless constrained, the automated algorithms are likely to overfit the data by extracting too many components that describe the noisy portion of the BOLD signal. To restrict the quantity of noisy components and thus "obtain familiar resting state networks that are more consistent with other studies in the literature," researchers typically "manually set the number of components to a lower number" than it is possible to extract mathematically.[617] It should be noted that there is no consensus among experts concerning the optimal number of components to extract.[618] This means that in each study, researchers have to decide, somewhat arbitrarily, into how many independent networks their resting-state dataset should be decomposed. But despite such arbitrariness, determining the appropriate number of components is a crucial interpretational decision "because networks extracted with ICA can sometimes be split or combined."[619] This, in turn, can make the identification of the resulting networks difficult, thus rendering them effectively uninterpretable.

Yet even after the algorithms have extracted the number of components researchers had specified, the analysis is far from over. At this point, researchers have to decide

613 In lay terminology, the ICA's assumption of statistical independence—hence the name of the method—means that one component cannot be predicted based on the knowledge of another component. In purely mathematical terms, it means that the algorithms search for non-Gaussian components in the dataset. For details, see Bijsterbosch, Smith, and Beckmann, 55–57. See also Poldrack, Mumford, and Nichols, *Handbook*, 138–42.

614 Bijsterbosch, Smith, and Beckmann, *Resting State*, 61.

615 Lv et al., "Nonexperts," 1395.

616 Lv et al., 1395.

617 Bijsterbosch, Smith, and Beckmann, *Resting State*, 58.

618 Bijsterbosch, Smith, and Beckmann, 58.

619 Bijsterbosch, Smith, and Beckmann, 61.

which of the extracted components merely reflect noise and which represent resting-state functional networks that have been reproducibly shown to exhibit synchronous spontaneous activity when the brain is not engaged in an external task.[620] Apart from the DMN (default-mode network) we discussed in the previous chapter, several other resting-state networks have been described in the neuroimaging literature.[621] To decide which of the components identified by ICA represent resting-state networks, researchers combine computer-driven methods with visual inspection. They look for a sufficiently good spatial overlap between their extracted components and the maps of the known resting-state networks that have been published in previous neuroimaging studies.[622] In short, to identify specific functional networks among the extracted components, researchers have to rely on existing literature. Thus, although nominally a data-driven approach, ICA nevertheless requires human judgment. As we have seen, such judgment entails deciding into how many components to decompose the data and, even more importantly, differentiating between functionally meaningful components and structured noise.

In hysteria research, ICA has been deployed to search for potential differences in the spatial organisation of various resting-state networks between patients and healthy control subjects. For example, in their subsequent study, van der Kruijs et al. used ICA to re-analyse the resting-state fMRI dataset from their previous seed-based analysis discussed above.[623] Using this different analysis method, van der Kruijs et al. discovered in the same resting-state dataset a much more widespread pattern of abnormal functional connectivity than in the previous study. ICA revealed that, relative to healthy subjects, patients with non-epileptic seizures exhibited "increased coactivation of several regions in the resting-state networks associated with fronto-parietal activation, executive control, sensorimotor functioning, and the default mode."[624] Based entirely on reverse inference, the authors speculated about several possible cognitive mechanisms through which the identified aberrant patterns of coactivation across four different resting-state networks could contribute to the occurrence of non-epileptic seizures. The hypothesised cognitive processes included impaired movement planning and perception, as well as altered self-reflection.[625] In the end, in a broader but less speculative conclusion, the authors suggested that hysteria patients "lack optimal information-integration abilities."[626]

However, it is worth noting that, when used on its own, ICA did not always prove to be a particularly fruitful method for discovering hysteria-related alterations in resting-

620 Lv et al., "Nonexperts," 1395.

621 "There are several resting-state networks that commonly emerge from ICA analysis in rs-fMRI studies, including but not limited to the default mode network, auditory network, salience network, executive control network, medial visual network, lateral visual network, sensorimotor cortex, dorsal visual stream (frontoparietal attention network), basal ganglia network, limbic network, and precuneus network." Lv et al., 1394.

622 Lv et al., 1395. See also Otti et al., "Chronic Pain," 4, article 84.

623 See van der Kruijs et al., "Resting-State Networks," 127–28.

624 Van der Kruijs et al., 129.

625 Van der Kruijs et al., 130–31.

626 Van der Kruijs et al., 132.

state networks. For example, Otti et al. used ICA to compare the organisation of several resting-state networks between twenty-one patients with chronic functional pain and nineteen healthy controls subjects.[627] Yet, contrary to van der Kruijs et al., Otti et al. found no changes in the spatial configuration of functional connectivity within the sensorimotor, fronto-insular, or the default mode network (DMN) between patients and healthy controls.[628]

Undeterred by these negative results, Otti et al. went a step further and deployed an alternative analysis. Called power-spectra analysis, this additional method enabled the researchers to calculate the frequency with which the spontaneous neural activity fluctuated within each of the resting-state networks that they had isolated through ICA.[629] In doing so, Otti et al. managed to identify alterations in the temporal organisation of the DNM and the fronto-insular network. According to their findings, the spontaneous fluctuations of the activity within the DNM and the fronto-insular networks shifted to a higher frequency in patients relative to healthy controls. Otti et al. admitted that their findings did "not demonstrate causal relationships" between pain-condition and altered spectral power.[630] Nevertheless, based on reverse inference, they tentatively suggested that the alteration in the rhythmical dynamics of the two resting-state networks could reflect the patients' "impaired subjective emotional awareness."[631]

The power-spectra analysis performed by Otti et al. brings us to the third type of analysis used in fMRI hysteria research to characterise the patients' spontaneous brain activity at rest.[632] Whereas the seed-based analysis and ICA serve to identify either long-distance connectivity patterns or large-scale functional networks in terms of their spatial organisation, shape and size, the third group of methods enable researchers to zoom in on regional characteristics of the brain's resting-state activity. Strictly speaking, the methods entailed in the third group do not measure functional connectivity directly. Instead, they examine different aspects of synchrony in the spontaneous neural activity at the local level, either within predefined regions of interest or across the whole brain.

For example, one such method is called regional homogeneity (ReHo) analysis. Researchers use it to assess the synchrony of the brain's spontaneous resting-state activity across the nearest neighbouring voxels by measuring the similarity of their BOLD time courses.[633] Several studies have applied this method either to patients with functional pain or to those with multiple somatic symptoms, in each case comparing

627 Otti et al., "Chronic Pain."

628 Otti et al., 4, article 84.

629 For details regarding the power-spectra analysis, see Otti et al., 5–7, article 84. For other studies of hysterical symptoms that used ICA to extract one or more resting-state networks from their data but then, in the next step, applied a different type of analysis to characterise potential alterations within these networks, see, e.g., Otti et al., "Somatoform Pain"; and Wei et al., "Default-Mode Network."

630 Otti et al., "Chronic Pain," 6, article 84.

631 Otti et al., 7, article 84.

632 See, e.g., Huang et al. "Spontaneous Activity"; Li et al., "Regional Activity"; and Yoshino et al., "Regional Neural Responses."

633 Lv et al., "Nonexperts," 1392.

patients to healthy control subjects.[634] In each study, researchers computed whole-brain maps that showed multiple locations with aberrant regional homogeneity—both increased and decreased—in patients relative to controls. However, the locations of the abnormal regional resting-state activity differed significantly across the studies and, what was more problematic, the potential reasons for such inconsistencies have so far remained unclear.

Other studies used an alternative method called fALFF, which quantifies a different aspect of the brain's regional spontaneous activity. This method summarises the frequency characteristics of the BOLD signal in each voxel as a measure of the intensity of the local resting-state activity.[635] In one study, Su et al. used this method to detect regional abnormalities in the resting-state activity in patients with multiple somatic symptoms compared to healthy controls.[636] Su et al. chose to focus their regional connectivity analysis only on the brain areas that jointly constitute the default-mode network (DMN). Hence, before performing the fALFF analysis, the researchers first had to deploy ICA to identify the default-mode network in their subjects. Upon finished fALFF analysis, Su et al. discovered aberrantly increased regional intensity in one part of the network (the medial prefrontal cortex) and decreased regional intensity in another (the precuneus).[637]

In another study, Li et al. applied the fALFF to the whole brain, searching for regional changes in the resting-state activity in patients with non-epileptic seizures relative to healthy subjects.[638] Li et al. identified six brain areas with aberrant fALFF values, which meant that these areas exhibited abnormal synchronous regional activity.[639] Next, Li et al. used the thus identified six areas as regions of interest for the subsequent seed-based inter-regional connectivity analysis. The inter-regional analysis, in turn, disclosed additional widespread alterations in connectivity patterns. Taken together, the complex findings generated by Li et al. indicated that the patients' "changes in the regional cerebral functions are related to remote inter-regional network deficits."[640]

In effect, these two studies demonstrate that regional and interregional resting-state analysis methods are not mutually exclusive. Instead, the different methods can be variably and often fruitfully combined within a single study to generate complementary findings. However, it should also be noted that although both Su et al. and Li et al. could identify multiple abnormalities in the neural synchrony in their patient

634 Huang et al. "Spontaneous Activity"; Li et al., "Regional Brain Function"; Song et al., "Regional Homogeneity"; and Yoshino et al., "Regional Neural Responses."

635 In full, the method is called the fractional amplitude of low-frequency fluctuations. For a detailed description, see Bijsterbosch, Smith, and Beckmann, *Resting State*, 68–69.

636 Su et al., "Regional Activity."

637 Su et al., 3–4, e99273.

638 Li et al., "Regional Activity."

639 Specifically, "patients exhibited significantly increased fALFF in the left superior frontal gyrus (SFG), left precuneus, left paracentral lobule, right postcentral gyrus and left supplementary motor area (SMA). Patients showed decreased fALFF in a triangular part of the right inferior frontal gyrus (IFG)." Li et al., 2, article 11635.

640 Li et al., 1, article 11635.

sample, they were less successful in interpreting their findings in cognitive terms. The researchers struggled with the fact that "the exact physiological nature" and thus also the biological meaning of "fALFF is not entirely clear."[641] How exactly the discovered regional alterations of the brain's spontaneous activity were implicated in either the formation or the maintenance of hysteria patients' symptoms remained unresolved.

Finally, an increasing number of resting-state fMRI studies of hysteria have started to deploy a variety of more recent, highly sophisticated methods jointly referred to as node-based analyses.[642] All node-based analyses are rooted in graph theory, a branch of mathematics concerned with modelling complex networks and measuring their properties. In graph theory, any network can be mathematically represented—and subsequently visualised—as a system of points, called nodes, that are pairwise connected by lines, referred to as edges.[643] The resulting arrangement of nodes and edges is called a graph, and it can be used to model the brain's intrinsic functional organisation.

When used in resting-state fMRI, the graph's edges denote functional connections between nodes. The individual nodes, in turn, can be defined at very different spatial scales, ranging from single voxels over one or more functional brain regions to entire resting-state networks. Whether it consists of a single voxel or an entire resting-state network, a node is always "considered as functionally homogeneous region" in this type of analysis.[644] In short, regardless of its size, each node is treated as a single and discrete functional unit, which is connected to other nodes. Admittedly, such a "simplified summary of connectivity is not a fully accurate representation of the underlying complex hierarchical organization of the brain, but is nevertheless a useful model for studying it at a certain scale."[645]

To perform any node-based analysis, researchers first have to parcellate the brain into nodes on the spatial scale of their choice.[646] It is important to note that "node-based methods are only as good as the nodes fed into them, because the nodes are spatially fixed at the start of the analysis."[647] Hence, choosing which particular spatial scale and which available parcellation approaches to use are crucial interpretational decisions with significant epistemic consequences.[648] Having defined the nodes, researchers then extract the BOLD time series from each of them, and finally, calculate the connectivity between all possible pairs of nodes. The latter step is referred to

641 Su et al., "Regional Activity," 6, e99273.

642 See, e.g., Dienstag et al., "Motor Control"; Diez et al., "Fast-Tracking"; Ding et al., "Connectivity Networks"; and Wegrzyk et al., "Functional Connectivity."

643 See, e.g., Bassett and Bullmore, "Small-World Brain Networks," 513.

644 Bijsterbosch, Smith, and Beckmann, *Resting State*, 82.

645 Bijsterbosch, Smith, and Beckmann, 84.

646 Bijsterbosch, Smith, and Beckmann, 82. Of course, researchers do not parcellate an actual brain, but only the imaging data. Yet this metonymic expression is commonly used in the neuroimaging context, and I am adopting it here. See ibid., 84.

647 Bijsterbosch, Smith, and Beckmann, 85.

648 For the differences between the so-called atlas-based and data-driven approaches to parcellation and their respective advantages and disadvantages, see Bijsterbosch, Smith, and Beckmann, 86–89.

as defining the edges.[649] Once they have completed it, researchers have successfully constructed their graph. At this point, they can use a wide variety of mathematical measures that serve to quantify different topological aspects of the resulting graph. Among many others, such measures include the connectivity strength, the average path length between nodes, and the clustering of connections.[650]

The crucial advantage of the graph-theoretical framework is that it provides researchers with a high degree of analytical flexibility. It allows researchers to examine the organisation of whole-brain functional networks both locally, i.e., at the level of individual nodes, as well as globally, by measuring multiple characteristics of the graph as a whole.[651] Put simply, unlike the resting-state connectivity analyses discussed so far, the node-based methods place the focus on the brain's hierarchical functional organisation by enabling researchers to investigate both "the segregation of brain networks and the integration between them."[652]

Importantly, what is of interest in a node-based analysis are not the locations of the nodes themselves since these are predefined by researchers. Instead, what is of interest are various characteristics of the links among the nodes, such as their number, strength, length, and spatial clustering. This shift of perspective has had consequences on how the complex, multidimensional results of node-based analyses are visualised to enable researchers to explore and apprehend their results. The connections (i.e., edges) are typically visualised as lines.[653] "However, as the number of represented connections is increased, the underlying anatomical space runs the risk of becoming obfuscated by the connections. This problem was circumvented by recognizing that the path of connections in functional connectivity space is arbitrary" and, therefore, did not necessarily have to be visualised in anatomical terms.[654] As a result, new ways of visualising the outcomes of graphed-based connectivity analyses have been developed that "prioritize the clarity of connections."[655] Some visualisations of functional connectivity are still recognisable at a glance as brain maps as they consist of a transparent brain outline onto which the nodes and their edges are overlaid.[656] Others no longer bear any visual resemblance to the brain.

649 For a succinct overview of different mathematical approaches to defining edges, see Bijsterbosch, Smith, and Beckmann, 90–95.

650 For an overview of different measures researchers can compute, see Bijsterbosch, Smith, and Beckmann, 97–99.

651 For details, see, e.g., Lv, "Nonexperts," 1396; Bijsterbosch, Smith, and Beckmann, *Resting State*, 98–99; and Ding et al., "Connectivity Networks," 3, e63850. However, a potential disadvantage of the graph-theoretical methods is that "the nodes are defined prior to the analysis and their shape and size do not change as part of the analysis." Bijsterbosch, Smith, and Beckmann, *Resting State*, 105. Thus, unlike ICA, node-based methods cannot identify potential changes in spatial shape and size of resting-state networks. In effect, each resting-state method has its specific strengths as well as its limitations.

652 Diez et al., "Fast-Tracking," 930.

653 See, e.g., Diez et al., 931, fig. 1A; Wegrzyk et al., "Functional Connectivity," 166, fig. 1.

654 Margulies et al., "Visualizing the Human Connectome," 451.

655 Margulies et al., 451. See also ibid., 452, fig. 7.

656 See, e.g., Wegrzyk et al., "Functional Connectivity," 166, fig. 1.

Thus, in 2012, Irimia et al. developed more abstract visualisations, which they aptly named connectograms.[657] The connectograms' explicit aim is "to organize, inspect and classify brain connections in a visually-insightful and content-rich manner, and with the clear advantage of a high data-to-ink ratio."[658] Simply put, connectograms are highly schematised circular diagrams that can be flexibly used to visualise various aspects of brain connectivity.[659] Different brain regions (i.e., nodes) are first labelled with an abbreviation and a particular colour and then assigned a position on the arc of a circle.[660] The nodes' positioning is restricted by the fact that the left side of the circle refers to the left brain hemisphere and the right side of the circle to the right hemisphere. Inside the circle, pairwise connections among the nodes are visualised by lines. Significantly, the opacity, thickness, and colour of the lines can be used to encode various summary metrics that describe the computed characteristics of functional connections between the nodes. Such a circular diagram is meant to provide "a more intuitive" and thus, for an expert, more easily graspable visualisation of the brain's convoluted functional architecture.[661] Hence, even if it no longer visually resembles the brain, this novel type of visualisation has proven to be an effective epistemic tool. It allows researchers—who know how to 'read' the information encoded in a connectogram—to make sense of the highly complex and multidimensional empirical findings obtained through graph-theoretical analyses of their data.

During the 2010s, several different graph-theoretical approaches to analysing resting-state fMRI data have been deployed in hysteria research. For example, in three separate studies, Ding et al., Guo et al., and Su et al. computed the number of connections each voxel had to all other grey-matter voxels in the brains of hysteria patients relative to healthy controls.[662] The patients in these studies had either multiple somatic symptoms or non-epileptic seizures. Conversely, Otti et al., Dienstag et al., as well as Monsa, Peer, and Arzy investigated potential intra- and inter-network deficiencies underpinning functional pain, non-epileptic seizures, and partial one-sided paralysis, respectively.[663] The authors of the three latter studies used graph-theoretical analysis to search for the differential ways in which multiple large-scale resting-state functional networks interacted in patients compared to controls. In yet another study, Su et al. examined the differences in the so-called interhemispheric resting-state functional connectivity between patients with multiple somatic symptoms

657 Irimia et al., "Circular Representation." In developing connectograms, Irimia et al. deployed the freely available Circos software that visualises data in a circular format and was initially designed for displaying genomic data. "Introduction to Circos, Features and Uses // CIRCOS Circular Genome Data Visualization," Circos, accessed January 17, 2022, http://circos.ca/.

658 Irimia et al., "Circular Representation," 1341.

659 See, e.g., Szaflarski et al., "Facial Emotion Processing," 201, fig. 3.

660 For details, see Irimia et al., "Circular Representation."

661 Irimia et al., 1350.

662 See Ding et al., "Connectivity Density"; Guo et al., "Anatomical Distance"; and Su et al., "Connectivity Strength."

663 See Otti et al., "Somatoform Pain"; Dienstag et al., "Motor Control"; and Monsa, Peer, and Arzy "Self-Reference."

and healthy controls.[664] In doing so, Su et al. aimed to identify potential disruptions in the neural processing between the left and right brain hemispheres that were specific to hysteria patients.

Except for Otti et al., all the other studies listed above detected multiple statistically significant functional connectivity disturbances in patients compared to healthy control subjects.[665] But the findings across the individual studies were mutually inconsistent. Such inconsistencies may, in part, be attributed to the different hysterical symptoms these studies investigated. Yet, even more importantly, there was another caveat. Because the nodes in some of the studies were defined at the level of individual voxels and in others comprised entire functional networks, the resulting imaging findings were difficult to compare even when they addressed the same symptom.

Finally, two other studies, one by Ding et al. and another by Diez et al., deserve to be singled out due to the particularly sophisticated graph-theoretical analyses they used.[666] Comparing seventeen patients with epileptic seizures to twenty healthy controls, Ding et al. first parcellated their subjects' brains into ninety anatomically defined nodes. They then computed a host of both local and global properties of the thus constructed whole-brain functional network.[667] Summarising these different measures, Ding et al. concluded that, compared to healthy controls, patients lacked the network property called small-worldness. Small-worldness refers to the optimal topological organisation of a network into its nodes.[668]

Instead of having many random connections, nodes in an optimally organised network are densely connected locally and have only a few long-range connections. The consequence of such wiring is that each node in the network can be reached from any other node through a small number of connections, which, in specialist terms, is called a short path length. Small-worldness thus facilitates efficient neural wiring and supports an optimal balance between "segregated/specialized and distributed/integrated information processing."[669] It has been shown experimentally that this type of network configuration characterises the functional organisation of the healthy human brain.[670] According to Ding et al., the loss of small-worldness in hysteria patients' brains entailed both significantly increased local specialisation and decreased global integration. This altered topological organisation, in turn, led to considerably "less efficient information propagation" across the patients' brains.[671]

664 See Su et al., "Interhemispheric Connectivity."

665 As a notable exception, Otti et al. found no statistically significant difference in functional connectivity among networks associated with affective processing and memory function between patients with somatoform pain and healthy controls. See, Otti et al., "Somatoform Pain," 61.

666 Ding et al., "Connectivity Networks"; and Diez et al., "Fast-Tracking."

667 Ding et al., "Connectivity Networks," 2–3, e63850. Additionally, Ding et al. acquired diffusion tensor images and, in parallel to functional, also computed the patients' structural connectivity networks. For details, see ibid.

668 Bassett and Bullmore, "Small-World Brain Networks," 512.

669 Bassett and Bullmore, 514.

670 For details, see Ding et al., "Connectivity Networks," 5, e63850

671 Ding et al., 4, e63850.

In a similarly fine-grained study of thirty patients with various motor symptoms, Diez et al. applied a new graph-theoretical resting-state analysis called stepwise functional connectivity (SFC).[672] This method was specifically developed to "navigate across large-scale functional connections from particular areas to the rest of the brain" to study "how distributed systems bond together through multiple connectivity steps."[673] In effect, this novel method aims to identify the hierarchical organisation of neural processing in terms of its sequential propagation across different functional networks. Initially, the researchers used this method to delineate the connectivity pathways through which the information flow propagated from primary sensory and motor cortices to higher-order cognitive centres in healthy individuals.[674] Next, they decided to investigate if and how this functional stream of multimodal integration was altered in hysteria patients with heterogeneous motor symptoms.

Since the findings of the Diez et al. study in their full complexity are beyond the scope of our discussion, I will only summarise their major points. Diez et al. discovered that, compared to controls, patients exhibited enhanced resting-state propagation from the primary motor cortex and the amygdala to multiple higher-order multimodal integration areas, including the insula.[675] Using reverse inference, the authors conjectured that these alterations in the information flow led to the patients' aberrant processing of attention, "interoception, stress responses and self/emotional awareness."[676] Admittedly, in terms of the implicated cognitive processes, the conclusions drawn by Diez et al. remained somewhat vague. However, the main contribution of Diez et al., as I see it, is their novel approach to delineating potential disturbances in the intrinsic hierarchical organisation of the hysteria patients' brains. Their sophisticated graph-theoretical analysis method has enabled the researchers to pose a highly specific question about the potential neural basis of hysterical motor symptoms by analysing the pathways of information processing that connect primary sensorimotor cortices to higher-order regions of multimodal integration.

***

Summing up my analysis in this section, it can be said that the multifaceted action-guiding concept of resting-state functional connectivity considerably enriched the fMRI-based hysteria research by enabling it to move beyond the purely task-based paradigm. The deployment of this action-guiding concept has opened up the possibility of delineating potential disturbances in the spontaneous neural activity across multiple functional regions and networks, as well as at different levels of the brain's intrinsic organisation in hysteria patients. Whereas the acquisition of resting-state fMRI data is

672 Diez et al., "Fast-Tracking," 929–30. Patients had positive motor symptoms, functional weakness, and non-epileptic seizures.

673 Sepulcre, "Functional Steams," 2.

674 For the study of healthy subjects, see Sepulcre et al., "Stepwise Connectivity."

675 Compared with controls, patients exhibited increased stepwise functional connectivity "from motor regions to the bilateral posterior insula, TPJ, middle cingulate cortex and putamen." Patients also showed enhanced connectivity from the right amygdala "to the left anterior insula, periaqueductal grey and hypothalamus among other areas." Diez et al., "Fast-Tracking," 929.

676 Diez et al., 936.

relatively straightforward, we have seen that researchers make crucial interpretational decisions by choosing among the many available analysis methods.

Throughout this section, I have underscored that the various analysis methods operate with distinctly different perspectives on resting-state functional connectivity. Each method quantifies a particular aspect of the temporal synchrony in the spontaneous fluctuation of the BOLD signals stemming from differently defined spatial units. Therefore, each method results in a different type of functional connectivity map. I have aimed to show that the generation of such diverse functional connectivity maps from the same resting-state fMRI dataset in each case hinges on the inscription of very different assumptions about the functional organisation of the brain into the resulting map. Hence, as I have argued, even in the so-called data-driven methods, such as ICA, the production of the visibility of resting-state connectivity patterns cannot be discussed without paying attention to the implicit assumptions that informed the data analysis. It has also been equally important to me to emphasise that the richness of these multiple co-existing perspectives on functional connectivity is what makes the current resting-state investigation of hysteria such a dynamic area of research. As the multiple examples discussed above have demonstrated, the different definitions and methods of computing functional connectivity are not mutually exclusive. Instead, they can be productively combined even within a single study.

This brings us to the point where we need to consider the concrete empirical results that resting-state fMRI research on hysteria has delivered within the first decade of its existence. Despite the mutually inconsistent findings that the individual resting-state fMRI studies of hysterical symptoms have generated, one critical insight has already emerged from this relatively new strand of hysteria research. Generally speaking, all the studies analysed in this section suggest that the functional disturbances underlying hysterical symptoms may not be limited to overactivation or underactivation of several isolated regions or even to their two-way interactions. Rather, the implication arising from the current resting-state fMRI research is that the neural disturbances underpinning hysterical symptoms appear to involve a skewed integration of synchronous activity both within and across multiple functional networks. In short, the symptoms' neurophysiological basis might not only be more complicated than initially presumed but also considerably more dynamic.

There is one caveat, however. As discussed above, the individual resting-state fMRI studies of hysteria have isolated different patterns of altered connectivity within and across various functional networks involving many widespread brain areas. Although potentially epistemically significant, the exact meaning of these aberrant patterns remains elusive. This is because "the biological and physiological mechanisms that give rise to the changes in fMRI connectivity are poorly understood."[677] Unlike task-based studies in which the mapping of a cognitive function onto the correlated brain activity is guided by a priori assumption about the cognitive components that a specifically designed task isolates,[678] resting-state studies lack such an interpretation framework.

677 Bijsterbosch, Smith, and Beckmann, *Resting State*, 130.

678 For a detailed discussion, see section 3.1.1.

In fMRI research, 'rest' is an uncontrolled and essentially uncharacterised state. It thus remains unknown what kind of cognitive processes the subject is engaged in while 'resting' inside an MRI scanner.[679] As outlined in the examples above, researchers typically revert to reverse inference when interpreting their resting-state results in cognitive terms. Yet, this interpretational strategy is not without problems. For instance, the higher-order brain regions that are often implicated in these studies are known to partake in multiple cognitive functions, with their exact role changing depending on the particular context.[680] Since 'rest' lacks a clearly defined context, in many resting-state studies, the interpretations of how the identified disturbances in the correlational structure of hysteria patients' spontaneous neural activity relate to cognitive processes necessarily remain vague, tentative and, at times, even speculative. Hence, despite the multiplicity of methods that enable productive exploratory investigation of the hysteria-related loss of temporal coherence in the brain's intrinsic dynamic organisation, what is currently missing is a theoretical synthesis of the so far mostly fragmentary and often mutually divergent results. Such interpretational challenges might explain why, regardless of the continually growing number of resting-state studies, the intensity of the task-based fMRI hysteria research, with its reliance on precisely tailored experimental manipulation, shows no signs of abating.

As mentioned earlier, the authors of most fMRI studies of hysterical symptoms published in the first two decades of the twenty-first century chose to deploy either a task-based or a resting-state approach.[681] It remains to be seen if directly combining these two mutually complementary approaches within single studies might perhaps prove epistemically more promising than using them separately. But to facilitate their truly effective combined use, it would appear necessary to design studies that do not merely deploy these two approaches parallel to one another. Instead, it might be more pertinent to look for ways of more closely interweaving these two approaches within single studies so that each approach can offset the disadvantages of the other.

4.4.2 Tracing Functional Neurological Changes Associated with Treatment-Induced Recovery

Although it entered hysteria research only recently, we have seen how resting-state functional connectivity has quickly advanced to a highly productive action-guiding concept. In this section, we will examine functional neuroplasticity, another concept adopted from cognitive neuroscience, whose application in hysteria research has had a distinctly different trajectory. In neuroscience, functional neuroplasticity denotes the brain's intrinsic ability to continually undergo modifications in its

679 Bijsterbosch, Smith, and Beckmann, *Resting State*, 7.

680 For a detailed discussion of problems entailed in reverse inference, see Poldrack, "Cognitive Processes."

681 For notable exceptions, see, e.g., Baek et al., "Motor Intention"; Dogonowski et al., "Recovery"; Morris et al., "Avoidance"; and Szaflarski et al., "Facial Emotion Processing."

functional organisation in response to experience.[682] Notably, the concept of functional neuroplasticity already informed the experimental design of the first functional neuroimaging study of hysteria by Tiihonen et al., which, as discussed in chapter 2, was published in 1995.

In their pioneering study, Tiihonen et al. conjectured that the spontaneous remission of hysterical paralysis should be associated with localisable changes in the patient's pattern of brain activity.[683] Drawing on this conjecture, they used SPECT to measure their single patient's cerebral blood flow during the electric stimulation of the affected limb, first before and then after recovery. In a PET study published in 2001, Vuilleurmier et al. took up this pre-recovery and post-recovery comparison. Yet, Vuilleurmier et al. applied the comparison to a sample of four patients whose hysterical paralysis fully remitted after several months of "supportive physiotherapy and psychotherapy."[684] After that, not a single comparable neuroimaging study of hysteria appeared over the next ten years. This hiatus clearly indicated that the interest of the research community in delineating recovery-related neuroplastic changes in hysteria patients' brain activity had died down. Instead, the focus shifted to cross-sectional studies that, as in all examples analysed thus far, acquired fMRI data for each patient in a single session only. Hence, by its very design, all cross-sectional studies necessarily ignore the hysterical symptoms' potential temporal evolution.

However, in 2011, two new fMRI studies appeared. One of the studies examined a single case of hysterical mutism (i.e., the loss of the ability to speak) and another a group of patients with multiple somatic symptoms.[685] In both studies, the researchers aimed to delineate the changes in the patients' brain activity associated with recovery that had been explicitly induced through respective targeted therapies. In effect, these two studies reactivated the deployment of functional neuroplasticity as an action-guiding concept in fMRI research hysteria. By the end of the decade, the number of fMRI studies relating symptom improvement to neuroplastic changes in the brain function had grown slowly but steadily.[686] That this number will continue to increase is suggested by several large-scale studies of this type, which were in various stages of development in the early 2020s.[687] Significantly, ever since the revival of this strand of fMRI hysteria research in 2011, most studies have focused on identifying neuroplastic changes associated with therapy-induced rather than spontaneous recovery.[688]

---

682 For details, see von Bernhardi, von Bernhardi, and Eugenín, "Neural Plasticity"; and Sharma, Classen, and Cohen, "Neural Plasticity."

683 Tiihonen et al., "Altered Cerebral Flow." This study was briefly discussed in section 2.3.2.

684 Vuilleumier et al., "Sensorimotor Loss," 1079.

685 Bryant and Das, "Neural Circuitry"; and de Greck et al., "Reward."

686 See Becker et al., "Conversion Blindness"; Diez et al., "Fast-Tracking"; Dogonowski et al., "Recovery"; Espay et al., "Neural Responses"; LaFaver et al., "Before and After"; Roy et al., "Dysphonia"; Shimada et al., "Cerebellar Activation"; Spengler et al., "Voice Loss"; and Yoshino et al., "Therapy."

687 See LaFrance and Szaflarski, "Biomarkers for Seizures"; and Perez, "Biomarkers of Prognosis." Another planned study aims to investigate hysteria "patients with different symptoms and follow changes in brain activity patterns as a function of clinical follow-up." Bègue, "Emotion Processing," 258.

688 See Becker et al., "Conversion Blindness"; and Shimada et al., "Cerebellar Activation."

At a superficial glance, it may appear surprising that after only two studies, researchers abandoned this particular action-guiding concept and then, years later, suddenly rekindled its use. But even if I cannot fully explain this seemingly contradictory development, I can describe some of the key contributing factors. First, in my opinion, what made recovery-related neuroplastic changes challenging to study was the initial focus on the symptoms' spontaneous remission. Although in principle possible, clinical data suggest that spontaneous recovery is very rare and highly unpredictable.[689] Hence, shifting the focus to clinical therapy, as Vueilleumier et al. did in 2001, seemed logical.

Yet the shift to therapy-induced recovery did not immediately resolve the problem. At that point, there was hardly any agreement among medical practitioners on how to clinically manage hysterical symptoms. This, in turn, led to widespread scepticism regarding the symptoms' treatability, thus effectively leaving the patients in "the therapeutic vacuum."[690] In this therapeutic vacuum, the clinical management strategies were reduced to "relatively minimalistic interventions, focused more on conserving health care resources than improving patient symptoms and functioning."[691] Somewhat paradoxically, the reason for this situation was not the lack of available treatment options in itself. In fact, various treatment options, including different forms of psychotherapy, physiotherapy, hypnosis, transcranial magnetic stimulation, and antidepressants, were routinely used for managing other psychiatric disorders.[692] But the hysteria-specific therapeutic vacuum was due to the lack of understanding about this disorder's underlying cause, as well as "the paucity of controlled clinical trials examining" the potential benefit of available treatment modalities.[693] Moreover, it appears to me that the medical practitioners' at the time still pronounced tendency to regard hysteria patients as simulators additionally reinforced the perceived untreatability of the purportedly unreal symptoms.[694]

By the late 2000s and continuing into the 2010s, the situation had begun to change. Hysteria's varied somatic manifestations have gradually gained the status of genuine instead of merely feigned symptoms, a transition in which, as I have argued previously, fMRI research played a decisive role.[695] We have also discussed how this newly attained status has led to a revival of broader medical research into hysteria. In this new context, an increasing number of clinical studies into the application of various therapeutic approaches to hysteria have started to appear. Such studies, in turn, have generated empirical evidence for some level of efficacy of tailored psychotherapy, cognitive behavioural therapy and, in the case of motor symptoms, physiotherapeutic intervention aimed at retraining voluntary movements.[696] As a

689 For details, see Gelauff and Stone, "Prognosis."

690 Kroencke and Swindle, "Cognitive Behavioral Therapy," 206.

691 Kroencke and Swindle, 206. See also Kroencke, "Efficacy," 881.

692 Aybeck, Kannan, and David, "Neuropsychiatry of Conversion Disorder," 279.

693 Espay et al., "Opinions and Clinical Practice," 1372.

694 See section 2.2.3.

695 See section 2.4.2.

696 In the context of today's evidence-based medicine, the validation of any treatment is typically accomplished through specific kinds of clinical studies referred to as randomised control

result, hysterical symptoms have come to be viewed not only as medically treatable but also, at least potentially, as fully reversible.[697] This new context made it feasible for there to be sustained fMRI research into neuroplastic changes underlying therapy-induced recovery. I thus argue that the gradual validation of available treatment options was a necessary precondition for the revival of fMRI research into the neuroplastic modulation of the brain activity associated with symptom remission. Using validated treatment interventions, researchers could more reliably and controllably induce recovery and then use fMRI to study its neural effects.

However, although progress has been made recently in the clinical research on hysteria, effective treatments remain limited. According to the current recommendations, an optimal treatment entails a combination of multidisciplinary interventions that, depending on the type of the symptom, includes "physiotherapy, psychiatry/psychology, speech therapy and occupational therapy."[698] But since different patients have heterogeneous and often multiple concurrent symptoms, there is no one-size-fits-all approach to treatment. How to best select patients with a particular set of symptoms for specific treatment modalities remains an open question.[699] Consequently, a sizeable proportion of patients, particularly those with longstanding symptoms, fail to respond sufficiently to the currently used treatment options.[700]

A potentially more promising approach would entail developing new treatments informed by a deeper medical understanding of the symptoms' underlying neuropathophysiology. The necessary insights for such future developments could, at least in theory, be delivered by the ongoing fMRI hysteria research. Yet, from this treatment-oriented perspective, a significant drawback of the fMRI research conducted so far is that it has almost exclusively relied on a cross-sectional approach. Inconveniently, this approach cannot differentiate between the so-called trait and state abnormalities in the patients' brain activity.[701] By definition, trait disturbances are those neural processes that play a predisposing or even a causal role in the symptom development and are, therefore, thought to have been present even before any clinical symptoms become manifest.[702] In short, trait disturbances are regarded as more or less permanent and may not respond to any form of treatment. Conversely, state

trials. In these studies, subjects are randomly assigned to two or more groups to test the efficacy of the medical intervention under investigation. For details, see, e.g., Sessler and Imrey, "Clinical Research." For individual clinical studies into the effectiveness of different treatment options for various hysterical symptoms, see, e.g., Czarnecki et al., "Successful Treatment"; LaFrance et al., "Treatment Trial"; Kroencke and Swindle, "Cognitive Behavioral Therapy"; Nielsen et al., "Physio4FND"; Nielsen, Stone, and Edwards, "Systematic Review"; and Reuben et al., "Psychotherapy."

697 Espay et al., "Current Concepts," 1139.

698 Stone, "Assessment as Treatment," 14. Interestingly, the current understanding is also that potential therapeutic success "hinges on diagnostic delivery that validates the patient's symptoms and disability and allows full understanding and acceptance of the diagnosis by the patient." Espay et al., "Current Concepts," 1137.

699 Espay et al., "Current Concepts," 1137.

700 Espay et al., 1139.

701 Voon et al., "Functional Neuroanatomy," 186.

702 Voon et al., 186. See also Diez et al., "Fast-Tracking," 936.

abnormalities refer to those aberrant patterns of brain activity and connectivity that are associated with the acute condition of having an active symptom. Hence, it is this type of potentially more transient disturbance that a tailored treatment should target. However, based on cross-sectional fMRI studies of symptoms, it is impossible to determine to which extent the isolated patterns of aberrant activations and connectivity reflect either state or trait aspects of hysteria or possibly even their mixture.[703]

By contrast, experiments that deploy the concept of functional neuroplasticity appear to be better suited to disentangling the potential, currently still unknown trait and state deficits in the functioning of the hysteria patients' brains. This is because fMRI studies informed by the concept of functional neuroplasticity are necessarily longitudinal. To identify therapy-induced neuroplastic changes, researchers must compare the pre-treatment and post-treatment brain activities in the same sample of patients.[704] With this aim in mind, the initial set of fMRI data is acquired while patients have an acute symptom. Then a separate fMRI dataset is acquired after the symptom has clinically remitted due to successful treatment. The pattern of the therapy-induced neurophysiological changes isolated through the comparison of these datasets is regarded as "being essential for symptom generation" and taken to represent a state marker of the symptom in question.[705] Conversely, those patterns of activation and connectivity that remain unchanged across the longitudinal comparison are thought to reflect the trait markers of hysterical symptoms.[706]

It is interesting to note that through this distinction between trait and state neural disturbances, fMRI research on hysteria appears to implicitly revive one of Charcot's major tenets. That is, Charcot categorically differentiated between, on the one hand, purportedly hereditary and thus irreversible deficits that predispose patients to develop hysterical symptoms and, on the other hand, the reversible functional brain lesion. Similarly to the currently presumed state disturbances, Charcot conjectured that the appearance of a functional brain lesion was related to the development of clinically observable hysterical symptoms, whereas the lesion's disappearance correlated with recovery.[707]

Yet, notwithstanding the parallels to Charcot's research, fMRI studies of neuroplastic changes associated with the treatment-induced recovery are thought to have a double epistemic potential in the current medical context. First, from the perspective of basic research, such studies are hailed as holding the key to attaining a clearer understanding of hysteria's underlying neural mechanisms. Crucial in this respect is the presumed ability of such studies to establish an unambiguous difference between the irreversible trait and reversible state aspects of this disorder at the neural level.[708] Second, fMRI studies of therapy-related neural changes in hysteria patients

703 Voon et al., "Functional Neuroanatomy," 186.

704 Unlike cross-sectional studies that "may analyse multiple variables at a given instance," longitudinal ones "employ continuous or repeated measures to follow particular individuals over prolonged periods of time." Caruana et al., "Longitudinal Studies," E537.

705 Diez et al., "Fast-Tracking," 936.

706 See Conejero et al., "Brain Metabolism," Conclusions.

707 See sections 1.3.2 and 1.3.3.

708 Diez et al., "Fast-Tracking," 936.

are expected to generate findings that will enable researchers to develop tailored clinical interventions in the near future.[709] To fulfil this expectation, fMRI studies are meant to provide neurophysiological explanations as to why and to what extent the currently available treatments work. Accordingly, fMRI studies aim to distinguish which state aspects of hysterical symptoms a particular treatment option successfully targets and where it fails. However, I intend to show that, despite harbouring high hopes, in actual practice, the endeavour to unambiguously isolate therapy-induced changes in the hysteria patients' brain activity has faced multiple epistemic challenges, hence resulting in inconsistent imaging findings across studies.

Attempting to identify neuroplastic changes associated with therapy-induced recovery, most fMRI studies have deployed the task-based method.[710] But the types of the tasks they used and the details of each task's implementation have differed significantly across the individual studies. In fact, my analysis will show that by taking into account the different perspectives from which their authors approached the concept of therapy-induced functional neuroplasticity, the individual fMRI studies published in the 2010s can be divided into three different groups. These different approaches include, first, directly engaging the sensorimotor deficits entailed in the hysterical symptom of interest; second, addressing the symptom-related disturbances in emotion processing; and third, focusing on the prognostic potential of the patients' pre-treatment neural patterns. It is to these three approaches that we will now turn.

Three single-case fMRI studies are representative of the first approach to delineating treatment-induced neuroplastic changes in brain activity by deploying experimental tasks that directly engaged hysteria patients' symptom-specific sensorimotor deficits.[711] Interestingly, all three studies addressed some form of functional motor disturbance. Specifically, Bryant and Das, as well as Roy et al. investigated functional voice or speech loss, whereas Dogonowski et al. examined partial paralysis. Due to their focus on these specific symptoms, the tasks these studies deployed to identify the patients' recovery-related neuroplasticity involved controlled speech production and cued limb movement, respectively.

At the point when her initial fMRI dataset was acquired, the single patient in the Bryant and Das study could not speak, "utter a sound," or even whisper—and this condition had existed for four years.[712] During this period, the patient could only communicate through sign language and written messages. Extensive clinical assessment excluded any detectable "pathology to her larynx [i.e., the voice box] or vocal tract," thus leading to a diagnosis of hysterical mutism.[713] The diagnosis of mutism meant that the study's authors placed emphasis not on the patient's accompanying voice loss (i.e., aphonia) but on her inability to produce vocal speech despite her preserved

709 Perez, "Biomarkers of Prognosis," n.p.

710 As an exception, two studies used the resting-state method. See Diez et al., "Fast-Tracking"; and Yoshino et al., "Therapy."

711 Bryant and Das, "Neural Circuitry"; Dogonowski et al., "Recovery"; and Roy et al., "Dysphonia."

712 Bryant and Das, "Neural Circuitry," 290.

713 Bryant and Das, 290.

ability to both understand language and use it in the written or gestural form.[714] Tellingly, throughout her mutism, the patient reportedly retained her ability to sing.[715]

Having linked the patient's loss of speech to work-related stress, Bryant and Das chose to treat her with a cognitive-behavioural therapy tailored to remove her "motivation to not speak."[716] The treatment consisted of counselling sessions. During these sessions, the patient was told "her brain had learned not to speak because it had felt threatened in her previous workplace."[717] The therapist emphasised that this 'learning' had "occurred outside the level of awareness and was unintentional."[718] In addition to psychological counselling, the treatment also entailed a specifically tailored speech therapy. The therapy comprised karaoke exercises, during which the patient was encouraged to sing along to her favourite songs. The singing as a playful activity served to remove "the perceived threat" the patient associated with speaking and thus induce speech production while avoiding any "effortful attempts to achieve" the desired goal.[719] Within a few weeks, this therapy led to the full recovery of the patient's ability to speak. Seven months after the initial pre-therapy scan, another fMRI dataset was acquired of the now fully recovered patient.

Both during the pre-treatment and post-treatment data acquisition, the patient carried out the same task, which Bryant and Das developed explicitly for this study.[720] The patient was instructed to loudly enunciate the letters of the alphabet while keeping her lips and teeth together to minimise any head movement in the scanner.[721] It was only during the post-treatment scanning session that the patient was able to produce audible sounds in the scanner. By contrast, during the initial data acquisition, despite trying to loudly enunciate the letters, she remained mute. Interestingly, although Bryant and Das attributed the patient's speech loss to emotional motivation factors that they directly targeted through therapy, their task-based study entirely circumvented this aspect. Instead, they used an emotionally neutral vocalisation task to measure the recovery-related changes in the patient's brain activity. It is even more interesting

714 Notably, most aphonic patients, unlike those with mutism, can still produce verbal output by whispering. See Charcot, "Hysterical Mutism," 363; and Baker, "Voice Disorders," 397. Hence, as a form of speech disorder, hysterical mutism is distinct from functional voice loss, which we will discuss in the following case study. Interestingly, the clinical description of the patient in the Bryant and Das study is remarkably similar to the one Charcot had delivered in his lecture on the case of hysterical mutism. See Charcot, "Lecture 26: Mutism."

715 Patients with mutism typically retain the ability to produce "[a]utomatic phrases and utterances with minimal communicative responsibility." Baker, "Voice Disorders," 397, table 34.5.

716 Bryant and Das, "Neural Circuitry," 290.

717 Bryant and Das, 291.

718 Bryant and Das, 291. Evidently, the therapy was implicitly informed by Freud's concept of secondary gain we discussed in section 4.3.1. Interestingly, in this version, Freud's concept has apparently undergone a neurological update since, as Bryant and Das formulated it, 'the brain'—and not the subject—purportedly felt threatened.

719 Bryant and Das, "Neural Circuitry," 294. Initially, the patient could not sing in therapy. Therefore, she was asked "to imagine herself singing along with the soundtrack, including mouthing the words" until her perception of the soundtrack fused with her imagined voice. Ibid., 291.

720 Bryant and Das, 295.

721 Bryant and Das, 291–92.

to note that, although they explicitly aimed to isolate the changes in brain activity associated with speech recovery, the task they developed did not entail an articulation of any meaningful phrases or full sentences. Instead, the task consisted in voicing disconnected vowels and consonants. The authors provided no explanation for their decision to use this particular task.

Next, Bryant and Das computed fMRI activation maps for both the pre-treatment and post-treatment scanning sessions separately. Additionally, to isolate the session-specific differences, they also computed another map for the contrast between the pre-treatment and post-treatment measurements. The separately calculated maps disclosed that the vocalisation task induced a similar pattern of activation across the speech-related networks, both before and after recovery. Most significantly, this pattern included a bilateral activation in the inferior frontal gyrus (IFG), which on the left side encompasses Broca's area.[722] However, it was the map computed for the direct comparison between the pre-recovery and post-recovery sessions that disclosed statistically significant differential task-induced activations. These included higher activity in the bilateral IFG, anterior cingulate cortex (ACC), and right amygdala before treatment, as well as increased activity "at a more dorsal region of the right IFG" after treatment.[723] Bryant and Das also conducted the PPI analysis to quantify how the vocalisation task influenced the functional connectivity of the IFG with the ACC and amygdala, both before and after treatment. The resulting connectivity map showed no coupling between the regions of interest during the patient's mutism. Yet, the connectivity map computed after recovery delivered a different result. In it, the bilateral IFG showed negative connectivity with the bilateral amygdala and positive connectivity with the ACC.[724]

Drawing their imaging findings together, the authors concluded that the key insight was delivered by the fMRI maps calculated separately for each scanning session. These maps disclosed "comparable neural activation" in the left and right IFG during mutism and after speech recovery.[725] Based on these maps, the authors conjectured that throughout the patient's chronic mutism, the functional capacity of the relevant neural circuitry remained intact, so that the reason for the loss of speech had to be localised elsewhere. To localise the potential reason, Bryant and Das then turned to interpreting the changes in the connectivity patterns across the scanning sessions. They set out by quoting neuroimaging literature according to which the ACC/amygdala network is seen as "pivotal to the anxiety response" in the sense that "the ACC generally functions to regulate fear reactions in the amygdala."[726] Next, they suggested that the changes in their patient's connectivity pattern after treatment were "consistent with the notion that recovered speech was neurally associated with successful regulation of anxiety networks."[727] Conversely, they speculated that the absence of this pattern

722 As discussed in chapter 2, Broca's area has been associated with speech production since the 1860s.
723 Bryant and Das, "Neural Circuitry," 291–92.
724 Bryant and Das, 293.
725 Bryant and Das, 295.
726 Bryant and Das, 295.
727 Bryant and Das, 295.

during mutism could be attributed to the symptom-specific "dysregulated connectivity between the affected functional networks (in this case speech) and anxiety-related circuitry."[728]

But apart from the by now often repeated fact that the findings of a single-case study are not generalisable, there are several other caveats to the above seemingly clear-cut and elegant interpretation. First, Bryant and Das remained emphatically evasive about the differential activations they computed through the direct statistical comparison of the patient's pre-recovery and post-recovery fMRI data. Of the four different fMRI maps they had calculated in their study, this was the only one not visualised in the published paper.[729] Such an omission appears particularly significant since, strictly speaking, this was the very map that isolated the recovery-related changes in the patient's brain activity in statistically rigorous terms. Moreover, apart from not visualising it, Bryant and Das also wholly ignored this map in the overarching interpretation of their imaging findings I outlined above.

As I see it, the reason for this selective exclusion is that Bryant and Das were unable to account in cognitive terms for their patient's greater brain activity in the bilateral IFG, ACC and amygdala during mutism. It also appears to me that the researchers were unable to incorporate the hyperactivity of the patient's right IFG after recovery into the interpretation they had constructed for the rest of their fMRI findings. In a side comment, which is easily overlooked, Bryant and Das admitted that in the previous neuroimaging literature, apart from being associated with the speech production, the bilateral IFG, and the right IFG in particular, have been linked not only to the inhibition of motor responses but also, more specifically, to speech inhibition.[730] In other words, due to its multifunctional character, the IFG is thought to partake both in the speech and the frontal inhibitory networks.[731] The problem was that, based on the task they had used, it was "difficult to ascertain" if the recovery-related changes in the IFG's activation and connectivity patterns were attributable to speech production or to its inhibition.[732] In effect, this meant two things. First, the shifts in the brain activations across the imaging sessions were uninterpretable. Second, the authors' apparently clear-cut interpretation of the changes in the connectivity patterns is questionable. In short, the imaging findings of the Bryant and Das study were very ambiguous. This ambiguity was probably due to the researchers' choice of the experimental task that was inadequate for isolating the patient's recovery-related neuroplastic changes in the brain function.

In a more recent study, Roy et al. also set out to identify the shift in the neural activation patterns after the full recovery of a single female patient with a related yet slightly different symptom. The woman in the Roy et al. study had retained the ability

728 Bryant and Das, 295.

729 Admittedly, the published paper included the numerical table for this map listing the Cartesian coordinates and statistical values for the differential activations. Bryant and Das, 293. However, unlike the other three fMRI maps, this table was not accompanied by a figure visualising the anatomical locations of the activations listed in the table.

730 Bryant and Das, 295. See Xue, Aron, and Poldrack, "Inhibition."

731 As discussed previously, the IFG also partakes in the attentional networks. See section 4.2.2.

732 Bryant and Das, "Neural Circuitry," 295.

to produce connected speech but had a year-long history of partial voice loss, i.e., dysphonia. The central clinical feature of her symptom was "a strained high-pitched breathy voice quality with transient aphonic voice breaks."[733] In this case, the onset of the symptom was not associated with any apparent psychological factors, but seemed to have developed after a sinus infection.[734] Roy et al. attributed the dysphonia to the "dysregulated muscle activity" of the patient's larynx, which, in turn, so they presumed, was caused by aberrant "commands originating in the central nervous system."[735] Simply put, in their opinion, the ultimate cause of the patient's voice loss was a potentially reversible and still to be detected dysfunction of the brain.

Based on this diagnosis, Roy et al. decided to implement a particular form of manual therapy to rebalance the patient's aberrant use of her voice box muscles. After a single one-hour therapy session, during which her "habitual pattern of muscle misuse" was corrected, the patient regained her normal voice.[736] Roy et al. conjectured that the patient's recovery induced through the reposturing of her laryngeal muscles would be associated "with a shift in brain activations underlying voice and speech production."[737] Hence, their patient underwent the scanning before and directly after the single therapy session. This meant that the pre-recovery and post-recovery fMRI datasets in this study were acquired on the very same day.

What is of particular interest to our discussion is that although their experimental manipulation also directly engaged the speech production as in the previous study, Roy et al. chose a somewhat different approach. Instead of one, they used two tasks. One was a simple voice task that consisted of producing a single vowel 'ah' repeatedly. The other task required the patient to read aloud "declarative, emotionally neutral sentences."[738] Drawing on the previous neuroimaging literature, Roy et al. posited that, unlike simple vocalisation, the sentence reading task, "given its complexity, is arguably a more valid task to evaluate" the use of voice in speech production.[739] Therefore, they hypothesised that the sentence reading task would engage more extensive networks of brain areas than vocalisation. Having calculated the fMRI activation maps that compared the pre-treatment and post-treatment scanning sessions for each task separately, Roy et al. obtained empirical support for their conjecture. The resulting maps showed that "the overt sentence reading task was associated with greater variety and number of activation patterns" than the voice task.[740] Consequently, the rest of their study dealt exclusively with the interpretation of the recovery-related shifts in the patient's brain activity isolated through sentence reading.

Roy et al. did not perform a standard whole-brain analysis of their fMRI data. They focused instead only on ten preselected regions of interest (ROIs) that, according to

733 Roy et al., "Dysphonia," 185.

734 Roy et al., 185.

735 Roy et al., 183.

736 Roy et al., 186.

737 Roy et al., 187.

738 One example of such sentences was: "They put the dirty dishes in the sink." Similarly: "She put toothpaste on her toothbrush." Roy et al., 185.

739 Roy et al., 185. See also Xue, Aron, and Poldrack, "Inhibition," 1923.

740 Roy et al., "Dysphonia," 187.

the extant literature, are "involved in emotion and action regulation, self-evaluation, and sensorimotor control for voice."[741] The resulting fMRI map showed hyperactivity across all the ROIs in the direct comparison of the pre-treatment and post-treatment conditions. Roy et al. interpreted this activation pattern as "suggesting a role for emotion, arousal, or inhibitory mechanisms to interfere with voluntary control over phonation contributing to disordered voice."[742] Based on this map, Roy et al. hypothesised that during her symptomatic state, the patient may have been "locked in an aberrant default sensorimotor neural program."[743] This programme entailed, so they speculated, the overactivation of the PAG, hypothalamus, amygdala, and ACC, i.e., the "limbic system structures involved in emotion regulation and in particular identification of threat signals."[744] The overactive limbic system, in turn, triggered the inhibition of laryngeal muscle activity, thus suppressing ongoing voice and speech production.[745]

In effect, whereas Bryant and Das vaguely implicated the potential role of prefrontal top-down inhibitory regions (i.e., the right IFG) in hysterical speech loss, Roy et al. explicitly postulated the key contribution of a different type of inhibitory mechanism that was mediated by "bottom up alerting to response-relevant cues."[746] However, Roy et al. also had to admit that, based on their imaging results, they could not explain how exactly these different brain regions interacted to perpetuate the voice disorder. Nor could they delineate "the precise mechanism of action" through which the treatment succeeded in re-establishing "the neural signature for normal voice."[747]

This brings us to the third example of single-case studies in which researchers used a task intended to directly engage the functionally affected brain areas thought to underpin the hysterical symptom of interest. In this study, Dogonowski et al. examined a single patient's therapy-induced recovery from the acute onset of one-sided conversion paralysis of hand.[748] The authors provided no details about the therapy except mentioning that the "patient entered a rehabilitation programme once weekly."[749] Typically, "rehabilitation strategies aim to help the patient to establish normal control of movement through physiotherapy, occupational therapy or speech therapy."[750] We can thus presume that a form of physiotherapy focused on retraining motor function was a central part of the treatment.

---

741 Roy et al., 186. Specifically, Roy et al. chose the "areas involved in the freeze response to fear (PAG [periaqueductal gray]), emotion processing (amygdala, hypothalamus, hippocampus), self-awareness (BA 10 [Brodmann area 10]), top-down emotion regulation (dlPFC, mPFC [dorsolateral and medial prefrontal cortex]), conflict monitoring and initiation of behavior (ACC, MCC [anterior and midcingulate cortex]), and premotor and motor control (SMA [supplementary motor area] and sensorimotor cortex)." Ibid., 191.

742 Roy et al., 192.

743 Roy et al., 192.

744 Roy et al., 191.

745 Roy et al., 192.

746 Roy et al., 192.

747 Roy et al., 192.

748 Dogonowski et al., "Recovery."

749 Dogonowski et al., 270.

750 Espay et al., "Current Concepts," 1138.

Dogonowski et al. were primarily interested in tracing the recovery-related activity changes in the patient's motor system. Accordingly, they "chose a simple sensorimotor task devoid of cognitive or emotional content to minimise the functional engagement of prefrontal or limbic areas."[751] The task consisted of cued finger tapping that involved either a single or both hands, one of which was unaffected. Yet Dogonowski et al. introduced one crucial innovation. They collected the patient's fMRI data not only before and after her full recovery but also throughout the process of her gradual treatment-induced symptom improvement. The measurements took place at five different time points. The first measurement was performed seventeen days and the last nine months after the onset of partial paralysis.[752] Each time, the researchers also quantitatively assessed the patient's behavioural task performance and, additionally, collected a resting-state fMRI dataset.

The analysis of the behavioural data showed that both the bimanual and the one-sided tapping with the affected hand progressively improved across the five sessions. The same data also confirmed that, as expected, the one-sided task performance with the unaffected hand remained unchanged. The researchers then analysed the serially collected fMRI data to find out in which brain areas the changes in task-related activity across the five sessions scaled linearly with the symptom improvement for each type of tapping separately. The resulting fMRI map showed that the dorsal premotor cortex on both sides of the patient's brain was deactivated in the acute symptomatic phase.[753] During the subsequent symptom resolution, this very same area exhibited increased task-based activation in proportion to motor recovery. Additionally, the right medial prefrontal cortex (mPFC) exhibited the opposite pattern of dynamic change—its initially increased activation in the acute phase gradually decreased with recovery.[754] Significantly, this aberrant pattern of brain activity that normalised parallel to the clinical remission of the symptom was present "during tapping with the affected or non-affected hand as well as during bimanual finger-tapping."[755] The crucial implication of this finding is that brain dysfunction underlying one-sided hysterical paralysis is not limited to the affected limb but also has an impact on the apparently healthy side of the body.[756]

Next, by grounding their inference in the previously published studies, Dogonowski et al. conjectured that the overactivation of the mPFC during the patient's acute phase might reflect the aberrant triggering of its otherwise normal role as a 'veto' region.[757]

751 Dogonowski et al., "Recovery," 270.

752 Dogonowski et al., 270.

753 Dogonowski et al., 272.

754 Dogonowski et al., 272.

755 Dogonowski et al., 271.

756 Although Dogonowski et al. did not explicitly state this, their finding has called into question the validity of all previous fMRI studies of one-sided paralysis that were based on the within-patients comparison between the task-based activations for the affected and unaffected side of the body. All such studies, including the two case studies discussed in the previous chapter, are grounded in the assumption that the apparently healthy side of the patients' bodies functions normally at the neural level.

757 Dogonowski et al., 272.

Dogonowski et al. thereby explicitly drew on the influential model of intentional action proposed by Brass and Haggard in 2008. This model distinguishes three major components of intentional action: "a component related to the decision about which action to execute (what component), a component that is related to the decision about when to execute an action (when component), and finally the decision about whether to execute an action or not (whether component)."[758] Using fMRI, Brass and Haggard came to the conclusion that the mPFC controlled "the 'whether' component of intentional action which may involve a final check whether or not the action goes ahead."[759] Hence, quoting Brass and Haggard, Dogonowski et al. suggested that during the acute phase of hysterical paralysis, the mPFC executed an excessive top-down "endogenous inhibition of [the] intentional action," which had been generated in the already functionally deficient dorsal premotor cortex.[760]

Significantly, contrary to the two studies discussed above, Dogonowski et al. implicated yet another type of motor inhibition as the potential neural substrate of a hysterical symptom. To substantiate this hypothesis, Dogonowski et al. further calculated both task-based and resting-state connectivity maps using the aberrantly activated areas as two regions of interest. Interestingly, the patient's clinical improvement was associated with increased task-based connectivity between mPFC and dorsal premotor cortex. The resting-state connectivity, however, showed precisely the opposite pattern.[761] In the end, the researchers were unable to provide an unambiguous interpretation as to why different imaging and analysis methods appeared to uncover mutually conflicting patterns of recovery-related neuroplastic changes. Instead, they concluded that their results "illustrate that the relationship between task-associated activation, task-based and resting-state functional connectivity is not straightforward and needs to be addressed further in future prospective fMRI studies."[762]

In sum, my analysis thus far in this section has delineated the discrepancies across the therapy-induced neuroplastic changes in the patients' brain activity patterns isolated by each of the three single-case studies we discussed. I have highlighted the interpretational ambiguities of the studies' seemingly straightforward imaging findings. I have also underscored how, although they all addressed different types of motor symptoms, from voice and speech loss to limb paralysis, each study more or less directly attributed the patient's acute symptomatic state to aberrantly activated inhibitory neural processes.[763] We have also seen that the exact type of the presumed inhibition process, and the brain regions thought to subserve it varied considerably from study to study. In all likelihood, these discrepancies can, at least in part,

758 Brass and Haggard, "What, When, Whether," 319.

759 Dogonowski et al., "Recovery," 273.

760 Dogonowski et al., 273.

761 Dogonowski et al., 273.

762 Dogonowski et al., 273.

763 In effect, these longitudinal studies have taken up the still unresolved debate about the potential role and the nature of inhibitory processes in motor symptoms of hysteria. As discussed previously, this debate has been going on in the interpretation of findings from cross-sectional fMRI studies of hysterical symptoms over the last twenty years. See sections 3.5.3, 4.1.1, and 4.1.2.

be attributed to notable differences in the type and chronicity of the symptoms examined. Additionally, there were sizeable disparities in the time scale of each study's longitudinal framework that varied from a few hours to several months. Nevertheless, I think that the main cause of the mutually contradictory findings must be sought elsewhere.

It appears to me that the problem lies in using the tasks imported from cross-sectional studies and merely transposing them into the longitudinal context to first directly engage the compromised motor function during the symptomatic state and then again after that function has been successfully restored through therapy. This approach is too broad and unconstrained to isolate recovery-related symptom-specific changes in the patient's brain activity. Various studies we discussed so far have repeatedly suggested that hysterical symptoms arise from widely distributed multi-component neural disturbances. If we are to take their findings seriously, then we must also presume that the temporary remission of hysterical symptoms, and even more so their full clinical recovery, necessarily encompasses a highly complex multi-stage process. Hence, to delineate the changes in the brain activities that underlie such a complex process, it might be necessary to use experimental tasks that break this process down into its potential components. This, in turn, would require researchers to make more specific hypotheses about the neurocognitive components underpinning recovery and to develop more targeted tasks for their investigation.

A potential step in this direction can be found across several fMRI studies that, unlike the three examples analysed above, chose to examine recovery-related changes in the patients' brain activity by taking a different approach to experimentally framing the remitted hysterical symptoms. Instead of broadly engaging the affected functions, several studies narrowed the focus by using tasks that targeted the hypothesised, symptom-relevant disturbance of emotion processing.[764] In other words, these studies experimentally operationalised the hypothesis that dysfunctional emotion processing underpins hysterical symptoms and that the associated patterns of aberrant brain activity and connectivity could be measurably modified through a successful therapeutic intervention.

For example, de Greck et al. investigated the therapy-induced changes in the neural processing of rewarding external events in patients with multiple somatic symptoms.[765] The treatment of choice in this study was multimodal psychodynamic psychotherapy. As explained by de Greck et al., this type of psychotherapy "aims to provide understanding of the stress-causing conflicts and to enable patients to utilize other coping strategies" by restoring "the balance between the processing and emotional valuing of internal and external stimuli."[766] To identify the effects this therapy had elicited at the neural level, de Greck et al. deployed a so-called reward anticipation task. In this task, the participants were required to react quickly to a visual "target stimulus in order to

764 See de Greck et al., "Reward"; Espay et al., "Neural Responses"; and LaFaver et al., "Before and After."

765 De Greck et al., "Reward," 298.

766 De Greck et al., 297.

obtain monetary rewards."[767] However, the task also entailed a control condition during which quick responses were decoupled from any positive outcome. In the first scanning session, de Greck et al. used this task to compare how the ability to emotionally evaluate external stimuli differed at the neural level between twenty patients with acute symptoms and healthy controls. In the second session, de Greck et al. used the same task to examine how the aberrant brain activity changed in fifteen patients after psychotherapy, which had reduced not only their somatic symptoms but also the comorbid depression scores.[768]

The fMRI maps computed for the data from the first session showed that the patients with acute symptoms as opposed to healthy controls exhibited "decreased responsiveness of a set of brain regions crucially involved" in the neural differentiation between rewarding and non-rewarding external stimuli.[769] Interestingly, despite such differences at the neural level, both patients and healthy controls reported similar feelings of contentedness during the reward task. The activation map based on the data from the second session revealed that the successful therapy induced "a significant normalization" of the patients' brain activity in the regions involved in processing external rewarding stimuli.[770] Based on these maps, de Greck et al. concluded that, during the acute phase, patients with multiple somatic symptoms have a diminished ability to evaluate the emotional salience of external stimuli at the neural level. They further argued that the therapeutic intervention resulted in the re-balancing of the patients' "disturbed reward processing of external stimuli."[771]

Their specific finding aside, another aspect of the de Greck et al. study is of particular importance to our discussion. By shifting the focus to using emotional instead of symptom-specific tasks to examine the recovery-related neuroplasticity, Greck et al. were not only able to include subjects with more heterogeneous symptoms but also to perform a direct comparison between patients and healthy controls. This comparison permitted them first to isolate the aberrant pattern of activity that was specific to patients and then examine how this particular neural pattern changed as the effect of therapy. Hence, this shift of focus enabled a move away from single-case to more generalisable group studies with more complex levels of comparisons. However, despite such significant advantages, this approach is not without its disadvantages. As in all task-based studies analysed so far, in this case, too, the extent to which the resulting fMRI maps are able to isolate the potential recovery-related neuroplastic changes hinges on the kinds of neural and cognitive processes that the implemented task is designed to isolate. Since not much is known about the aberrant emotion

767 Thevisual stimuli consisted of a black circle within which another white circle occupied different positions. Each position indicated one of the three possible results—gaining money, losing it, or achieving no monetary outcome. Every trial required the subject to press a button "within a certain time during the presentation of the target image." De Greck et al., 299. Depending on the trial type and their ability to respond within the given time, the subject could win, lose, or neither win nor lose.

768 De Greck et al., 300.

769 De Greck et al., 304. These regions included the primary somatosensory cortex and thalamus. Ibid.

770 De Greck et al., 296.

771 De Greck et al., 303.

processing underlying hysterical symptoms, to begin with, different studies examining therapy-induced recovery have tested different types of emotional tasks. This, in turn, has led to mutually inconsistent imaging findings.

For example, a study by LaFaver et al. examined emotional and motor responses in a group of nine patients with mixed positive motor symptoms before and after a one-week rehabilitation treatment. This study produced findings that diverged from those by de Greck et al.[772] Importantly, the treatment used in the de Greck et al. study consisted entirely of a psychological intervention. By contrast, the patients in the LaFaver et al. study underwent a short-term rehabilitation programme that placed a distinct focus on "relearning normal movement control" through systematic physical training, with only a relatively limited concurrent use of psychotherapy.[773] Moreover, in their fMRI study, LaFaver et al. also used a different emotional task to determine if their motor retraining treatment had led to a reorganisation of neutral patterns in hysteria patients. Called an emotional go/no-go task, it required the subjects to either respond to a stimulus by pressing a button (go trials) or to withhold their response (no-go trials). During both types of trials, the subjects viewed standardised images of the facial expressions of basic emotions (i.e., fearful, happy, and neutral). The purpose of this task was to examine if and how the implicit processing of basic emotions interferes with motor control.[774]

The clinical assessment of the patients following the treatment demonstrated that the therapy resulted in a significant improvement. In accordance with the clinical changes, the whole-brain fMRI maps that compared pre-treatment and post-treatment measurements indicated a change "from stimulus driven 'bottom-up' activity to 'top-down' control of motor regions."[775] In neuroanatomical terms, the pattern of activation shifted from the ventral visual cortices, cerebellar vermis, and hippocampus "to caudate, putamen, premotor, pre-SMA (supplementary motor area), and SMA."[776] Additionally, the fMRI map obtained through seed-based connectivity analysis showed that the symptom improvement correlated with the increased functional interaction between the amygdala, considered to be part of the 'emotional circuitry,' and the motor planning regions. LaFaver et al. attributed the registered changes in the activity pattern to a shift from the patients' pre-treatment reactive focus on incoming stimuli to a more goal-

772 LaFaver et al., "Before and After." The paper by LaFaver et al. was published in 2018 as a report of the conference presentation that provided insights into, at the time, still ongoing study. The completed study was published two years later as Faul et al., "Inpatient Rehabilitation." My analysis focuses on this initial report because the cut-off point for my analysis in this book is December 31, 2019.

773 Jacob et al., "Motor Retraining," 1165. "The treatment team consists of a neurologist, physiatrist, psychologist, physical, speech, and occupational therapists and a social worker. Patients are admitted to the program on Sunday evening and discharged on the following Saturday. Therapy takes place Monday through Friday, consisting of 3 hours per day of physical, occupational, and speech therapy (if applicable) and 1 hour of psychotherapy." Ibid.

774 For a detailed description of the task, see Faul et al., "Inpatient Rehabilitation," 2–3, article 111125.

775 LaFaver et al., "Before and After," Conclusions.

776 LaFaver et al., Results.

directed behaviour after recovery.[777] Notably, their interpretation thus contradicted the finding by de Greck et al., according to which the recovery resulted in the increased neural responsiveness to external stimuli. Conceivably, these contradictions arose both from the different types of emotional tasks used in the two studies and the different types of therapeutic interventions to which their patients were exposed.[778] How to reconcile such discrepancies remains an open question.

Moreover, a recent fMRI study pointed to yet another potential problem that faces all studies using emotional tasks to identify neuroplastic changes associated with the therapy-induced recovery from hysterical symptoms. This additional problem lies in the fact that most hysteria patients have comorbid psychiatric conditions such as depression, anxiety, panic disorder, and different phobias.[779] It is highly likely that currently used therapeutic approaches aimed at treating hysterical symptoms also affect the accompanying psychiatric conditions. This is especially the case in studies that deploy some form of psychological intervention, such as cognitive behavioural therapy. Consequently, some of the shifts in the patients' brain activity isolated through the comparison between the pre-treatment and post-treatment fMRI data "may be related to changes in associated psychiatric comorbid conditions rather than changes in the severity" of the hysterical symptom under investigation.[780]

But regardless of such unresolved questions, I would like to draw attention to one other aspect of the LaFaver et al. study. In effect, LaFaver et al. generated preliminary imaging findings in support of the conjecture that systematic retraining of voluntary movement through targeted physical exercise not only leads to symptom amelioration but also elicits changes in the hysteria patients' neural activity. As discussed in chapter 1, this very same conjecture informed Charcot's development and use of the dynamometric exercise as a form of rehabilitation therapy. Accounting for the apparent success of this therapy and using images to prove it, Charcot hypothesised that the retraining of motor control resulted in the normalisation of the local neural activity in the motor and sensory cerebral centres and the re-establishment of their mutual hierarchy.[781] Admittedly, based on their imaging findings, LaFaver et al. posited a somewhat different mechanism. As we have seen, they suggested that the retraining

777 LaFaver et al., Results.

778 Interestingly, the authors of another study that used resting-state fMRI to investigate the effects of cognitive behavioural therapy on a group of patients with chronic somatoform pain came to a comparable conclusion as LaFaver et al. See Yoshino et al., "Therapy," 1153. Specifically, although they deployed a different treatment approach than the one used by LaFaver et al., focused on an entirely different hysterical symptom, and used the resting-state instead of a task-based fMRI method, Yoshino et al. also concluded that the therapy-induced improvements in their patients correlated with the reinforcement of the top-down neural processing. Despite implicating different areas of the prefrontal cortex than LaFaver et al., Yoshino et al. also argued that successful treatment leads to the normalisation of the patients' prefrontal activity. Moreover, in their sample of patients with chronic pain, Yoshino et al. found that the therapy-induced recovery additionally correlated with the normalisation of functional connectivity within the sensorimotor network. Ibid., 1148.

779 See Espay et al., "Neural Responses," e1792, table 1.

780 Espay et al., e1795.

781 For details, see section 1.3.2.

of voluntary movement resulted in the normalisation of the previously aberrant interactions between motor and emotion circuitries, including the shift from bottom-up to top-down neural processes. Yet, despite the differences in the implicated brain regions, the two proposed mechanisms have one significant point in common. Both Charcot and LaFaver et al. essentially argued that a targeted physical intervention could reinstate the normal hierarchical organisation of multiple functions that underpin the execution of voluntary movement at the neural level.

Finally, a potentially promising new approach to the concept of recovery-related neurosplasticity has recently begun to take shape within the fMRI research on hysteria. By the end of 2019, it was implemented in only three published studies—LaFaver et al., Diez et al., and Yoshino et al. In each case, this novel approach served to expand the main imaging findings of these studies that we already discussed.[782] This nascent approach appears to me significant because, as I will show, it frames the recovery-related functional neuroplasticity in different temporal terms by emphasising its prognostic potential. For example, in the LaFaver et al. study, the researchers submitted the pre-treatment fMRI data to an additional statistical analysis. In doing so, they aimed to identify the pre-treatment task-based activation and connectivity patterns that positively correlated with quantified measures of the patients' post-treatment symptom recovery. The resulting map indicated that, across their nine subjects, increased "activation in pre-SMA [pre-supplementary motor area] and motor cortices at pre-treatment scanning predicted improved [treatment] outcomes."[783]

Similarly, Diez et al. correlated the prospectively collected six-month outcome measures of patients' therapy-induced clinical improvement with their pre-treatment resting-state link-step functional connectivity maps.[784] Their aim was to determine how individual differences in the patients' altered information flow across neural systems during the acute phase were related to variations in the post-treatment recovery levels. This analysis showed that the subgroup of patients with the most pronounced recovery had increased stepwise connectivity between the amygdala and insula in the pre-treatment scanning. Diez et al. speculated that this pattern "may be a marker of preserved emotional awareness that potentially aids treatment response."[785] Finally, Yoshino et al. assessed correlations between the treatment-induced symptom amelioration and the pre-treatment resting-state connectivity strength in twenty-nine patients with chronic somatoform pain who underwent a 12-week cognitive behavioural therapy (CBT).[786] The researchers thus determined that lower resting-state functional connectivity strength in the dorsal posterior cingulate cortex (PCC) prior to treatment

782 For the discussion of the main findings in the Diez et al. study, see the previous section. For the discussion of the main findings in the Yoshino et al. study, see footnote 778 above.

783 LaFaver et al., "Before and After," Results.

784 Significantly, in this study, the researchers did not collect any post-treatment fMRI data but only quantified the clinical changes in the symptom severity six months after the initial resting-state scanning. Treatments were individualised and included a combination of cognitive-behavioural therapy and physiotherapy. Diez et al., "Fast-Tracking," 930.

785 Diez et al., "Fast-Tracking," 936.

786 Yoshino et al., "Therapy," 1148.

was predictive of the greater "improvement of clinical symptoms via CBT" in patients with chronic pain.[787]

As these three examples demonstrate, the novel analytical approach entails the following unspoken implication. Although the still unknown underlying neuropathology of hysterical symptoms is viewed as potentially reversible, the adaptive therapy-induced neuroplasticity required for recovery is neither physiologically unconstrained nor exclusively dependent on the adequacy of the treatment modality. In fact, I argue that this nascent search for prognostic imaging indicators is informed by the assumption that the brain's potential for recovery in a hysteria patient is constrained by the nature and spatial extent of the initial symptom-specific functional neuropathology. Hence, this strand of hysteria research focuses on identifying—in purely biological and thus quantifiable terms—what could be designated as the potential capacity for neuroplasticity of a patient's brain. The underlying hypothesis is that such capacity for therapy-induced neuroplasticity can be determined by isolating a particular pattern of the patient's pre-treatment activity which correlates with post-treatment recovery. If discovered, the pattern thus isolated could then, at least in principle, be used to predict the level of responsiveness to treatment in other patients who, prior to therapy, also exhibit the same neural pattern.

My impression is that this novel approach is potentially reductive, as it disregards the possible role in the recovery of various subjective and socio-cultural factors that are not measurable during pre-treatment fMRI scanning. These factors include, for instance, patients' motivation and willingness to partake in the treatment, their trust in doctors and the level of social, economic and personal support available to them during the therapy. Yet, there is another aspect of this approach that I find particularly interesting. Unlike other analyses we have addressed in this chapter, the new approach does not entirely average out the individual differences in neural patterns among the study participants. Instead, it explicitly aims to first identify and then relate patients' different neural patterns to their divergent levels of post-treatment recovery. In this type of analysis, the differences in neural patterns among the patients are not viewed as mere noise. Rather, they are treated as the information of interest that holds the potential to predict the patients' future recovery.

***

To conclude my analysis in this section, it can be said that despite the methodological inconsistencies delineated above, after a prolonged period of dormancy, the action-guiding concept of recovery-related neuroplasticity has gradually advanced to the forefront of the current fMRI hysteria research. The growing epistemic relevance of this concept may be attributed to its double capacity to guide research in two distinct directions. First, it enables researchers to attempt to localise the hysterical symptoms' underlying neuropathology by retrospectively measuring recovery-related neuroplastic changes. And second, it also permits researchers to characterise how the prospective potential for treatment-induced reversibility differs across hysteria

787 Yoshino et al., 1148.

patients. Moreover, I think that this latest development of explicitly addressing potential neurobiological differences among individual patients is particularly relevant. In effect, this development is illustrative of the more general, gradually increasing conceptual sophistication of the fMRI exploratory research on hysteria, whose trajectory during the first two decades of the twenty-first century I have traced in this chapter.

Overall, this chapter has aimed to show that instead of arising from an undirected process of trial-and-error, the articulation of new epistemic insights in fMRI-based hysteria research has relied on the systematic experimental testing of a set of preliminary action-guiding concepts. On the one hand, these concepts have guided the selection of experimental parameters, thus informing the production of fMRI maps. On the other hand, these concepts have, in turn, been reshaped by the resulting image-based findings. Also, I have underscored how, to use Ludwig Jäger's term, this process of recursive semantic transcription has produced significantly different effects across the individual action-guiding concepts analysed in this chapter.[788]

As a result of this transcription, some of these preliminary concepts—such as malingering, sense of agency, and attention—have been experimentally implemented with increasing refinement over time, with each subsequent study building upon the imaging findings of those preceding it. Despite initially appearing epistemically promising, other action-guiding concepts, such as hypnosis and idiosyncratic traumatic memories, proved too ambiguous or too challenging to frame within the procedural logic of an fMRI experiment. The potential epistemic productivity of concepts such as resting-state connectivity and aberrant emotion processing remains to be determined by future research since the fMRI studies that have deployed them so far have delivered insufficiently consistent results. Such inconsistent results notwithstanding, both of these action-guiding concepts currently appear promising. We have also seen that not all concepts have followed a straight trajectory. This has been exemplified by the recovery-related neuroplasticity that, after a prolonged period of dormancy, has recently re-emerged as a potential "generator of surprises."[789]

Importantly, my in-depth analysis in this chapter has demonstrated that fMRI maps have played a constitutive role in the still ongoing gradual concretisation of the initially abstract action-guiding concepts by empirically relating them to particular hysterical symptoms. It is through and with images that researchers have explored the applicability of these preliminary theoretical and empirical concepts to hysteria. In some cases, the resulting images disclosed the epistemic deficits or vagueness of some of these action-guiding concepts in relation to hysteria. In other cases, researchers have succeeded in experimentally operationalising the action-guiding concepts with increasing specificity.

In sum, it seems to me that the dynamic process of systematically testing multiple action-guiding concepts, which not only frame the experimental image-based exploration of hysteria but are also continually changed by it, enables the current fMRI research to go about their business of gradually articulating the potential neural basis of

788 Jäger, "Epistemology of Disruptions," 80–82.

789 Rheinberger, *History of Epistemic Things*, 31.

hysterical symptoms. In fact, I suggest that this multiplicity of mutually complementary conceptual perspectives, some of which, as we have seen, can be fruitfully combined in a single study, is what currently makes this research field particularly vibrant.

Admittedly, as I have emphasised repeatedly in this chapter, all the insights that have emerged so far from the fMRI exploration of hysteria's underlying neural mechanisms are still preliminary, highly fragmentary, and even partly contradictory. It is, therefore, indisputable that, by the end of the second decade of the twenty-first century, the fMRI-based research has not been able to find any definitive, clinically implementable answers to the medical mystery of hysteria. And despite the currently high hopes among researchers, whether the fMRI-based research will ever be able to find such answers to hysteria remains to be seen. Yet, I have aimed to show that, within a decade and a half of its existence, this image-based research has continually grown and matured. As a result, those carrying out this research have learned to use fMRI to ask progressively more complex and fine-grained questions. In the process, they have managed to endow present-day manifestations of hysteria—under whichever current, continually changing terminology these heterogeneous somatic symptoms are grouped—with the status of a genuine disorder that arises from an as yet unknown but in principle reversible functional disturbance of the brain. It appears to me that this alone is no small achievement. And this achievement seems even more impressive if we consider that until recently, medical professionals have doubted the reality of these symptoms and accused the patients exhibiting them of malingering.[790]

Finally, a superficial observer might sceptically contend that contemporary researchers are merely using fMRI as a state-of-the-art imaging technology to illustrate and thus belatedly, and possibly even falsely, legitimise Charcot's old views on hysteria. The same observer could then go on to argue that these long discarded views include Charcot's claim that hysteria is attributable to a potentially curable functional brain lesion, is similar to hypnosis, and entails involuntary symptoms distinct from feigning. However, while underscoring multiple parallels and a shared focus on the image-based experimental search for hysteria's underlying neural mechanism, my analysis has aimed to show that the present-day research is beginning to produce new and unexpected insights. Moreover, as I have emphasised throughout this chapter, these new insights have reached the level of not only technological but also conceptual sophistication that has long surpassed what was possible in Charcot's time. The current, although still fragmentary and preliminary, findings suggest that the neural basis of hysterical symptoms cannot be reduced to isolated inhibition of one or more brain centres, as Charcot had conjectured. Instead, at the neural level, the symptoms appear to involve dynamic interactions among functional disturbances that simultaneously affect several anatomically widespread multifunctional brain networks. Hence, the fMRI research is not only creating a considerably more complex picture of hysteria or, to use the current medical terminology, functional neurological disorder. Just as importantly, this new image-based research has also begun to fill in the details that had eluded Charcot.

790 For a detailed discussion of the predominance of such dismissive attitude of medical professionals towards hysteria patients in the second half of the twentieth century, see section 2.2.2.