PSYCHOLOGY AND EDUCATION (2021) 58(4), ISSN 1553 - 6939
Article Received: 22th November,2020; Article Revised: 26th March, 2021; Article Accepted: 26th April, 2021

Attachment-Based Treatment for Chronic Mental Illness

Martin Fields, MD
Board Certified in Psychiatry and Neurology, University of Illinois, Rockford Campus, USA
mfields111@aol.com

ABSTRACT

Brain-to-brain communication between a therapist and the patient can resolve severe mental illness. This report demonstrates a model for accomplishing this.

Summary

Attachment is a primary factor in mental health rehabilitation programs. However, despite elucidating the underlying neurobiological basis regarding attachment, this knowledge is yet to be applied successfully to mental health or psychotherapy-based treatments. This paper examines the neurobiological basis of the most fundamental attachment process, the Basic Bond, and demonstrates how mother-infant brain-to-brain synchronizations may lead to its successful implementation in patients with chronic mental illness.

The purpose of theta wave brain-to-brain communication is to augment the hippocampal CA2 region's theta wave formation in infants. This communication increases theta wave activations, resulting in the transformation of meaningless electrical energy patterns into organized patterns. Furthermore, an infant associates its mother's meaningful organization of its theta brainwave patterns with safety. Consequently, the feeling of safety is then associated with the mother's presence, which is the underlying basis of mother-infant attachments. Inducing this phenomenon during therapy sessions is achieved to such a degree as to prove the brain-to-brain communications between patient and therapist. Consequently, the patients experience novel and logical meaning in the world around them.

Evidence suggests that patients with severe mental illness may have a defect in the basic bond formation process; however, in many instances this can be converted to a successful bond through psychotherapy. The patient can thus experience safety through a brain-to-brain communication with the therapist. Accomplishing this entails the modification of the ordinary psychotherapy situation from one that does not accommodate brain-to-brain communication to one that does. The basic process of altering psychotherapy to accommodate theta wave-based brain-to-brain communication requires a much less 'structured' setting than usual, and one that fits the communication needs of a patient.

Keywords

Schizophrenia, Brain-to-Brain Communication, Basic Attachment, Theta wave synchrony

Introduction

Although considerable efforts have gone in to help patients with severe mental illnesses, we are unable to determine definitive etiologies for their conditions or ways in which to cure them. According to the World Health Organization (2019), 45 million people worldwide have bipolar disorder while a further 20 million have schizophrenia and other psychoses. According to the World Health Organization (2011), mental illnesses are the leading causes of disability-adjusted life years worldwide, accounting for 37% of the healthy years lost due to non-communicable diseases. The global cost of mental illness amounted to $2.5 trillion in 2011, with two-thirds of this cost originating from indirect costs (lost productivity) in 2010; the projected cost for 2030 is calculated at $6 trillion.

Most of the treatments and research funding related to these severe disorders have been devoted to the use of psychotropic medication, despite the limited evidence supporting its efficacy (Hartling et al., 2012; Stafford et al., 2015; Thase, 2007). Despite the supporting evidence and modest effects sizes of modern psychotherapy methods, such as Cognitive Behavioral Therapy, they are still usually considered adjunctive to the use of psychotropic medication (Cuijpers et al., 2013; Hofmann et al., 2012). Therefore, the need for further improvements in the treatment of these disorders are imperative.

Modern neuropsychological research has generated a large body of information that applies to both our understanding of the genesis of chronic mental illness and toward a model for advancing psychotherapy treatments. This research can inform the clinical treatment of these patients by enabling us to structure their psychotherapy differently, thus enabling more effective treatment by helping them form an attachment with the therapist that was lacking earlier.

Body

The Hippocampus

The hippocampus controls the process of exploring novel environments and new experiences; these experiences are compared with previous ones and placed within a relevant frame of reference. Accordingly, we can understand where we are going and what to expect when we get there in any encountered situation which aligns with our frame of reference. Therefore, the hippocampus' function is integral to basic human development.

The hippocampus originally evolved as a way to navigate our environments by coding our movements in time and space; furthermore, it allows for the comparative coding of new environments vs ones we have already been in. New hippocampus cells are born in the entorhinal region[1] and start to migrate through the various regions of the hippocampus; at each phase of the migration they serve a different function. In the CA1 region the cells are involved in location placement (essentially functioning as our GPS system), directional coding, and our rate of movement when traveling within a specific time and space.

The CA2 region records changes in emotional and temporal rather than spatial modes. This region is involved in a process known as frame-of-reference formation, which is concerned with the integration of perceptual inputs to form an overall impression of an experience, and thereby determining whether it is safe, a novel experience, and how similar or different it is from previous experiences. Therefore, we record the social and emotional contexts of our experiences in this region; it is likely here where our attachments are created.

Finally, the CA3 region then transmits what has been learned to other brain regions—including the prefrontal cortex, the nucleus accumbens, the thalamus, and the amygdala—through so-called theta slow-wave impulses. The hippocampus is, therefore, wired to communicate whatever it learns to all major brain regions, thereby providing input that is essential for them to perform their functions. Without this information people cannot operate in the social contexts in which they live.

The Hippocampus CA2 Region Generates the Basic Bond, and Its Potential Failure Results in Severe Mental Disorders

The CA2 region of the hippocampus, activated by oxytocin and vasopressin, is elected as the primary region of the brain with regards to governing attachment. It provides an individual with the motivation to explore novel experiences and to seek out interactions with others. The CA2 region further enables individuals to form positive and secure frames of reference based on their initial attachments. However, if those initial attachments are insecure, the consequent frames of reference for social interactions will be negative or disorganized. Accordingly, these individuals will avoid relationships and display a lack of interest in exploring their surroundings; John Bowlby and Mary Ainsworth, the original attachment theorists, would call these individuals "avoidant-detached" types (Ainsworth, 1972).

It has been demonstrated that lesions in the hippocampal CA2 region will result in severe defects of social-recognition memory (Stevenson and Caldwell, 2014); it can provide a basis for the severest mental illnesses as well. Indeed, severe psychopathology, such as those present in bipolar disorder and schizophrenia, has been shown to affect the hippocampus and its connectivity to other brain regions (i.e. prefrontal lobes). These negative effects are likely associated with theta-wave (4-8 Hz) communication defects, particularly those involved in the attachment process. To further support this inference, severely ill patients have displayed volume depletion in the hippocampal regions (Li et al., 2018).

Weinberger (1999) outlined our understanding of cell morphological changes in the hippocampus of schizophrenia patients reduced sizes of neuronal cell bodies were uncovered. According to him, these findings suggest that a cellular defect is affecting the plasticity of hippocampal frontal circuitry and connectivity. Heckers and Konradi (2002) found that hippocampal cells, which vary in shape such that the variations are localized to certain subregions, send projections to the

[1] An area of the brain in the medial temporal lobe that functions as a network hub associated with memory, navigation, and the perception of time. It is the primary interface between the hippocampus and neocortex.

prefrontal cortex, the nucleus accumbens, the amygdala, and the thalamus. Using a high-dimensional computer template to compare hippocampal shape and volume in schizophrenic vs. normal patients, Narr et al (2004) confirmed that the disorder involved an impairment of hippocampal prefrontal connectivity. Therefore, the primary attachment bond that emanates from the CA2 region may be a primary cause in the genesis of severe mental illnesses.

Theta brainwaves (4-8 Hz/sec), which are generated by brain activity within the hippocampus (Ekstrom et al., 2005), are slow traveling waves that proceed along hippocampal regions. This wave is involved in spatial navigation (Watrous et al., 2011), memory formation (Lega et al., 2012), and in human attachments (Sloan et al., 2007). Therefore, can we assume that since the progressions of theta waves are associated with the same CA2 brain region of the hippocampus as basic attachments are, that they affect the formation of attachment bonds and the pathology associated with chronic severe mental disorders?

Qiu and colleagues (2015) reported that theta waves from the hippocampus can generate "endogenous" electrical fields throughout the cortex without direct transmissions from nerve to nerve. This extraordinary connectivity of low-frequency theta waves demonstrates that hippocampal communications exhibit an extraordinary range within the brain.

Furthermore, the formation of theta waves is also associated with brain-to-brain communications—i.e., theta waves represent the code for the novel neuronal firing patterns that are present between an infant and a mother. The familiarity is created by the similar firing pattern rhythm of this brainwave in mothers and their infant's brains. These brain rhythms, and the mode of communication associated with those rhythms, build the code from which an understanding of the world emanates. We can thus conclude that brain-to-brain synchronicity acts as the most basic form of communication between parents and their offspring. The communication code between mother and infant is similar to the code between the hippocampus and other brain regions, as well as between the hippocampus' internal structures. Therefore, this code may be the basis of attachment since it connects the brain's internal functions directly with the communication that takes part between the mother and infant.

Sarro et al. (2014) demonstrated the effectiveness of this form of communication between a mother rat and her pups. When the mother rat was in the nest with her pups, the rat pup's brain synchronicity — on the encephalogram — was significantly more synchronous with its mother's than during her absence. Furthermore, the theta wave levels were much higher as well. The researchers found that other mother-infant interaction types did not cause the same change in theta waves; these included grooming, nursing, and feeding through lactation. Only the communication between mother and infant generated this rise in theta brainwaves.

Leong et al. (2017) indicated a similar finding in human mother-infant communications. They recorded dual electroencephalograms between an adult and infant; the infant either viewed the adult directly or through a video of the adult, and the adult responded either with a direct gaze or an indirect gaze (adult's eyes averted the gaze of the infant). In all instances, the mother was singing the same nursery rhymes to the infant while this direct/indirect gazing went on. The researchers measured slow-wave brain activity (theta 4-6 Hz and alpha 6-9 Hz wave) and the coherence of brain activity between the adult and infant. They found that a direct gaze, especially when the infant returned the gaze, increased both the brain-based coherence between them and their overall brain activity.

Therefore, this stimulation was bidirectional in that each partner's brain was activating the other's. This stimulation occurred primarily when they made direct eye contact with one another. The communication occurred in the brain's slow wave (alpha and theta) regions, which are associated with the hippocampus' natural conduction pattern. The researchers found that the direct gaze condition triggered infant vocalizations, and that the greater the brain synchronization was between the adult and infant the more vocalizations were triggered. Therefore, the brain-to-brain synchronization increased the activation of internal theta wave patterns in the infant's hippocampus, which in turn induced a psychological event — the infant's

communicativeness. Without this increase in theta wave activation, the infant would not psychologically have been at a communicative level. In summation, the brain-to-brain synchronicity between mother and infant generated a mode of communication (the theta wave mode, which we can call the brain-to-brain synchrony mode) which shifted the infant out of its nascent neurobiological state into a more psychologically communicative one. I believe this is the underlying basis for attachment.

Wass et al. (2018) also recorded dual encephalograms of mothers and their twelve-month-old infants during solo and dual play. They found that parents' theta waves closely tracked changes in their children's attention, and that instances in which parents showed greater neural responsivity were associated with longer sustained attention in their infants. This suggests that the mothers' brain-to-brain communications were inducing psychological states of interest and attention, of the surroundings, in their infants.

How Failures in Basic Bond Formations Lead to Severe Mental Illnesses

Researchers have uncovered a connection between a defect in hippocampal function and the development of schizophrenia (Heckers, 2001; Tamminga et al., 2010). Schizophrenia patients exhibit impaired hippocampal activity with regards to memory formation (Holthausen et al., 2003). Studies regarding schizophrenia patients have identified hippocampal activity reductions (Honea et al., 2005) in first episode psychosis patients (Narr et al., 2004) and in drug-naïve patients (Szeszko et al., 2003).

This hippocampal defect in schizophrenia patients has been shown to affect the development of coherent brainwaves within the hippocampus and other brain regions that are connected to it. Chen et al. (2016) identified increased theta and delta waves in the frontal lobes of patients with severe mental disorders, including those with schizophrenia. Mitra et al. (2017) revealed that increased slow-wave activity over the left frontotemporal region correlates with negative schizophrenia symptoms. Similarly, Rockstroh et al. (2007) measured slow-wave activity (theta and alpha waves) over the frontal lobes in normal and affective disorder controls compared with schizophrenic patients and found that the latter group exhibited high levels of slow-wave activity. However, further studies have not confirmed these high levels of theta and alpha wave activity. These apparently contradictory findings were reconciled by Sigurdsson et al. (2010), who indicated that decreases in hippocampal connectivity with other brain regions may be an indicator of psychopathology, such as schizophrenia. This connectivity decrease may result in higher intensity, but less meaningful, theta and alpha waves as compared to the waves that reflect a direct communication from hippocampus to prefrontal cortex. Therefore, increased theta wave intensity in the frontal lobe is an ineffective overreaction to the hippocampal failure of meaningful theta wave communication.

Siekmeier and Stufflebeam (2010) conducted a metanalysis of magnetoencephalographic activity in Schizophrenia patients from 1993-2009; they found that 11 out of 12 studies showed increased theta (4-8 Hz) and delta (1-4 Hz) band oscillations in the patients' temporal lobes, and a correlation between temporal lobe theta activity and positive schizophrenic symptoms. Moran and Hong (2011) conducted a metanalysis of high vs low frequency brainwave abnormalities found in schizophrenia patients; they found that high frequency gamma wave abnormalities often occur concurrently with low frequency abnormalities (theta waves), as such, it is unclear which abnormality is the primary contributor to the failure of cross frequency coupling — which is critical for key cognitive functions.

On the basis of the above findings, Lee et al. (2014) proposed a 'discoordination' hypothesis in which schizophrenia patients' cognitive impairments result from aberrant coordination of neural activity; a rat model was created where they made neonatal hippocampus lesions in rat pups to test this hypothesis. They found inter-hippocampal dyssynchrony in the rats' theta and beta bands, which correlated with their active place avoidance performance. The anticonvulsant ethosuximide was used to attenuate the rats' abnormal spike wave activity, as well as improve their cognitive control and reduce hyperlocomotion. It was found that the anticonvulsant not only normalized the task associated theta and beta synchrony between two

independent rat hippocampi, but also increased synchrony between the medial prefrontal cortex and the hippocampus above control levels. These researchers suggest that normalizing aberrant hippocampal synchrony — through the use of medication — can be beneficial and should be considered as a new way to treat schizophrenia. These findings also support the idea that a hippocampal defect may be involved in abnormal theta wave communication within the hippocampus itself, as well as in the disruption of hippocampal prefrontal lobe communication patterns. While the hippocampal frontal lobe circuit enables a person to derive basic meaning from relationships, this failure of the theta wave results in an absence of meaning.

Theta-gamma coherence abnormalities have been identified within the hippocampi of schizophrenia patients (Andreou et al., 2015; Cousijn et al., 2015; Ford et al., 2002; Uhlhaas and Singer, 2010); communication problems within the hippocampus can result from this failure in these patients. Tamminga et al. (2010) asserted that a defect in hippocampal formation and its generating coupled gamma and theta waves may be the source of schizophrenia patients' abnormal memories. This defect may arise from a failure in the plasticity process in the cornu ammonis (CA3) accompanied by an increase in activity (triggered by reduced afferent stimulation of CA3 neurons from the dentate gyrus). Furthermore, the researchers cited evidence for a loss of mnemonic functions specific to the dentate gyrus; this causes pattern separation in the developing theta and gamma waves before they reach the CA3 region.

Consequently, once these waves reach the CA3, the hippocampus produces illusory memories according to the defective brainwave-based development process instead of real memories. Tamminga et al. (2010) suggested that this will result in a 'run-away' CA3 producing abnormal memories rather than accurate ones. Interestingly, the evidence implies that the actual defect in these patients may lie in the process of forming these theta waves, which may involve the CA2 region. This evidence suggests that the cognitive abnormalities and psychotic symptoms in schizophrenia may be a result of malformed theta waves emanating from the CA2 region of the hippocampus and the subsequent generation of overcompensated malformed theta waves that are transmitted to the rest of the brain.

The CA2 brain region may be more involved in the inhibitory circuitry of the hippocampus than the CA1 and CA3 regions, furthermore, this region has a higher total percentage of inhibitory interneurons than any other region of the hippocampus (Botcher et al., 2014, Dudek et al., 2016). A study by Manahan-Vaughan (2018) explored the distribution of inhibitory cell types in the hippocampus; it was found that the CA2's pyramidal cell layers contained the highest density of pyramidal cell GABAergic neurons in the hippocampus. Therefore, if a problem were to arise in the CA2 region of the hippocampus, perhaps due to a brain-to-brain communication failure, it would result in a failure of these inhibitory interneurons; this, in turn, would cause a failure in the flow of theta waves to the CA3 hippocampal cells, resulting in a subsequent interruption of the hippocampal prefrontal lobe communication system.

Recent studies have linked the CA2 region of the hippocampus to the genesis of severe mental disorders, especially schizophrenia. Piskorowski et al. (2016) implemented a mouse model of autism and schizophrenia, in which the density of parvalbumin expressing interneurons (inhibitory interneurons) were decreased in adult mice. They found that the CA2 pyramidal neurons displayed a highly hyperpolarized resting membrane potential, which made them less sensitive to input stimulation. Similarly, a reduction in the parvalbumin immunoreactivity of the CA2 region was also observed in Schizophrenia patients (Wesson et al., 2006; Wetmore et al., 1994). Falkai et al. (2016a,b) observed reduced oligodendrocytes and interneuron density in hippocampal CA2 regions, which is associated with cognitive defects in Schizophrenia patients — post mortem.

The CA2 brain region is also associated with social dysfunction (Mou, 2016). Furthermore, this region is essential to the recognition of novel or familiar conspecifics, which constitutes part of an individuals' social recognition memory ability (Tzakis and Holahan (2019). Social recognition memory is essential to the recognition of various elements: social hierarchy, mate, and offspring recognition; territorial defense and interspecies

recognition; and for the general establishment and maintenance of groups (Ferguson et al., 2002; Jacobs et al., 2016), Richter et al., (2005) conducted a study on recognition memory in the olfactory bulb of juvenile rats, which was blocked by anisomycin (a protein synthesis inhibitor) that they injected into the rats' olfactory bulb system. This may be representative of a human hippocampus since, in juvenile rats, the olfactory bulb constitutes a part of the rats' hippocampus. Social recognition in rats and primates are known to be dependent on hippocampal functions since ablations of the hippocampus can block social recognition. (Baker and Kim, 2002; Kogan et al., 2000). Van Wimersma and Maigret (1996) injected either oxytocin or anti-vasopressin into the hippocampi of rats and found significant increases in their recognition memory; suggesting that the attachment process may be associated with the recognition memory process of the hippocampus.

Gao et al. (2008) found that social recognition memory was disrupted by ketamine, an NMDA antagonist; this effect was partially attenuated by Haldol and olanzapine. This suggests that the interneurons in the hippocampus — which are predominantly located in the CA2 region of higher mammals and humans — may be responsible for social recognition memory, furthermore, when they are disrupted it could cause this recognition memory to fail. Tirko et al. (2019) showed that oxytocin receptor activation drives pyramidal cells in the CA2 hippocampal region to fire bursts to the CA1 region, which supports the CA2's role in the attachment process. Mice lacking oxytocin or oxytocin receptors display impaired sociability and social memory (Choe et al., 2015, Ferguson et al., 2001, Lin et al., 2018), altered oxytocin serum levels (Striepens et al., 2011), and reduced oxytocin receptor expression (Uhrig et al., 2016); this problem may account for the symptoms related to social behavior in schizophrenic patients. Therefore, the disruption of the hippocampal frontal lobe circuit associated with the generation and use of theta slow waves may be responsible for positive and negative schizophrenia symptoms and for the social and cognitive disabilities associated with the disorder. Although this problem may exist in other severe mental disorders, it may be to a lesser degree.

The use of an attachment deficit model has been applied to schizophrenic patients in several studies (Dozier et al., 2001; Dozier, 1990; Dozier and Lomax, 1994; Tyrrell et al., 1999). By recognizing that attachment deficits may be associated with a wide variety of psychiatric disorders, Liotti and Gumley (2009) focused on finding correlations between schizophrenia and a severe subtype of attachment disorder, the disorganized subtype. Aydin et al. (2016) focused on the metacognitive deficiencies of schizophrenic patients. They compared patients who exhibited deficits in terms of attachment style, childhood trauma, and caregiver attitudes and found that schizophrenic patients had greater degrees of metacognitive deficiencies (they were unable to gain insight into their illness). Furthermore, it was found that these deficiencies, the anxious attachment style, overprotection during childhood, and childhood emotional abuse were all associated with metacognition failures in the schizophrenic group. Favaretto et al. (2001) found that parents of adults with psychosis reported that the parenting they had received was less caring compared to non-clinical control.

According to Read and Gurnley (2008), who reviewed studies using the PBI (parental bonding instrument), found that psychotic and schizophrenic patients were rated high on the affectionless control pattern, which pertains to the low care and high over-protection exhibited by parents. This would characterize a particular type of parental bonding style with which none of the currently characterized styles fit.

These authors summarized the literature on schizophrenia, severe mental illnesses, and psychosis as it centers around an insecure and disorganized form of attachment; they also discussed how this was associated with the onset of disease. Furthermore, they argue that the significance of using the attachment model, to understand the genesis of these severe mental disorders, is in the fact that it keeps our focus on the 'ongoing circumstances of childhood'. However, this type of characterization does not lend itself to improve the efficacy of treatment, especially psychotherapy interventions. How differently would we treat someone with a disorganized form of attachment deficit as opposed to any other form? The cause of this

problem may be found in the way we understand attachment deficits in general.

Accordingly, we may need a more dynamic model of attachment: one in which we understand the underlying basis of attachment failure as well as how that failure can be resolved through treatments, including psychotherapy treatments. The current focus on the CA2 region of the hippocampus, and its relationship with communication and social awareness, may contribute to the conceptualization of the attachment process — i.e. focusing on possible reasons for the region to fail. Therefore, the reason for a failure in this region may, inversely, be due to a failure of the attachment process; caused, in part, by a failure in the brain-to-brain synchronicity needed to generate the growth of the CA2's inhibitory interneurons — which would have led to the further generation of theta brainwaves and an increase in the communication with hippocampal CA3 and other brain regions. Failure of this system can account for every type of symptom in schizophrenia and other severe mental disorders.

Schizophrenia and Other Severe Mental Disorders as Disorders of Brain-to-Brain Attachment-Based Communication.

A study by Pais-Vieira et al. (2013) demonstrated the existence of brain-to-brain communication in rats, in which the communicator rat shared real-time sensorimotor information with a conspecific. This communication has been demonstrated between humans as well (Rao et al., 2014). Since that discovery, there has been a large upsurge in research regarding human brain-to-brain communication (Kinreich et al., 2017, Wheatley et al., 2012); it has been used to demonstrate the concurrence of brain-to-brain synchronicity and attachment in mother-infant pairs. (Lenzi et al., 2015). This brain-to-brain synchronicity, and the likely attachment associated with it, is instrumental in the creation of 'meaning' from communications for all parties involved (Stolk et al., 2014). Moreover, this neural synchrony is inherent in the development of neural networks (Uhlhaas et al., 2009) which, in turn, expands our functional capacity to communicate in this manner.

Basic attachments may be based on fundamental brainwave-based communications. Accordingly, Pratt et al. (2018) examined the brain patterns of 11-year-old children while they viewed films of their own mother-child naturalistic attachment experiences; these brain patterns were compared to those observed when the children viewed films of other mother-child pairs. They found that theta and gamma wave bands were predominant in the viewings of the children's own films when contrasted with the strangers' films. They also compared the strength of the mother-infant attachments; measured by both the degree of their social synchrony and their brain activation patterns. The researchers found that the degree of social synchrony that the children experienced with their mothers was significantly related to the viewing of their own mother-child interactions, this was reflected by the oscillatory intensity of the theta and gamma frequency bands. Although this study observed various attachment levels through several attachment related brain regions and brainwave activations, theta and gamma brainwaves proved the most significant when the children viewed the videos.

Pratt et al. (2018) concluded that the theta band oscillation increases were based on the familiarity of the individuals faces (Weibert, 2016), which were more stimulating in theta wave activation even when contrasted with the faces of famous individuals (Gobbini et al., 2004). The frontal gyrus region was most reflective of this increase in theta waves since it is associated with the hippocampal prefrontal cortex brain circuit. Moreover, the authors cited that both the frontal gyrus and theta rhythms are imperative to the processing of salient emotional cues and memory retrieval. They attributed the activation of gamma wave bands to areas of the temporal lobe and to higher brain regions associated with attachment, such as the mentalizing and empathy networks. Hence, the theta wave pattern was consistent with the most basic type of attachment. This finding is consistent with similar findings by other researchers, namely the study mentioned earlier by Wass et al. (2018) with the dual electroencephalography study between mothers and their twelve-month-old infants, and Feldman (2020) who outlined the basic strengths of the

attachment model and emphasized the basic theta band basis for that attachment.

Consistent with the literature which supports the CA2 hippocampal brain region as a potential region of defects in severe mental disorders, studies of EEG based brainwave patterns have found defects in this same wavelength. Similar to the abnormalities that Pratt, Goldstein, and Feldman (2018) found in bonding pairs, EEG abnormalities in high frequency gamma and low frequency theta bands have been found in scans of Schizophrenia patients (Moran and Hong, 2011).

In a recent review, Newson and Thiagarajan (2018) found intensity increases in lower frequency delta and theta bands and found lower intensities across the higher frequencies for schizophrenia patients (alpha, beta and gamma). Howells et al. (2018) also discovered a similar divergence between high and low frequency bands in schizophrenia patients. This suggests that brainwaves in the lower frequency domains, especially the theta and delta domains, may have certain primary abnormalities associated with them, which corresponds to the following: the region of attachment, the hippocampus CA2 region, and the CA2 region's projections through CA3 to the prefrontal lobe. Therefore, attachment deficits may be associated with the genesis of schizophrenia and the bipolar disorder. Furthermore, it is noteworthy that studies have shown a correlation between schizophrenia and hippocampal shrinkage; the use of oxytocin, a bonding hormone in the treatment of schizophrenia, has also demonstrated this correlation (Macdonald and Feifel, 2012). This evidence suggests that this shrinkage, which may be the result of a failure of attachment, results in the inability to find meaning in communication with others. This kind of primary frame of reference for understanding the world results in a constant sense of insecurity and a basic inability to effectively communicate with others, which results in deficits related to negative and positive symptoms and the psychoses associated with severe mental disorders.

Using Psychotherapy to Reverse Brain-to-Brain Synchrony Defects in Patients with Severe Mental Illness

The mode of relating, or brain-to-brain synchrony, is arguably the most fundamental mode of therapy. With the utilization of this mode, as opposed to other more advanced modes, we can 'complete the sentences and thoughts' of the patients at the same time that they utter them. It is this simultaneous communication that distinguishes the mode of relating from more advanced therapeutical modes. Additionally, certain patients struggle to communicate their issues verbally with therapists without the incorporation of the mode of relating. This will be demonstrated in the first case study with Jill. When they begin treatment, these patients' communication abilities consist of formal language usage that does not necessarily convey any emotional meaning. Their ability to function in society has been hindered primarily because they do not 'get it' or understand the purposes behind human communication or attachment. Their lives are, therefore, devoid of emotional 'meaning.' We can conclude that their 'frames of reference' for organizing their world do not enable them to derive meaning from their relationships.

Additionally, in order to conduct meaningful communications with these patients, the treatment situation needed to be structured very differently than with other types of patients; accommodations needed to be made for the integration of brain-to-brain communication. That is, the structure of the psychotherapy treatment was modeled, in part, in accordance with the workings of the basic brain-to-brain network. Consequently, it resembled a very unstructured model, similar to basic mother-infant communications. This was necessary to ensure the optimal receptiveness of the basic forms of communication employed between a communicator and someone who does not understand the intricacies of human communication. These principles will be illustrated in the following case reports. Although neither patient would be considered schizophrenic, both would be understood as having profound mental issues, and neither would be amenable to any other treatment besides the one provided. Moreover, both individuals had profound deficits in understanding the basic

meaning of emotion-based communication, albeit for different reasons. Once I was able to form a meaningful attachment with each of them, they began to find meaning in human communication, and their ability to communicate started to develop dramatically.

Case History: Jill

When Jill started treatment with me, she was forty-nine years old and married with three children. She worked as a potter but had never achieved any success with her work. She had seen many other psychotherapists before; however, she never achieved any improvements. At the outset of our sessions, Jill could not tell me what she needed help with, nor could she adequately describe her past. Instead, she spoke in a confusing way—she felt the need to follow every statement that she made with an opposite or contradictory one. I did not know how to help her. When she suggested that I allow her to stay after her sessions for a few minutes, I agreed with the hope that it may give me a clue on how to connect with her. I told her that I was willing to try this, provided that she leaves readily after the extra few minutes as I needed to see my next patient, to which she agreed.

Jill spent much of this extra time sitting silently and facing away from me so it was difficult to pinpoint what actually transpired. However, as the weeks went by, Jill began to open up in her regular sessions. She said that her therapy was becoming valuable to her and that she felt close to me, which she attributed to the periods of "staying after." Instead of talking apparent nonsense, with each phrase followed by a contradictory one, she started to engage meaningfully. I was gradually able to prompt a real history regarding the circumstances of her life. She told me that her father had divorced her mother when she was an infant, and that she was raised by her mother and grandmother. She was an only child and her mother had conflicting views on how to manage her. Jill knew that if her mother believed one thing, her grandmother was sure to believe the opposite. We were able to reconstruct the conflict between the mother and aunt as it replayed itself in her contradictory statements, one after the other.

I also learned that she was in her second marriage and that she was seeking a relationship that worked; apparently was always dissatisfied in her relationships. She had left the father of her children because he was unstable, unreliable, and lived a confused and disorganized life. Her current husband, however, was much more consistent in his affection towards her, and a far better provider. Despite this she felt no affection for him; it was a marriage of convenience. In fact, she claimed to have never felt any real emotional ties with anyone, including her own children. Moreover, their lives were not going well, and except for her eldest, the children were struggling in school and had no real interests or friends.

Jill told me that the period when she stayed after her sessions allowed her to feel connected to me in a way that she had never felt with anyone before, and that her work with me was more meaningful to her than any of her prior treatments. I could often anticipate what she would say and vice versa; this communication simultaneity and the absence of a communication lag between us confirmed to me that we had established a brain-to-brain synchronicity (i.e. we were communicating telepathically). Jill said she felt safe in her therapy sessions and that this was the first time she had felt safe anywhere. Once her basic attachment was established, it became the foundation and frame of reference from which a deeper attachment could evolve.

About one year into her treatment, she got angry with me for being a few minutes late to one of her appointments. She picked up a model clipper ship I had built, which was in my waiting room, and threw it. She told me she had no idea it would upset me — which it did — when she broke my ship; however, she was later so remorseful that she had it repaired professionally. As her treatment proceeded, she learned to use more appropriate means of expressing her anger within a therapeutic context. To a great extent, her treatment was primarily focused on helping her to understand what communications were appropriate in various contexts; this was mostly achieved through our brain-to-brain mode of communication.

Later in the treatment, I could help her extend her understanding to other frames of reference. She began using her skill as a potter to

communicate; she ended up producing pieces that people appreciated, instead of the eccentric and strangely shaped works she had crafted previously. Accordingly, she was able to start selling her work. Regarding her marital life: where she had once asked her husband's best friend out on a date, she was completely unaware of the gesture's inappropriateness, she now realized how disruptive this type of behavior was to her marriage — a marriage that she really had no desire to leave. Her growing understanding of context and frame of reference vastly improved her marriage, as well as the relationships with her children and friends.

One day, Jill would not leave her stay-after session when I asked her to. Since my next patient was waiting, I was angry and demanded that she leave or I would not continue to see her.[2] I had already sensed that these stay-after sessions would have to come to an end since her ability to communicate with me was already evident during our normal session times. As her treatment progressed, our therapeutic alliance improved and we were able to resolve the behavior that had caused me to be ambivalent.

Even though Jill's reaction could be ascribed to her acting out her ambivalent attachment with her mother, this formulation (while correct) would be limited because it does not explain how she developed an attachment for me in our stay-after sessions. Usually, patients who act out develop attachments when they are not acting out; they also know when they are "misbehaving." These patients know how to behave appropriately but they just do not, whereas Jill really did not know. I was helping her learn what was appropriate in various social contexts.

By the end of her treatment, Jill had learned to connect with many people in her life; she had developed the frames of reference she needed to relate to them appropriately, even without my assistance. When her husband died, she could call me and share her grief, moreover, she called upon her friends to help arrange his funeral and sort out her finances.

The brain-to-brain mode of communication is our guidance system, from which we can organize all the other modes of relating that we will use in our lives. Failure in telepathic communications, towards building attachments, will result in the loss of understanding certain contexts. Treatment modifications that emphasize telepathic communication can help restore patients' attachments and modes of relating.

Case History: Morgan

Morgan was a fifty-year-old married woman with two children. She had suffered from severe depression and anxiety for a very long time. Despite her difficulties, she used to be a successful office manager. However, she had to retire because the later severity of her anxiety and depression inhibited her ability to function. She divorced her first husband because he had been unfaithful. However, after she remarried, to her immense pain, she discovered that her second husband had an affair. This event caused her depression to deepen to a point where she could no longer function. This failure in her most intimate attachments had a significant and profound effect on her life. She was living with both her current and former husband; an odd situation she justified on the economic grounds that neither she nor her husband or ex-husband were able to work. However, this also reflected her apparent lack of ability to attach herself to either one. The situation aggravated the constant conflicts among them, which generated the constant anxiety, tension, and depression from which she suffered.

However, her main attachment deficit was due to a frame-of-reference failure: her every experience and perception, whether internal or external, was interpreted on the basis of insecurity or anxiety. For example, if her current husband had an episode of back pain, she would regard it as one of his rages, which she interpreted as *her* failure. Even if the weather was cloudy on any day, she regarded it as grounds for activating her fears. The difference between this client's anxiety and that of regular anxious patients, is that regularly anxious patients can attach themselves to others much more successfully than she could. Moreover,

[2] She left, and we subsequently constructed that my ambivalence toward her was an enactment of her mother's early ambivalence toward her during their early attachment period. Her father had left the mother shortly after her birth and Jill believed her mother blamed her for that. This became the basis of our ending the stay-after phase of her treatment.

patients with anxiety disorders normally find relief in a whole variety of interventions: psychotropic medications, psychotherapy, and other life experiences. For Morgan, on the other hand, every moment was a different anxiety episode. Even though she phoned me constantly for support, she never really experienced any relief. Furthermore, while ordinary anxious patients seek relief from anxiety, this client actively sought to justify reasons for being anxious in every situation she encountered. Compared with her, other patients' frames of reference seem much more secure. An analogy would be that their holding environments were basically secure, while hers was insecure.

As is true for every client with an attachment deficit, Morgan was unable to take advantage from traditional psychotherapy; no intervention could offer her a reduction in anxiety. Accordingly, the moment someone helped her, the next apparent cause for anxiety would immediately surface to take the place of the quelled one. The only interpretation that "worked" or seemed to fit her situation was that her entire worldview was based on a defective frame-of-reference in which she understood every stimulus and experience in terms of insecurity. Her life was a relentless pursuit of insecurity.

After I explained this to her for some time, she finally understood it. She also noticed that she was looking forward to coming to her sessions. Gradually, she described feeling more secure than she had during any previous treatment situation. However, I could sense (telepathically sense) that when she phoned me this new mode of communication was not helpful but in fact disruptive for her. I could not put my finger on why I felt this way, but I was so sure of it that I introduced a structural modification to her treatment: I would not take phone calls from her unless her husband called me on her behalf, indicating that it was a real emergency.

I was right to act on my sense of the situation; she became much more invested in her treatment sessions and increased their frequency from monthly to once every other week. This structural shift was exactly what she needed. During her sessions we did not focus on the ever-present anxiety-generating situations, instead we focused on why she had so many of these. Morgan recalled that, earlier in her life, her mother was very insecure. She also told me with pain and anguish how she was considered a "fat" teenager. Her best friend would not hang out with her because, due to her weight, she had a negative effect when it came to boys. She recalled that when she tried to diet, her mother would be so jealous that she sent her to the store to buy banana splits for the entire family, including one for herself. She was very distressed by this recollection.

She tested me on my phone policy on several occasions. Once she called to announce that her husband had called my office staff. When I called her back, she told me she had to see if I would call in response. On another occasion, she was so anxious that her husband did call, and I was able to provide her with real relief by responding. I always used my sense of when something would be disruptive versus when it would be helpful to her. In my judgement of when she needed me to call versus when it was unnecessary, I was using my brain-to-brain communication sense of her. I had no cue to base my judgement upon; I just 'knew' my response was correct. It was similar to how we feel when we just 'know' how to respond to an infant at any time or to someone with whom we are so close that we think we can complete their sentences and they ours. Additionally, while Morgan's mother was indiscriminate in her "help" (for example, by giving her daughter money to buy a banana split when she was on a diet), I used far more discrimination in my telepathic reading of what to react to, and in which circumstances.

This behavioral pattern reflected a subtle, but very important, difference between the psychopathology of Jill and that of Morgan. Jill had me staying after her sessions, while Morgan had me decide when it was appropriate to take her phone calls and when it was not. In Jill's case, the reason was that her parents were ambivalent toward her, which was the cause of the attachment failure. By letting her stay after sessions, I was simulating that pathology; having my next client waiting in my waiting room while she stayed certainly simulated ambivalence. Morgan's problem, on the other hand, was less chronic. Her mother was able to attach to her but was too self-absorbed to tell when and when not to be involved. Similarly, I was having to decide when

to contact her and when not to. At times, we were able to reconstruct when I had failed in this role and how that reenacted her mother's pathology.

During her psychotherapy sessions, Morgan would often ask me why I made a particular decision in calling her back or not. I told her I had a general "feel" for her and a sense of what I needed to do, or not do, to help her; I knew when my presence would help and when it would be intrusive. I explained that I was using the same instincts that a mother uses to know when to hold her infant and when not to—precisely what her mother could not do. Morgan was trying to get everyone in her environment to repeat her early life experiences, in which her mother would indiscriminately pick her up to provide comfort whether she needed it or not. I would not follow that pattern. She understood how this type of intervention was more beneficial than seeking answers to the repeated demands for solutions regarding her constant anxiety issues.

Morgan was ultimately able to express considerable distress at the recollections of her mother's constant anxiety and how much it had affected her early life. At a certain point, I had a sense that the treatment situation had changed. Morgan started to find places outside of my office where she could find tranquility. One such place was a quiet lake in a forest; she and her husband would go fishing there. She noticed how she gained a sense of happiness doing this, and we were able to connect that experience to the those with me in my office. From this point on, I knew she needed me to call her back when she called me, and I did so. I used the same telepathic judgment as earlier, only now I found it was not interfering with her treatment but helping it.

Morgan started to reverse her lifelong anxieties associates with being overweight. She went to Weight Watchers and became an active, contributing member. Her attachment to the Weight Watchers group was markedly different from the previous failed attachments in her life. She lost over 120 pounds, looked dramatically better, and felt happier than she ever had. About two and a half years into the treatment she no longer needed all her psychotropic medications and really started working on being happy. She got a dog and taught it tricks, and it slept with her. She took considerable joy in playing with him and shared this with her husband. We laughed together at the pictures and videos of these tricks that she proudly showed to me. She was able to confront her fears head-on; she got over her fear of not passing her driver's license exam, instead of worrying about it incessantly. She abandoned almost all of her anxieties and instead found activities to enjoy. Morgan's attachment to her husband, who was always at her side, became one of genuine trust. This replaced the previous dynamic of the relationship in which he had to constantly reassure her.

This treatment proceeded for many years with very productive gains. At one time, she became very distressed as she helped her husband with some of his needs; she cried, "No one ever meets my needs." She was shocked to realize that she had never communicated that to anyone before. Her husband, who was in that session with her, was unaware of her needs or that she felt so unloved. I explained to both of them that for her to be aware these needs, or to consider that they were unmet as she did then, was a very long road from where her treatment began. At the beginning of her treatment she was only aware of constant anxiety and that was the only thing she or her husband usually dealt with. Now she could experience the needs that she was never aware of before. This was a key turning point for this client and the richness of her life dramatically improved from then on.

Discussion

It is apparent to me that we utilize brain-to-brain synchronizations all the time in order to understand how to relate to others appropriately within various contexts. We know how to act when we see a family member, a friend, a colleague, or a stranger because we apply the appropriate frames of reference automatically, unconsciously, and as soon as we see them. This is what gives us a sense of safety — which we must have in order to grow. This process lends meaning to our communications with others, putting our relationship with them on a psychological plane. Patients with severe mental illness are not always aware of the contexts of their communications, nor do they find the meaning in those communications that we assume everyone does. Consequently, they often appear to

go through life robotically; they often do not know how to behave in one context as opposed to another, nor do they attempt to learn how to communicate effectively with others. This results in a form of psychosis—periods when their stress levels become unmanageably high and their attempted communications do not connect with others on any level. Alzheimer's patients have a similar issue.

In each of these two case studies, a less structured setting was used to enable the establishment of a brain-to-brain mode of communication. This mode was characterized by the patient and myself experiencing similar, and otherwise unprompted, thoughts at the same time. There were differences to the manner in which this unstructured setting evolved as it was based on the specific inner need of each patient. In one situation it required the patient to stay after her sessions for a few minutes, while the other situation required me to sense when or when not to answer the patient's calls.

The key to the success of these treatments lay in the unstructured 'flow' of the treatments as they naturally resulted from the brain-to-brain communication process. In each case, that 'flow' lead to a patient-specific resolution method because the patients became more capable of relating to others in their world. This, in turn, lead to an enactment within the treatment that allowed us to understand and resolve the original problem associated with the basic bonding failure in the first place.

In both cases I was able to find the structure shift that was needed to access the patient's failed mode of brain-to-brain synchronies with the use of my own brain-to-brain functions. We can regard this phenomenon as the patient 'leading me to it'; we can see that it is no different than when a mother is 'led' to address her infant's needs using her brain-to-brain communication sense. The basic aspect of the treatment situation, however, is that the use of brain-to-brain synchronies required a more unstructured situation than what is usually employed in psychotherapy. In each case, I could 'tell' we were on the 'right track' when I modified the treatment because I learned when I was relating to the patient in a brain-to-brain mode; we would experience similar, but otherwise unprompted, thoughts at the same time during these sessions. Additionally, I could tell we were moving towards progress because the treatment would become much more meaningful to the patients. It was at these times when they would suddenly find themselves able to relate to others as they had never before. In Jill's case, she was able to communicate in a clearer and more meaningful way with the people in her life; Morgan was able to reduce her constant anxieties. Most importantly, both patients were able to form attachments with me and their significant others, which they had not been able to do prior to the treatments.

Although there are other forms of attachment, this first and most basic attachment requires the greatest modification within treatment settings; they are also the most difficult to manage due to the lack of overt guideposts informing us on how to conduct the treatment. However, it is the sense of our connectedness, our brain-to-brain synchronies with the patients, and our intuition that guides us during this process.

This study demonstrates, for the first time, that brain-to-brain based psychotherapy can enable patients with chronic mental illnesses characterized by a marked deficit in basic attachment to form such attachments. This is the first demonstration of a way to resolve a chronic mental illness based on an in depth understanding of the genesis of that disorder. The cases presented here were uniquely suited for this treatment, as they involved patients who were highly motivated and intellectually flexible enough to benefit from it. Psychotherapy research needs to develop new ways of facilitating this type of treatment so that others can also benefit. This process could also include integrated treatments incorporating other modalities such as deep brain stimulation. Further work on the neurobiological roots of chronic mental illness, including gene/environment interactions, will help to further improve the effectiveness of our treatment.

References

[1] Ainsworth, M. D. (1972). *Attachment and dependency: A comparison.* In J. L. Gewirtz, *Attachment and dependency*. V. H. Winston & Sons.

[2] Andreou, C, Leicht, G, Nolte, G, Polomac, N, Moritz, S, Karow, A, Hanganu-Opatz, IL, Engel, AK, Mulert, C (2015). Resting-state theta-band connectivity and verbal memory in

schizophrenia and in the high-risk state. Schizophrenia Research, 161(2-3):299-307. doi: 10.1016/j.schres.2014.12.018. PMID: 25553979.

[3] Aydin, O, Balikci, K, Tas, C, Aydin, PU, Danaci, AE, Brüne, M, Lysaker, PH (2016). The developmental origins of metacognitive deficits in schizophrenia. Psychiatry Research, 245:15-21. doi: 10.1016/j.psychres.2016.08.012. PMID: 27526312.

[4] Baker, KB, Kim, JJ (2002). Effects of stress and hippocampal NMDA receptor antagonism on recognition memory in rats. Learning and Memory, 9(2):58-65. doi: 10.1101/lm.46102. PMID: 11992016. PMCID: PMC155932.

[5] Begus, K, Bonawitz, E (2020). The rhythm of learning: theta oscillations as an index of active learning in infancy. Developmental Cognitive Neuroscience, 45:100810. doi: 10.1016/j.dcn.2020.100810.

[6] Botcher, NA, Falck, JE, Thomson, AM, Mercer, A (2014). Distribution of interneurons in the CA2 region of the rat hippocampus. Frontiers in Neuroanatomy, 8(8):104. doi: 10.3389/fnana.2014.00104. PMID: 25309345. PMCID: PMC4176080.

[7] Chen, YH, Stone-Howell, B, Edgar, JC, Huang, M, Wootton, C, Hunter, MA, Lu, BY, Sadek, JR, Miller, GA, Cañive, JM (2016). Frontal slow-wave activity as a predictor of negative symptoms, cognition and functional capacity in schizophrenia. British Journal of Psychiatry: the Journal of Mental Science, 208(2):160-167. doi: 10.1192/bjp.bp.114.156075.

[8] Choe, HK, Reed, MD, Benavidez, N, Montgomery, D, Soares, N, Yim, YS, Choi, GB (2015). Oxytocin mediates entrainment of sensory stimuli to social cues of opposing valence. Neuron, 87(1):152-163. doi: 10.1016/j.neuron.2015.06.022. PMID: 26139372. PMCID: PMC4689302.

[9] Cousijn, H, Tunbridge, EM, Rolinski, M, Wallis, G, Colclough, GL, Woolrich, MW, Nobre, AC, Harrison, PJ (2015). Modulation of hippocampal theta and hippocampal–prefrontal cortex function by a schizophrenia risk gene. Human Brain Mapping, 36(6):2387-2395.

[10] Cuijpers, P, Hollon, SD, van Straten, A, Bockting, C, Berking, M, Andersson, G (2013 Apr 26). Does cognitive behaviour therapy have an enduring effect that is superior to keeping patients on continuation pharmacotherapy? A meta-analysis. BMJ Open, 3(4):e002542. doi: 10.1136/bmjopen-2012-002542. PMID: 23624992. PMCID: PMC3641456.

[11] Dozier, M (1990). Attachment organization and the treatment use for adults with serious psychopathological disorders. Development and Psychopathology, 2(1):47-60.

[12] Dozier, M, Tyrrell, C (1997). Attachment and communication among persons with serious psychopathological disorders, in Attachment Theory and Close Relationships, (eds J.A. Simpson and W.S. Rholes). New York: Guilford.

[13] Dozier, M, Lomax, L, Tyrrell, CL, Lee, SW (2001). The challenge of treatment for clients with dismissing states of mind. Attachment and Human Development, 3(1):62-76.

[14] Dudek, SM, Alexander, GM, Farris, S (2016). Rediscovering area CA2: unique properties and functions. Nature Reviews. Neuroscience, 17(2):89-102. doi: 10.1038/nrn.2015.22.

[15] Ekstrom, AD, Caplan, JB, Ho, E, Shattuck, K, Fried, I, Kahana, MJ (2005). Human hippocampal theta activity during virtual navigation. Hippocampus, 15(7):881-889. doi: 10.1002/hipo.20109. Erratum in: Hippocampus (2006). PMID: 16114040, 16(1):101.

[16] Falkai, P, Malchow, B, Wetzestein, K, Nowastowski, V, Bernstein, HG, Steiner, J, Schneider-Axmann, T, Kraus, T, Hasan, A, Bogerts, B, Schmitz, C, Schmitt, A (2016a). Decreased oligodendrocyte and neuron number in anterior hippocampal areas and the entire hippocampus in schizophrenia: A stereological postmortem study. Schizophrenia Bulletin, 42, *Suppl 1*. Suppl:S4-S12:S4-S12. doi: 10.1093/schbul/sbv157.

[17] Falkai, P, Steiner, J, Malchow, B, Shariati, J, Knaus, A, Bernstein, HG, Schneider-Axmann, T, Kraus, T, Hasan, A, Bogerts, B, Schmitt, A (2016b). Oligodendrocyte and interneuron density in hippocampal subfields in schizophrenia and association of oligodendrocyte number with cognitive deficits. Frontiers in Cellular Neuroscience, 10:78. doi: 10.3389/fncel.2016.00078. PMID: 27065804. PMCID: PMC4811909.

[18] Favaretto, E, Torresani, S (1997). Il legame genitoriale come fattore predittivo dello

sviluppo di disturbi psichiatrici in eta adulta. Epidemiologia e Psichiatria Sociale, 6(2):124-138.

[19] Feldman, R (2020). What is resilience: an affiliative neuroscience approach. World Psychiatry: Official Journal of the World Psychiatric Association, 19(2):132-150. doi: 10.1002/wps.20729.

[20] Ferguson, JN, Aldag, JM, Insel, TR, Young, LJ (2001). Oxytocin in the medial amygdala is essential for social recognition in the mouse. Journal of Neuroscience: the Official Journal of the Society for Neuroscience, 21(20):8278-8285. doi: 10.1523/JNEUROSCI.21-20-08278.2001. PMID: 11588199. PMCID: PMC6763861.

[21] Ferguson, JN, Young, LJ, Insel, TR (2002). The neuroendocrine basis of social recognition. Frontiers in Neuroendocrinology, 23(2):200-224. doi: 10.1006/frne.2002.0229. PMID: 11950245.

[22] Ford, JM, Mathalon, DH, Whitfield, S, Faustman, WO, Roth, WT (2002). Reduced communication between frontal and temporal lobes during talking in schizophrenia. Biological Psychiatry, 51(6):485-492.

[23] Gao, XM, Elmer, GI, Adams-Huet, B, Tamminga, CA (2009). Social memory in mice: disruption with an NMDA antagonist and attenuation with antipsychotic drugs. Pharmacology, Biochemistry, and Behavior, 92(2):236-242. doi: 10.1016/j.pbb.2008.11.016.

[24] Gobbini, MI, Leibenluft, E, Santiago, N, Haxby, JV (2004). Social and emotional attachment in the neural representation of faces. Neuroimage, 22(4):1628-1635. doi: 10.1016/j.neuroimage.2004.03.049. Erratum in: Neuroimage, 2006 Sep;32(3):1484. PMID: 15275919.

[25] Hartling, L, Abou-Setta, AM, Dursun, S, Mousavi, SS, Pasichnyk, D, Newton, AS (2012). Antipsychotics in adults with schizophrenia: comparative effectiveness of first-generation versus second-generation medications: a systematic review and meta-analysis. Annals of Internal Medicine, 157(7):498-511. doi: 10.7326/0003-4819-157-7-201210020-00525. PMID: 22893011.

[26] Heckers, S (2001). Neuroimaging studies of the hippocampus in schizophrenia. Hippocampus, 11(5):520-528. doi: 10.1002/hipo.1068. PMID: 11732705.

[27] Heckers, S, Konradi, C (2002). Hippocampal neurons in schizophrenia. Journal of Neural Transmission, 109(5-6):891-905. doi: 10.1007/s007020200073.

[28] Hofmann, SG, Asnaani, A, Vonk, IJ, Sawyer, AT, Fang, A (2012). The efficacy of cognitive behavioral therapy: a review of meta-analyses. Cognitive Therapy and Research, 36(5):427-440. doi: 10.1007/s10608-012-9476-1.

[29] Holthausen, EA, Wiersma, D, Sitskoorn, MM, Dingemans, PM, Schene, AH, van den Bosch, RJ (2003). Long-term memory deficits in schizophrenia: primary or secondary dysfunction? Neuropsychology, 17(4):539-547. doi: 10.1037/0894-4105.17.4.539. PMID: 14599267.

[30] Honea, R, Crow, TJ, Passingham, D, Mackay, CE (2005). Regional deficits in brain volume in schizophrenia: a meta-analysis of voxel-based morphometry studies. American Journal of Psychiatry, 162(12):2233-2245. doi: 10.1176/appi.ajp.162.12.2233. PMID: 16330585.

[31] Howells, FM, Temmingh, HS, Hsieh, JH, van Dijen, AV, Baldwin, DS, Stein, DJ (2018). Electroencephalographic delta/alpha frequency activity differentiates psychotic disorders: a study of schizophrenia, bipolar disorder and methamphetamine-induced psychotic disorder. Translational Psychiatry, 8(1)**:**75. doi: 10.1038/s41398-018-0105-y.

[32] Jacobs, SA, Huang, F, Tsien, JZ, Wei, W (2016). Social recognition memory test in rodents. Oi:10.21769/BIOPROTOC.1804Corpus ID: 63112350.

[33] Kinreich, S, Djalovski, A, Kraus, L, Louzoun, Y, Feldman, R (2017). Brain-to-brain synchrony during naturalistic social interactions. sci. rep.:17060. Scientific Reports Dec 6, 7(1):17060. doi: 10.1038/s41598-017-17339-5. PMID: 29213107. PMCID: PMC5719019.

[34] Kogan, JH, Frankland, PW, Silva, AJ (2000). Long-term memory underlying hippocampus-dependent social recognition in mice. Hippocampus, 10(1):47-56. doi: 10.1002/(SICI)1098-1063(2000)10:1<47::AID-HIPO5>3.0.CO;2-6. PMID: 10706216.

[35] Lee, H, Dvorak, D, Fenton, AA (2014). Targeting neural synchrony deficits is sufficient to improve cognition in a

schizophrenia-related neurodevelopmental model. Frontiers in Psychiatry, 5:15. doi: 10.3389/fpsyt.2014.00015.

[36] Lega, BC, Jacobs, J, Kahana, M (2012). Human hippocampal theta oscillations and the formation of episodic memories. Hippocampus, 22(4):748-761. doi: 10.1002/hipo.20937. PMID: 21538660.

[37] Lenzi, D, Trentini, C, Tambelli, R, Pantano, P (2015). Neural basis of attachment-caregiving systems interaction: insights from neuroimaging studies. Frontiers in Psychology, 6:1241. doi: 10.3389/fpsyg.2015.01241.

[38] Leong, V, Byrne, E, Clackson, K, Georgieva, S, Lam, S, Wass, S (2017). Speaker gaze increases infant–adult connectivity. Proceedings of the National Academy of Sciences of the United States of America, 114(50):13290-13295. doi: 10.1073/pnas.1702493114.

[39] Li, W, Li, K, Guan, P, Chen, Y, Xiao, Y, Lui, S, Sweeney, JA, Gong, Q (2018). Volume alteration of hippocampal subfields in first-episode antipsychotic-naïve schizophrenia patients before and after acute antipsychotic treatment. NeuroImage. Clinical, 20:169-176. doi: 10.1016/j.nicl.2018.07.008.

[40] Lin, YT, Hsieh, TY, Tsai, TC, Chen, CC, Huang, CC, Hsu, KS (2018). Conditional deletion of hippocampal CA2/CA3a oxytocin receptors impairs the persistence of long-term social recognition memory in mice. Journal of Neuroscience: the Official Journal of the Society for Neuroscience, 38(5):1218-1231. doi: 10.1523/JNEUROSCI.1896-17.2017. PMID: 29279308. PMCID: PMC6596267.

[41] Liotti, G, Gumley, A (2009). An Attachment Perspective on Schizophrenia: the Role of Disorganized Attachment, Dissociation and Mentalization. 10.1002/9780470699652.ch9.

[42] Macdonald, K, Feifel, D (2012). Oxytocin in schizophrenia: a review of evidence for its therapeutic effects. Acta Neuropsychiatrica, 24(3):130-146. doi: 10.1111/j.1601-5215.2011.00634.x.

[43] Manahan-Vaughan (2018) Recording field potentials and synaptic plasticity from freely behaving rodents. In: Manahan-VaughanD, editor. *Handbook of in vivo neural plasticity techniques* London: Academic Press, pp. 1–42.

[44] Mitra, S, Nizamie, SH, Goyal, N, Tikka, SK (2017). Electroencephalogram alpha-to-theta ratio over left fronto-temporal region correlates with negative symptoms in schizophrenia. Asian Journal of Psychiatry, 26:70-76. doi: 10.1016/j.ajp.2017.01.013.

[45] Moran, LV, Hong, LE (2011). High vs low frequency neural oscillations in schizophrenia. Schizophrenia Bulletin, 37(4):659-663. doi: 10.1093/schbul/sbr056.

[46] Mou, X (2016). Hippocampal CA2 region: A new player in social dysfunctions. Journal of Neurology and Neurophysiology, 07(1). doi: 10.4172/2155-9562.1000357.

[47] Narr, KL, Thompson, PM, Szeszko, P, Robinson, D, Jang, S, Woods, RP, Kim, S, Hayashi, KM, Asunction, D, Toga, AW, Bilder, RM (2004). Regional specificity of hippocampal volume reductions in first-episode schizophrenia. NeuroImage, 21(4):1563-1575. doi: 10.1016/j.neuroimage.2003.11.011.

[48] Newson, JJ, Thiagarajan, TC (2018). EEG frequency bands in psychiatric disorders: a review of resting state studies. Frontiers in Human Neuroscience, 12:521. doi: 10.3389/fnhum.2018.00521.

[49] Pais-Vieira, M, Lebedev, M, Kunicki, C, Wang, J, Nicolelis, MA (2013). A brain-to-brain interface for real-time sharing of sensorimotor information. Scientific Reports, 3**:**1319. doi: 10.1038/srep01319.

[50] Piskorowski, RA, Nasrallah, K, Diamantopoulou, A, Mukai, J, Hassan, SI, Siegelbaum, SA, Gogos, JA, Chevaleyre, V (2016). Age-dependent specific changes in area CA2 of the hippocampus and social memory deficit in a mouse model of the 22q11.2 deletion syndrome. Neuron, 89(1):163-176. doi: 10.1016/j.neuron.2015.11.036.

[51] Pratt, M, Goldstein, A, Feldman, R (2018). Child brain exhibits a multi-rhythmic response to attachment cues. Social Cognitive and Affective Neuroscience, 13(9):957-966. doi: 10.1093/scan/nsy062.

[52] Rao, RPN, Stocco, A, Bryan, M, Sarma, D, Youngquist, TM, Wu, J, Prat, CS (2014). A direct brain-to-brain interface in humans. PLOS ONE, 9(11):e111332. doi: 10.1371/journal.pone.0111332.

[53] Read, J, Gumley, A (2008). Can attachment theory help explain the relationship between

childhood adversity and psychosis? Attachment: new directions in psychotherapy and relational psychoanalysis, 2:1-35.

[54] Richter, K, Wolf, G, Engelmann, M (2005). Social recognition memory requires two stages of protein synthesis in mice. Learning and Memory, 12(4):407-413. doi: 10.1101/lm.97505.

[55] Rockstroh, BS, Wienbruch, C, Ray, WJ, Elbert, T (2007). Abnormal oscillatory brain dynamics in schizophrenia: a sign of deviant communication in neural network? BMC Psychiatry, 7(1):44. doi: 10.1186/1471-244X-7-44.

[56] Sarro, EC, Wilson, DA, Sullivan, RM (2014). Maternal regulation of infant brain state. Current Biology: CB, 24(14):1664-1669. doi: 10.1016/j.cub.2014.06.017.

[57] Siekmeier, PJ, Stufflebeam, SM (2010). Patterns of spontaneous magnetoencephalographic activity in patients with schizophrenia. Journal of Clinical Neurophysiology: Official Publication of the American Electroencephalographic Society, 27(3):179-190. doi: 10.1097/WNP.0b013e3181e0b20a.

[58] Sigurdsson, T, Stark, KL, Karayiorgou, M, Gogos, JA, Gordon, JA (2010). Impaired hippocampal–prefrontal synchrony in a genetic mouse model of schizophrenia. Nature, 464(7289):763-767. doi: 10.1038/nature08855.

[59] Sloan, EP, Maunder, RG, Hunter, JJ, Moldofsky, H (2007). Insecure attachment is associated with the alpha-EEG anomaly during sleep. BioPsychoSocial Medicine, 1:20. doi: 10.1186/1751-0759-1-20.

[60] Stafford, MR, Mayo-Wilson, E, Loucas, CE, James, A, Hollis, C, Birchwood, M, Kendall, T (2015). Efficacy and safety of pharmacological and psychological interventions for the treatment of psychosis and schizophrenia in children, adolescents and young adults: a systematic review and meta-analysis. PLOS ONE, 10(2):e0117166. doi: 10.1371/journal.pone.0117166. PMID: 25671707. PMCID: PMC4324833

[61] Stevenson, EL, Caldwell, HK (2014). Lesions to the CA2 region of the hippocampus impair social memory in mice. The European Journal of Neuroscience, 40(9), 3294–3301. doi: 10.1111/ejn.12689.

[62] Stolk, A, Noordzij, ML, Verhagen, L, Volman, I, Schoffelen, JM, Oostenveld, R, Hagoort, P, Toni, I (2014). Cerebral coherence between communicators marks the emergence of meaning. Proceedings of the National Academy of Sciences of the United States of America, 111(51):18183-18188. doi: 10.1073/pnas.1414886111. PMID: 25489093. PMCID: PMC4280639.

[63] Striepens, N, Kendrick, KM, Maier, W, Hurlemann, R (2011 Oct). Prosocial effects of oxytocin and clinical evidence for its therapeutic potential. Frontiers in Neuroendocrinology, 32(4):426-450. doi: 10.1016/j.yfrne.2011.07.001. PMID: 21802441.

[64] Szeszko, PR, Goldberg, E, Gunduz-Bruce, H, Ashtari, M, Robinson, D, Malhotra, AK, Lencz, T, Bates, J, Crandall, DT, Kane, JM, Bilder, RM (2003). Smaller anterior hippocampal formation volume in antipsychotic-naive patients with first-episode schizophrenia. American Journal of Psychiatry, 160(12):2190-2197. doi: 10.1176/appi.ajp.160.12.2190. PMID: 14638589.

[65] Tamminga, CA, Stan, AD, Wagner, AD (2010). The hippocampal formation in schizophrenia. American Journal of Psychiatry, 167(10):1178-1193. doi: 10.1176/appi.ajp.2010.09081187. PMID: 20810471.

[66] Thase, ME (2007 Dec). STEP-BD and bipolar depression: what have we learned? Current Psychiatry Reports, 9(6):497-503. doi: 10.1007/s11920-007-0068-9. PMID: 18221631.

[67] Tirko, NN, Eyring, KW, Carcea, I, Mitre, M, Chao, MV, Froemke, RC, Tsien, RW (2018). Oxytocin transforms firing mode of CA2 hippocampal neurons. Neuron, 100(3):593-608.e3. doi: 10.1016/j.neuron.2018.09.008.

[68] Tyrrell, CL, Dozier, M, Teague, GB, Fallot, RD, G.B. and Fallot (1999). R.D. Journal of Consulting and Clinical Psychology, 67(5):725-733.

[69] Tzakis, N, Holahan, MR (2019). Social memory and the role of the hippocampal CA2 region. Frontiers in Behavioral Neuroscience, 13:233. doi: 10.3389/fnbeh.2019.00233.

[70] Uhlhaas, PJ, Pipa, G, Lima, B, Melloni, L, Neuenschwander, S, Nikolić, D, Singer, W (2009). Neural synchrony in cortical

networks: history, concept and current status. Frontiers in Integrative Neuroscience, 3:17. doi: 10.3389/neuro.07.017.2009. PMID: 19668703. PMCID: PMC2723047.

[71] Uhlhaas, PJ, Singer, W (2010). Abnormal neural oscillations and synchrony in schizophrenia. Nature Reviews. Neuroscience, 11(2):100-113.

[72] Uhrig, S, Hirth, N, Broccoli, L, von Wilmsdorff, M, Bauer, M, Sommer, C, Zink, M, Steiner, J, Frodl, T, Malchow, B, Falkai, P, Spanagel, R, Hansson, AC, Schmitt, A (2016). Reduced oxytocin receptor gene expression and binding sites in different brain regions in schizophrenia: A post-mortem study. Schizophrenia Research, 177(1-3):59-66. doi: 10.1016/j.schres.2016.04.019. PMID: 27132494.

[73] van Wimersma Greidanus, TB, Maigret, C (1996). The role of limbic vasopressin and oxytocin in social recognition. Brain Research, 713(1-2):153-159. doi: 10.1016/0006-8993(95)01505-1. PMID: 8724986.

[74] Wass, SV, Noreika, V, Georgieva, S, Clackson, K, Brightman, L, Nutbrown, R, Covarrubias, LS, Leong, V (2018). Parental neural responsivity to infants' visual attention: how mature brains influence immature brains during social interaction. PLOS Biology, 16(12):e2006328. doi: 10.1371/journal.pbio.2006328.

[75] Watrous, AJ, Fried, I, Ekstrom, AD (2011). Behavioral correlates of human hippocampal delta and theta oscillations during navigation. Journal of Neurophysiology, 105(4):1747-1755. doi: 10.1152/jn.00921.2010. PMID: 21289136.

[76] Weinberger, DR (1999). Cell biology of the hippocampal formation in schizophrenia. Biological Psychiatry, 45(4):395-402. doi: 10.1016/s0006-3223(98)00331-x.

[77] Wesson, DW, Keller, M, Douhard, Q, Baum, MJ, Bakker, J (2006). Enhanced urinary odor discrimination in female aromatase knockout (ArKO) mice. Hormones and Behavior, 49(5):580-586. 47:(Ar.KO).

[78] Wetmore, C, Olson, L, Bean, AJ (1994). Regulation of brain-derived neurotrophic factor (BDNF) expression and release from hippocampal neurons is mediated by non-NMDA type glutamate receptors. Journal of Neuroscience: the Official Journal of the Society for Neuroscience, 14(3 Pt. 2):1688-1700. doi: 10.1523/JNEUROSCI.14-03-01688.1994. PMID: 8126563. PMCID: PMC6577587.

[79] Wheatley, T, Kang, O, Parkinson, C, Looser, CE (2012). From mind perception to mental connection: synchrony as a mechanism for social understanding. Social and Personality Psychology Compass, 6(8):589-606.

[80] World Health Organization (2011). Global Status Report on Non-Communicable Doseases.2010. Geneva: WHO.

[81] World Health Organization (2019). Mental disorders https://www.who.int/news-room/fact-sheets/detail/mental-disorders.