Chapter 11
Clinical Neuroscience Meets Second-Person Neuropsychiatry

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Abstract Disturbances of social and affective processes are at the core of psychiatric disorders. Together with genetic predisposing factors, deprivation of social contact and dysfunctional relationships during development are some of the most important contributors to psychiatric disorders over the lifetime, while some developmental disorders manifest as aberrant social behavior early in life. That the cause of mental illness is rooted in the brain was long held as a truism, yet finding the causes for and neurobiological correlates of these conditions in the brain has proven and continues to be difficult (Venkatasubramanian G, Keshavan MS, Ann Neurosci 23:3–5. https://doi.org/10.1159/000443549, 2016). In clinical practice, psychiatric disorders are diagnosed based on categorical manuals, such as the DSM and ICD, which form a useful guide for clinical diagnosis and interventions. Yet, understanding the specific neural mechanisms leading to or characterizing distinct psychiatric conditions through this categorical approach has been slow (see, for example, Lynch CJ, Gunning FM, Liston C, Biol Psychiatry 88:83–94. https://doi.org/10.1016/j.biopsych.2020.01.012, 2020). Findings in the brain often do not seem to lend support to common mechanisms for the defined disorder categories. This is not particularly surprising because, in these diagnostic manuals, multiple combinations of symptoms can often lead to the same diagnosis, which is reflected in highly variable phenotypes of psychiatric disorders.

Keywords Psychiatric disorders · Second-person neuroscience · Neuropsychiatry

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Introduction

Disturbances of social and affective processes are at the core of psychiatric disorders. Together with genetic predisposing factors, deprivation of social contact and dysfunctional relationships during development are some of the most important contributors to psychiatric disorders over the lifetime, while some developmental disorders manifest as aberrant social behavior early in life. That the cause of mental illness is rooted in the brain was long held as a truism, yet finding the causes for and neurobiological correlates of these conditions in the brain has proven and continues to be difficult (Venkatasubramanian & Keshavan, 2016).

In clinical practice, psychiatric disorders are diagnosed based on categorical manuals, such as the DSM and ICD, which form a useful guide for clinical diagnosis and interventions. Yet, understanding the specific neural mechanisms leading to or characterizing distinct psychiatric conditions through this categorical approach has been slow (see, for example, Lynch et al. 2020). Findings in the brain often do not seem to lend support to common mechanisms for the defined disorder categories. This is not particularly surprising because, in these diagnostic manuals, multiple combinations of symptoms can often lead to the same diagnosis, which is reflected in highly variable phenotypes of psychiatric disorders. Coupled with the complexity of the brain and its capacity for compensating regional disturbances through plastic changes makes it harder still to find causes and neural mechanisms of heterogeneous disorder labels. Moreover, evaluating the low-level contributors to psychiatric disorders is complicated as animal models for psychiatric conditions often cannot capture the complexity of these disorders in humans.

Recently, calls have been made for transdiagnostic approaches, such as the Research Domain Criteria (RDoC) framework (Insel et al., 2010), where mental illness is approached through specific behavioral domains rather than lists of specific symptoms and diagnostic labels. However, the majority of clinical research still relies on the categorization of patients, and even studies explicitly applying the RDoC framework to analyze neuroimaging data have mainly focused on finding correlates for a limited subset of the domains (Carcone & Ruocco, 2017). To address the variability of disorder phenotypes and to delineate particularly relevant transdiagnostic domains, a focus on social and affective processes relevant for mental health and illness appears to be crucial for improving our understanding of the brain basis of psychiatric disorders in a way that maximally benefits the patients. This is motivated by the insight that social impairments are some of the most debilitating facets of psychiatric disorders and the conceptual consideration that ascriptions of psychopathology always make reference to intersubjective conventions, which has led to the construal of psychiatric disorders as "disorders of social interaction" (Schilbach, 2016).

In this chapter, we will outline major approaches of studying the brain basis of psychiatric disorders, mainly focusing on our own work and related functional magnetic resonance imaging (fMRI) studies while briefly considering evidence from structural and brain stimulation studies as well. Furthermore, we will discuss recent methodological developments inspired by the above-described focus on social interaction, which has been described as a possible convergence of clinical neuroscience and psychiatry that could be described as the development of a second-person neuropsychiatry. This development highlights the importance of quantitatively measuring behavioral characteristics of patients during real-life social interaction and moving toward studying active behavior in addition to passive processing of social and affective information (Lahnakoski et al., 2020; Schilbach, 2019). Finally, we will consider when and why it is important to measure also the brain function of two (or more) people during real-time interaction and how the quantification of behavior becomes even more important under such complex conditions.

Structural Abnormalities and Functional Connectivity Correlates of Psychiatric Disorders

If we follow the long-standing logic that psychiatric disorders are "disorders of the brain" (Insel & Cuthbert, 2015), it is reasonable to assume that these disorders are reflected as physical and functional abnormalities in the brains of the affected individuals. In some cases, such direct links exist, as witnessed by specific deficiencies or behavioral alterations due to brain injury and lesions in specific brain areas. Brain lesions can also lead to psychiatric symptoms in some cases, and, for example, mood disorders are often reported after traumatic brain injury. Yet, findings on specific, focal abnormalities appear to be inconclusive for most psychiatric conditions. One notable exception is a focal target which is a region in the subgenual cingulate cortex that, when stimulated intracranially, can lead to a reduction of symptoms at least in some patients suffering from treatment-resistant depression (Mayberg et al., 2005). This effect is likely not mediated only by changes in local activity, but in the way this region modulates activity in other brain regions through its connections.

In addition to studying focal differences, structural abnormalities of white matter bundles or functional hubs of the brain, i.e., brain regions with a high number of connections, can disturb the functional architecture of the brain. This is clearly visible in some neurological conditions, such as multiple sclerosis that affects the myelin sheath of neurons, thereby disturbing the electrical conduction of signals between brain regions. Functional connectivity, usually measured through temporal correlations of hemodynamic activity with fMRI, is thought to reflect the organization of brain connections and their functional integration. Repeatable patterns of connectivity have been produced in a multitude of studies reflecting plausible functional networks. Often, this connectivity is studied in the absence of a task, with the (implicit or explicit) assumption that the connectivity reflects relatively stable properties underlying anatomy and physiology. Indeed, the effects of task-induced activity on the functional connectivity patterns are reasonably subtle compared with the large-scale network structure (Gratton et al., 2018; Simony et al., 2016). Some evidence exists that reliable group-level differences exist in psychiatric disorders, such as autism spectrum disorder (Holiga et al., 2019) across multiple studied populations. Yet, the variability between individuals in local connectivity measures tends to be high both in patients and in control populations highlighting the difficulty of finding common neural underpinnings for these disorders. Moreover, the temporal fluctuations of connectivity have recently gained more interest leading to an ongoing debate on whether state transitions and meta-states of connectivity at shorter timescale are a reliable or a more sensitive predictor of psychopathology than time averaged connectivity or, alternatively, an artifactual property of the analyses methods on slow and noisy signals.

Recently, other approaches looking at more global network or subnetwork properties, rather than local differences, have been gaining more attention. For example, differences in the subnetwork structure of functional networks including limbic regions have been reported that seem reliable across samples both during resting state and movie viewing paradigms (Glerean et al., 2016). However, the implications of these findings at the level of an individual remain unclear. Most network analyses rely critically on thresholding of the connectivity matrices (Garrison et al., 2015), and network properties can change considerably by a small change in the selected threshold. This can be alleviated, for example, by using relative thresholds (Garrison et al., 2015) or considering different ranges of connectivity values separately rather than setting a single threshold (Bassett et al., 2012), which can help in detecting connectivity patterns that are predictive of psychopathology.

One recent development has combined lesion studies with connectivity measures, where functional connectivity in patient groups sharing similar symptoms yet having distinct focal brain lesions suggests the connectivity of the lesioned areas may be particularly important to determine the functional consequences for the patients. For example, two aspects of "free will," volition and agency, appear to be differentially affected depending on the connectivity of the lesion site (Darby et al., 2018), with the former being associated with lesions in regions that connect to the anterior cingulate cortex and the latter with regions connecting to the precuneus. These results suggest that aberrant structure or function of different sets of brain regions may potentially have common effects through their connections in a region that is not directly affected by the lesion. However, whether these findings prove helpful for patients suffering from psychiatric disorders remains unclear.

Importantly, it seems that differences in functional brain networks, compared to a healthy population, are highly overlapping between multiple psychiatric disorders. Indeed, rather than being disorder-specific, measures of general level of psychopathology, the so-called p factor (Caspi et al., 2014), can often explain much of the neuroimaging findings. It has been argued that there may be a common underlying contributor that predisposes individuals to developing a range of psychiatric disorders, which may also be reflected in the overlap of genetic findings across psychiatric disorders, which is supported by recent findings of shared neurobiological and cellular mechanisms of at least six different psychiatric disorders reported by the relevant working groups of the Enigma project (Patel et al., 2020). Controlling for these disorder-general correlates of psychiatric disorders may help in pinpointing the disorder-specific mechanisms. However, if the brain is studied through static anatomical and connectivity properties without any behavioral readouts beyond a categorical label, understanding the significance of these findings to the social life and general well-being of patients is not straight forward.

Stimulation-, Task-, and Model-Based Studies

Most of social cognitive neuroscience, particularly neuroimaging studies, have focused on simplified stimulus- and task-based designs. The goal here is to isolate and systematically manipulate particular constituent features or task components that together could enable more complex tasks to be performed. In a clinical context, one might then compare how strongly particular brain regions are activated by a given task across different diagnostic groups or if the activity level is correlated with certain symptom dimensions.

This approach has clear benefits for the interpretation of potential group differences because the observed brain activity can be linked to specific cognitive functions, in particular when mathematical modeling allows to predict brain activity change, which can be taken to suggest that the brain realizes similar computations to generate and control behavior. One example of this approach is a suite of recent studies by Henco and colleagues (2020b, b), in which they investigate the effect of implicit social cues (e.g., gaze shifts of a face) to bias decision-making in a probabilistic learning task, even though study participants were not asked to the social cues into account. Intriguingly, the way these social cues affect decision-making appears to be mechanistically different in individuals with borderline personality disorder and schizophrenia compared to both healthy controls and patients with major depressive disorder (Henco et al., In press), suggesting that the study of implicit social processes in combination with computational modeling might be particularly helpful in elucidating the neural mechanisms that differentiate these disorders.

Importantly, these kinds of experimental task use a fixed reward and learning schedule, which offers high levels of experimental control, and lend themselves to data analytic approaches that use mathematical models to describe cognitive and putatively neural mechanisms that underlie participants' behavior. Using hierarchical Gaussian filter models, Sevgi and colleagues (Sevgi et al., 2020) demonstrated how participants integrate social and nonsocial information to come up with their decisions and how this differs as a function of interindividual variance of autistic traits. The parameters derived from computational modeling can also be used to inform neuroimaging analysis, which has become known as model-based fMRI: here, it can, for instance, be assessed whether trial-to-trial changes of modeling parameters are related to brain activity changes. Using this approach, Henco et al. (2020a, b) demonstrated that interindividual differences in social belief computations, i.e., whether participants tend to use social cues during decision-making, even when not explicitly instructed to do so, were related to brain activity levels in the putamen and insula, areas that have previously been associated with habitual behaviors and interoception.

Naturalistic Passive Observation

While the conventional approaches described above have allowed us to gain completely new insights into relevant brain processes, many of them tend to rely on the assumption of “pure insertion,” at least approximately (Friston et al., 1996). That is, it is assumed that effects of the manipulation of individual features or processes are essentially independent of each other and, in more complex or naturalistic conditions, these effects sum up to produce more complex processes or behaviors. In some cases, findings of simplified experiments generalize to more natural conditions, at least to some extent. For example, contrast edges of video images correlate with activity in the early visual cortex (Lahnakoski et al., 2012a), as might be expected based on the properties of edge-detecting cells in the region, but the amount of variance explained is relatively low. Careful consideration of a range of stimulus features can reveal insight into the organization of the brain networks of naturalistic social observation, for example, highlighting regions such as the posterior superior temporal sulcus and surrounding temporoparietal regions as potentially key regions for integrating multiple types of socially relevant information (Lahnakoski et al., 2012b) as well as building coherent temporal sequences of related events (Lahnakoski et al., 2017). The amplitudes of responses to emotionally arousing events in these regions appear to be also related to individual differences of the endogenous opioid system (Karjalainen et al., 2019), which may prove helpful for assessing potentially aberrant neurotransmitter function in psychopathology. Importantly, however, it is less clear how complex intuitive social processes can be deconstructed into more basic constituents. Arguably, more naturalistic social processes are only observable in complex situations, and the underlying processes may not be directly accessible through the stimulus properties, event descriptions, or even simple dimensional models of emotion alone. For example, recent findings have shown that when participants share a point of view toward movie events, either experimentally (Lahnakoski et al., 2014) or through friendship in everyday life (Parkinson et al., 2018), the similarity of the brain activity is increased compared with individuals who do not share a perspective or do not know each other. Such similarity between friends appears not to be reflected in functional connectivity during rest (McNabb et al., 2020), although more sensitive measures may yet reveal such associations. Moreover, naturalistic stimulation may provide benefits for detecting aberrant brain activity related to psychiatric disorders (Eickhoff et al., 2020), and prediction of behavioral traits may prove to be more successful using connectivity measures derived from, particularly social, natural viewing paradigms rather than resting state data (Finn & Bandettini, 2020). Thus, more ecologically valid dynamic stimulation may not only highlight brain-behavior associations but also highlight the types of content that best reveal these associations to guide us to further our understanding of naturalistic brain processes beyond simple models of stimulus features or general emotion dimensions (see, for example, Finn et al. 2020).

However, despite this potential benefit in highlighting individual differences, the use of naturalistic stimuli in the study of psychiatric disorders is still relatively rare. Some of the earliest studies have shown that, for example, individuals with ASD tend to show idiosyncratic patterns of both eye gaze and brain activity during natural viewing conditions (Hasson et al., 2009; Salmi et al., 2013). This highlights a potential difficulty in understanding the brain mechanisms underlying psychiatric disorders mentioned earlier; if patients with the same diagnosis are highly variable, then group contrasts, and predictions are likely to fail. It, thus, appears particularly important to further characterize the participants' behavior and experiences, as well as the contents of the stimuli that are particularly relevant for detecting the disorders. For example, during movie viewing, aberrant brain activity related to positive symptoms of first-episode psychosis patients appears to be particularly observable during surreal, fantasy scenes, which may share aspects of the patients' symptoms (Rikandi et al., 2017). Further work is required to discover the limits of passive observation studies and to what extent specific neural functions can be studied in complex conditions, with more limited experimental control. Likely, a fruitful approach is to iteratively alternate between more exploratory findings in naturalistic experiments, working backward toward more controlled conditions to design experiments to test specific hypotheses on the low-level mechanisms of psychiatric disorders, and testing the mechanistic predictions again in more naturalistic conditions, potentially in interactive tasks mimicking real-life situations where the presumed mechanism is particularly important (cf. Schilbach, 2019).

Interactive Experiments, Second-Person Neuroscience, and Neuropsychiatry

While investigating more naturalistic social situations is beneficial to understand complex social cognition, it has been pointed out that a fundamental difference may exist between situations of social observation, i.e., social cognition from an observer's point of view, as compared to situations of social interaction, i.e., social cognition from an interactor's point of view (Schilbach, 2014, 2016; Schilbach et al., 2013). Contrary to the conventional stimulus-response paradigms described above, social interactions are characterized by behavioral reciprocity. That is, social perception leads to actions that, in turn, will be responded to by the interaction partner (and so forth). In order to investigate how these social contingencies and the ensuing dynamics of social interaction modulate brain activity, we, therefore, need truly interactive tasks, which allow for the participant to engage in such reciprocal social interactions. Following the call for a truly social or second-person neuroscience, recent years have seen a growing number of studies that have focused on core social-interactive behaviors, such as studies in which participants perceive communicative cues to engage them in interaction (e.g., direct gaze) all the way to studies that include reciprocal, face-to-face interactions with a social partner (real or perceived; see Redcay and Schilbach (2019) for a recent review). In addition to increasing the ecological validity of the task used and making the social encounters more lifelike and dynamic, for example, using real video recordings in place of computer-generated avatars (Brandi et al., 2019), second-person neuroscience has also focused on scanning interacting brains, which has been described as hyperscanning (e.g., Bilek et al. 2015; Dumas et al. 2010). Findings from these studies have helped to gain striking new insights into the workings of "social brains," which, indeed, indicate that the neural mechanisms supporting social interaction do, in fact, differ from those during social observation. Findings converge on a set of brain regions and large-scale neural networks that appear to play key roles and interact in intricate ways in order to support social behavior during social interaction. In addition, the use of two-person experiments and hyperscanning techniques allows us to take a completely new look at how social behavior is realized across persons and brains and to investigate phenomena such as interpersonal synchrony, mimicry, and other forms of alignment in more ecologically valid contexts (Bolis et al., 2017; Schilbach, 2015). These developments constitute important steps in the advancement of social neuroscience and will continue to provide new insights into how activity in large-scale neural networks is modulated by social interactions and also open up new avenues for future research.

In addition to this, a second-person neuroscience may also be relevant for neuroimaging research in the field of psychiatry and could, therefore, contribute to what might be called a second-person neuropsychiatry (Schilbach, 2016): Here, it has been increasingly recognized that it is social interaction rather than passive observation that is often most difficult for patients suffering from psychiatric disorders. For example, an individual may well understand an emotion depicted in a movie as the conventions that have been developed by the artists working in the movie industry are highly efficient in conveying emotions, whereas in real life emotional cues may be much subtler. Moreover, in real-time interactions, there is little time for explicit interpretations of the socio-emotional states of the interaction partner but rather relies on a practical "know-how" of how to deal with them. In other words, people often automatically understand, empathize with, and predict the words or actions of their partner enabling them to act appropriately without explicit reasoning. This has been demonstrated by a study by von der Lühe and colleagues (von der Lühe et al., 2016), in which it was shown that patients with high-functioning autism are able to recognize and explicitly label actions even when they are depicted by impoverished point-light displays but fail to use this information to predict the subsequent action of a potential interaction partner. In other words, it was only the complexity of a dyadic social interaction situation that brought about autism-specific deficits in predicting subsequent actions rather than difficulties in action perception, which was found to be intact. Following this lead, it appears important to introduce new methods and techniques that help us to quantitatively assess behavior during real-life social interactions as this may help to understand how social interaction difficulties might be related to alterations of cross-brain rather than single-brain network activity (Bilek et al., 2017; Bolis & Schilbach, 2018).

Behavioral Characterization of Psychiatric Disorders in Individuals, Dyads, and Social Networks in Everyday Life

Studying constrained social interactions in the laboratory has clear benefits for interpretability compared with trying to measure interactions “in the wild,” much like controlled task designs in neuroimaging studies often allow for more straightforward modeling and interpretation of results than more naturalistic experiments. Yet, constrained experiments can be rather poor approximations of real-life social behavior. Moreover, our initial systematic measures of behavior during dyadic interaction suggest that some behavioral characteristics of individuals may only manifest when they can interact freely, with minimal experimental constraints (Lahnakoski et al., 2020). Thus, enabling the systematic, quantifiable measurement of social behavior in natural interactions, i.e., interaction-based phenotyping, in the clinic as well as in the everyday life of patients may be crucial for understanding the individual as well as shared symptoms of psychiatric disorders (Schilbach, 2019). This type of extensive characterization of psychiatric disorders at the level of individual patients may be the key to disentangling general brain correlates of psychopathology from disorder- and symptom-specific brain mechanisms. Moreover, it may be the key to finally move toward individualized interventions in psychiatry, which to a large extent are still lacking.

Interestingly, behavioral measures, such as interindividual synchrony and mimicry, distance, gaze, and orienting of the face and the body, have been shown to be predictive of the subjective quality of interactions (Lahnakoski et al., 2020). Also, using measures of motion energy in videos between patients and their therapist, behavioral synchrony has shown promise in predicting short- and long-term therapeutic success for patients with schizophrenia (Ramseyer & Tschacher, 2014). It may also be possible to differentiate between patients with autism spectrum disorder (ASD) from control participants based on their behavioral synchrony with an interaction partner (Georgescu et al., 2019), although further work is needed to evaluate the practical applicability of these preliminary findings in larger cohorts. Importantly, however, using such simple measures of synchrony of motion lack specificity of what the people are doing during the interaction. Moreover, synchrony does not appear to always be useful for detecting differences in subjective interaction quality. In the study mentioned above (Lahnakoski et al., 2020), we showed that measures like distance and facial orienting behavior may be more indicative of the subjective enjoyment and effort invested into interactions, respectively. Moreover, these may be differently predictive in different conditions, so a single measure may not fit all questions.

While such systematic and quantitative characterizations of dyadic social interactions appear to be a fruitful avenue for evaluating, for example, dyadic behavior during interactions with a therapist in the clinic, the majority of social interaction problems manifest in everyday life. Anecdotally at least, patients may feel fine at the clinic and have severe relapses of symptoms after they are discharged and have to continue their daily lives. Thus, to get a picture of the causes of the daily difficulties patients face, beyond subjective evaluations, quantitative measurements should be extended to daily life of individuals. The recent widespread introduction of personal digital devices, such as smartphones, led to the development of digital phenotyping (Onnela & Rauch, 2016), where such devices, potentially complemented by, for example, wearable sensors, can be used to continuously measure the behavior of individuals in their everyday life. This approach can produce a wealth of data for detecting various social and behavioral characteristics of illnesses (Torous et al., 2016), which can be of great benefit for finding behavioral markers that may guide therapy and further scientific inquiry. Yet, much work is still required to detect consistent, meaningful patterns in this type of data. Moreover, pattern detections and behavioral prediction that are not informed by strong theoretical foundation cannot substitute a mechanistic understanding of the disorders.

On an optimistic note, the use of interaction-based phenotyping and other forms of digital phenotyping "in the wild" may help to investigate the social behavior and factors that are relevant and constitutive of psychiatric disorders. As the relevant classifications used in psychiatry today rely on intersubjective conventions of what should be considered as a nosological entity, the use of quantitative, data-driven approaches that integrate information about social, psychological, and biological factors may help to delineate disorder-general and disorder-specific profiles for what we take as separate disorders today. In addition, a major challenge for the future also lies in the definition of mechanistic models of psychiatric disorders that are grounded in the underlying neurophysiology and are able to make predictions of outcomes of specific disturbances of the system and interventions that alleviate such disturbances. So far, the existing models have yet to prove their usefulness in the larger scale. However, initial mechanistic insight into potential contributors to disordered social processing has started to shed light on underlying psychological mechanisms of psychiatric disorders. In the two studies mentioned earlier (Henco et al., 2020a, b, In press), we used a hierarchical learning models to demonstrate that not only do patients with schizophrenia and borderline personality disorder score lower in probabilistic learning task in the presence of implicit social cues but also expanded to the mechanisms of excessive weighting of social information during periods of uncertainty. Similar learning models can be used for various types of interactions. However, modeling unconstrained real-life interactions is a significant challenge for future research. Thus, a thorough exploration and systematic characterization of interactions seem crucial for guiding modeling efforts of social interaction disorders and eventually linking them to their underlying causes in the mind, brain, and body.

Eventually, to fully understand and empirically test the brain mechanisms of reciprocal social interactions, we will also need to not only correlate behavior with subsequent brain measures but also be able to measure the brains of two (or more) interacting individuals at the same time to directly link brain activity and behavior. Such hyperscanning studies have been slowly gaining momentum, as briefly described above. In this context, mobile electroencephalography (EEG) and functional near-infrared spectroscopy (fNIRS) offer the benefit of much reduced constraints on behavior compared to fMRI, although simultaneous fMRI experiments have been performed for some time, either by linking two separate MRI devices (Montague et al., 2002) or with specially designed head coils within one scanner

(Renvall et al., 2020). However, it is important to consider when it is necessary to measure multiple people at the same time and when it is sufficient to measure, for example, only one person during an interaction with another person outside of the scanner (cf. Redcay & Schilbach, 2019). Alternatively, brain imaging can be performed sequentially, by first measuring the brain activity and audio or video recording, e.g., a person telling a story (Smirnov et al., 2019) or performing hand actions (Smirnov et al., 2017), followed by a measurement of participants listening or viewing the recording. Hyperscanning studies are complex to run and analyze, and, thus, it may be counterproductive to design such studies when a simpler experimental design would suffice. Moreover, when people are measured while they participate in an interaction, it is particularly important to know how they are behaving (Hamilton, 2020) as no exact schedule for events during the interaction can be enforced. For example, neural synchrony, which to some extent appears to be associated with sharing "the social world," or state of mind with other people (Nummenmaa et al., 2018) may, during an interaction, also arise trivially when the interactants just look at the same stimulus at the same time. Thus, during an interaction, synchrony may arise in a similar manner as in the passive observation studies described above without any deeper sharing of mental states. For the latter, activity in the so-called mentalizing network of the brain has been implicated, in particular in situations of direct social interaction (Redcay & Schilbach, 2019). Moreover, because every interaction is different, direct comparisons based only on the brain activity of people are difficult to interpret without characterizing the interaction. Thus, a combination of detailed behavioral characterization and brain-based measures is crucial for a more complete understanding of the neural underpinnings of natural social interactions and disorders thereof in psychopathology.

Conclusions

In the past, reliance on heterogeneous disorder categories and an overemphasis on the brain have potentially limited the progress of our understanding of the behavioral and neural mechanisms of psychiatric disorders. Moreover, common predisposing mechanisms appear to be shared by multiple disorders, which can lead to nonspecific findings between disorders, and more specific measures of the disorders are required. While subjective mental suffering of patients is not directly accessible to researchers or therapists, disordered social interactions are some of the most severe symptoms of many psychiatric disorders that are, at least in part, detectable and measurable by an external observer. Differences in social behavior are often intuitively used by therapists while diagnosing and interacting with patients, yet rarely are these behavioral abnormalities systematically measured. By carefully characterizing individual behavioral manifestations of the disorders between patients, particularly in social interactions and everyday life, we may better understand the complex disorder phenotypes and their underlying mechanisms and, ultimately, move closer to individualized interventions.

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