From Squirrels to Cognitive Behavioral Therapy (CBT): The Modulation of the Hippocampus

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Abstract

The legitimacy of psychotherapy can often be thrown into doubt as its mechanisms of action are generally considered hazy and unquantifiable. One way to support the effectiveness of therapy would be to demonstrate the physical effects that this treatment option can have on the brain, just like psychotropic medications that physically alter the brain's construction leaving no doubt as to the potency of their effects. Beginning with the understanding of therapy as a behavior, this paper first questions the possibility of behavior effecting measurable change on the brain. Examining diverse samples of both animals and humans repeatedly shows that the excessive exercise of spatial memory and mapping activities, which rely on the hippocampus, correlates with targeted hippocampal growth and modulation. The hippocampus reliably enlarges when over exercised. With this correlation demonstrated, this paper returns to therapy to find that Cognitive Behavioral Therapy (CBT), of all psychotherapies, modulates the brain in the very same pattern effected by targeted spatial and mapping behavior. These twin correlations lend credence to each other and their surprising similarity is best explained by the hippocampus's chief role in declarative memory. Both spatial memory and CBT rely on skills and behaviors regulated by declarative memory, lunder the jurisdiction of the hippocampus. This paper aligns the strong evidence of the spatial memory- hippocampal growth correlation with the CBT- hippocampal growth observation to show that CBT does indeed leave observable effects on the brain and real impressions on the patient.

Introduction:

Objective

This paper will explore how targeted use of the hippocampus leads to its morphological modulation and growth, with the overall goal of demonstrating how targeted behavior can demonstrably alter the brain. Specifically, the hippocampal growth correlated to its cognitive-map character will be explored. The correlation between the practice of spatial mapping activities and hippocampal growth will be examined in animals and humans. With hippocampus growth in response to these specific activities firmly established, this paper will attempt to correlate this observation to an area where it can have real-world application: therapy. The therapy that will receive particular focus is Cognitive Behavioral Therapy (CBT). This focus is due to the observation that CBT, out of all psychotherapies, specifically effects brain modulation along the very same lines as spatial memory and practice of mapping skills.

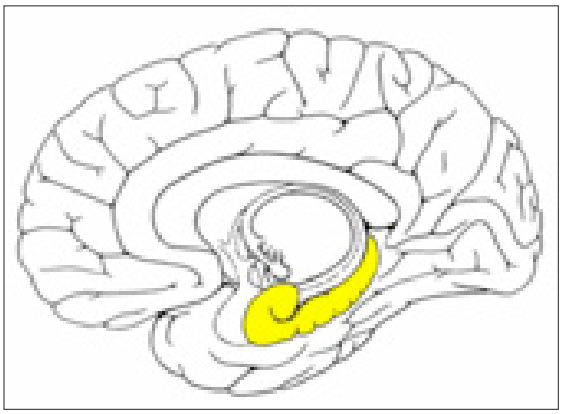

Figure 1: The human hippocampus, right lateral view (http://neurowiki.dk/images/8/83/Hippocampus0.png

What Is the Hippocampus?

The hippocampus is a seahorse shaped structure located in the medial temporal lobe of the brain. It has two lobes that each process a different type of memory. The right lobe is mainly responsible for viseo-spatial memory and the left lobe primarily works with verbal or narrative memory (Burgess, et. al. 2002). However, this lateralization is general; current research suggests that the storage and retrieval of both types of memories, especially the spatial subset, are more universally distributed across the whole hippocampus. This is evidenced by "cells coding for the same location [in reference to viseo-spacial memory] being distributed over the entire hippocampus." (Moser, Moser, 1998).

The hippocampus is considered the center of the declarative memory system. Declarative memory, also known as explicit memory, is the type of memory that can be consciously recalled and put into words, such as for facts and verbal knowledge (Ullman, 2004). It includes "episodic memories" which are autobiographical and personal, and "semantic memories," defined as general knowledge about the world (Burgess et. al. 2002, Schachter et. al. 2009). As part of its role in declarative memory "the hippocampus is central to the rapid acquisition of declarative knowledge about the environment, generating a so-called cognitive map." (Voermans et. al. 2004).

The cognitive map theory is the most current explanation for how organisms create and store memories of their environment. This theory "proposes that the hippocampus of rats and other animals represents their environments, locations within those environments, and their contents, thus providing the basis for spatial memory and flexible navigation." Essentially, the hippocampus builds a personal map of an organism's environment

as the organism navigates its way through it. Interaction with the frontal lobes of the brain "timestamps" each addition to the cognitive map, creating context and adding episodic character to the map (Burgess et. al. 2002).

The hippocampus has been observed to work in close conjunction with the caudate nucleus of the basal ganglia, a part of the brain responsible for forming associations between place and stimulus, thus leading to habitual behaviors. Both systems can work together, but non-competitively, in route recognition. When an organism returns to a previously visited location, the hippocampus uses its cognitive map to help recognize the location while the caudate contributes by recalling the personal memories of what occurred in this place the last time the organism was there. The hippocampus and caudate traverse different paths to come to the same conclusion: place or route recognition. Each are capable of recognizing a location on their own, via their alternative methods, but the possibility of enhanced recognition resulting from interaction between the two has been studied (Voermans et. al. 2004).

This is an example of the current trend in scientific research, in which many scientists study the interrelations and delocalization of brain function, based on the premise that "because the cognitive systems of the brain work in an integrated fashion, presumably the different memory systems do not work in isolation." (Voermans et. al. 2004). As such, much research has been done on the interactions and communication between the hippocampus and various other parts of the brain whereas, historically, focus had been placed on defining each brain area and its specific function. This makes focus on the morphology, function, and effects of one specific brain structure difficult but this paper will attempt to focus on the hippocampus specifically.

Methods

Information for this paper was obtained through various databases made available through the Touro College library. Relevant Internet searches, via Google, were also used to help lead to resources. Keywords included hippocampus, declarative memory, cognitive behavioral therapy, and brain modulation. Textbooks on therapy were consulted as well.

Discussion: Animal Studies of the Hippocampus

The clear effects of an organism's mapping behavior affecting physical changes on its hippocampus were initially observed in black-capped chickadees in Ithaca, NY. Chickadees are small, non-migratory, food-storing birds in the same family as jays and nutcrackers. These birds "showed a peak in relative hippocampal size in October, at the same time of year that food storing was reported to be greatest in this population of chickadees." (Sherry, Hoshooley, 2010). This peak was specific to the hippocampus; two other brain areas measured for control did not undergo any change at all. Additionally, this change was assuredly due to their increased mapping activity and not the alteration in day length (photoperiod) that occurs in the fall, as manipulating the day length experienced by captive birds had no effect on hippocampus size (Sherry, Hoshooley, 2010). Taking this together with previous studies that lesioned the avian hippocampus and observed how this specifically "disrupted memory for the locations of caches, because caching performance, feeding, and other behavior were not affected" assures the hippocampus's central role in cache mapping/memory (Sherry, Vaccarino, 1989). Therefore, it is safe to conclude that the correlation between the chickadees' behavior and their hippocampus size is causal. The chickadees' food storing activity, which involves tracking down nuts and seeds, hiding these finds in multiple caches, and most importantly recalling the location of each cache, exercises and expands the hippocampus.

In fact, the research team in this study worried that their observations may not be readily replicable because "in captivity, it may not be possible for birds to engage in enough food storing and cache retrieval to produce the changes in hippocampal size and neurogenesis observed in the wild." (Sherry, Hoshooley, 2010). This concern insinuates that once a certain threshold of practice of this behavior is reached, the hippocampal change is inevitable. It also shows that certainly it is some excessive level of practice of these activities, food storing and cache retrieval, that directly enlarges the hippocampus.

In a remarkably parallel finding, the hippocampi of Northeastern red squirrels, creators and hoarders of multiple caches of nuts, in an activity self-descriptively named "scatterhoarding," are larger than the hippocampi of their close cousins, the gray squirrels of the West Coast. The non-hoarding gray squirrels have no winter to contend with and so have no need to utilize the spatial mapping and recall skills specific to the hippocampus to scatterhoard for the future when food will not be available (Johnson et. al. 2010).

Notably, red squirrel hippocampus size has even been shown to fluctuate along with their hibernation patterns. When the squirrels are up and about, busily finding, hoarding, and creating mental maps of their caches, their hippocampi are larger than when their body temperature decreases to the point of initiating torpor, or hibernation, and thus cessation of all such activities (Millesi et. al. 2001). Like the chickadees, the red squirrels are clearly modulating their own hippocampi through their behavior.

Homing pigeons, known specifically for their mapping and spatial skills, are a natural species to look for the hippocampal

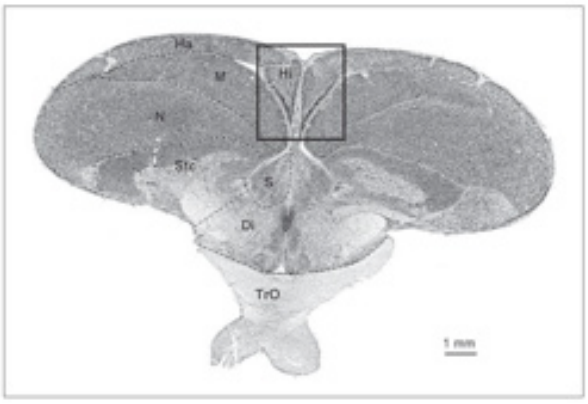

Figure 2: Coronal section through brain of homing pigeon with area of study, hippocampus, outlined. (Cnotka et. al. 2008)

growth observed in chickadees and squirrels. Citing studies similar to those discussed above, researcher Cnotka and her team hinge their study on the fact that "the hippocampus plays a critical role in processing spatial information both in birds and in mammals." (Cnotka et. al. 2008). And indeed, when these researchers examined the brains of the pigeonsthey found that homing pigeons possess disproportionately larger hippocampi for their body mass (Figure 2). A separate research team compounded this research by finding "morphological and histological differences in hippocampal tissue in homing and non-homing pigeons" (Shapiro, Wieraszko, 1996).

Additionally, comparing carrier pigeons that are allowed to fly, explore their barns, and map out new routes with pigeons that are confined to their cages, revealed the explorer pigeons to have measurably larger hippocampi (Cnotka et. al. 2008). The comparison between the explorer pigeons and the cage-confined pigeons directly parallels the above comparison between the red squirrels and gray squirrels. Both directly prove that when an animal stresses its hippocampus, the hippocampus will remodulate and enlarge.

Neurogenesis

Although it has been firmly established that animals who exercise their hippocampus directly affect their hippocampi's growth, the cause of this phenomenon has not been determined. The team of researchers who conducted the study on homing pigeons admit just that. They write, "in our study we have not determined what is responsible for this increase in volume, but it would be interesting to see why the hippocampus might be larger. Existing cells could increase their cell body size or build up larger dendritic arbors, new neurons or glia could be added, or there could be increased vascularization." (Cnotka et. al. 2008).

Meanwhile, the researchers who observed the hippocampus growth in New York chickadees were able to squarely implicate neurogenesis as the mechanism of growth. They did this by administering to wild birds "injections of tritiated thymidine, [3H] thymidine, which is incorporated into the nucleus of mitotic cells" (Sherry, Hoshooley, 2010). [3H]thymidine is a commonly used radioactive cell marker that newly forming cells incorporate into their DNA, thus differentiating the new cells from pre-existing cells (Toyohara et. al. 2002). The researchers then released the chickadees back into the wild. When they recaptured the birds, they found that "birds given [3H]thymidine in October had more labelled hippocampal cells when captured six weeks later than birds injected in August or February/March." (Sherry, Hoshooley, 2010). Evidently the birds generated more cells in their hippocampi in October, when their scatterhoarding activity levels were high, than in the months when they were not exercising their hippocampi excessively.

Neurogenesis would seem to be the most likely explanation for hippocampus growth but the possibility of new brain cells being created "on demand" should not be taken for granted. This is because "in most brain regions, the generation of neurons is generally confined to a discrete developmental period," and so growth would really not be possible at any time for most areas. Eriksson et. al., (1998), originally demonstrated the presence of progenitor cells, from which newborn neurons are generated and so the prerequisites for new cell growth, only in specific parts of the brain. Among these parts was the hippocampus. He showed this by injecting human cancer patients with "a thymidine analog, BrdU [that] is incorporated into the DNA of dividing cells" and then after the patients died, dissecting their brains to find labelled cells in the denate gyrus of the hippocampus (Eriksson et. al. 1998). These labelled cells indicate the presence of new neurons, and so progenitor cells, specifically in the hippocampus. This finding is crucial to correlating the animal studies to humans and offers the mechanistic explanation for how the hippocampus gets bigger. It shows that new neurons can indeed be grown in the hippocampus and that this growth can be initiated at any time – including whenever mapping skills are exercised. Eriksson's study essentially opened the door to neurogenesis and, as he ends off his report, "the potential to regulate human neurogenesis should prove to be an interesting area of investigation." (Eriksson et. al. 1998). The data in this paper enthusiastically supports this proposition.

Neuromodulation

In contrast, another research team focused on "the plastic processes that underlie long term potentiation" as the mechanism by which an organism can remodel its "mental map," or hippocampus. This team defines long-term potentiation as "a long-lasting, activity-dependent enhancement of synaptic strength that has been extensively studied in the hippocampus." (Kentros et. al. 1998). In their study, they observed how rats build their

mental maps by encoding each cell in their hippocampus with a different aspect of the place they are in. These programmable cells were appropriately named "place cells." It is then the "conjoint activity of place cells [that is] thought to be the basis of a map of the environment that the animal uses for solving spatial problems." (Kentros et. al. 1998). With this proposition for the construction of the mental map in place, the researchers then demonstrated that place cells, and the connections and interactions between them, can be reprogrammed based on the rat's activity. Essentially, the team demonstrated the ability of the hippocampus to remodulate, in addition to expand, in response to excessive use (Kentros et. al. 1998).

Taken together, notable hippocampal neurogenesis and neuromodulation correlates with the specific exercise of the hippocampus via practice of hippocampus-centric behaviors, namely those that rely on spacial mapping and recall activity.

Onward to the Humans

Having examined how the hippocampus specific behaviors of a wide range of animal species cause direct growth of the hippocampus, and accounting for this growth with evidence for neurogenesis and neuromodulation in the hippocampus, this paper turns to the likelihood of this causation occurring in humans as well. Are human brains, specifically the hippocampi, as manipulatable and malleable as those of rats, squirrels, chickadees, and pigeons?

Blithely referencing the sum of the extensive work that we have examined thus far, researcher Eleanor Maguire states, "the volume of the hippocampus in nonhumans is known to vary as a function of the demands placed on spatial memory." (Maguire et. al. 2006). With this firmly established, Maguire and her co-workers performed a landmark study comparing the brains of London taxi drivers with the brains of London bus drivers.

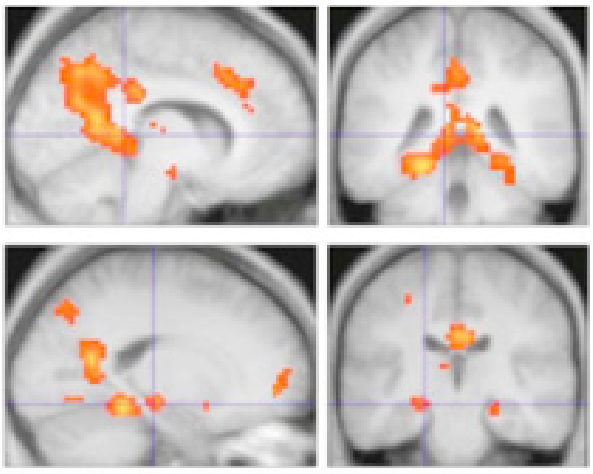

Figure 3: Hippocampal activation upon naviagtion through novel environments. (Maguire et. al. 2002

London is famous for its convoluted cityscape and so its taxi drivers are required to spend about two to four years studying its design and navigating its intricacies in order to be ready to pass the test required to get licensed as professional drivers. The taxi drivers' process to proficiency is rigorous and heavily reliant on the hippocampus. Just as it was observed with regard to the chickadees, squirrels, and pigeons, Maguire and her team report, "...years of navigation experience correlated with hippocampal gray matter volume only in taxi drivers [and not in London's bus drivers], with right posterior gray matter volume increasing and anterior gray matter volume decreasing with more navigation experience." (Maguire et. al. 2006). Since London bus drivers matched with London taxi drivers in "driving experience and levels of stress, but differed in that they follow a constrained set of routes," they provided the perfect comparison group to the taxi drivers who must learn and then navigate "25,000 streets and the locations of thousands of places of interest." (Maguire et. al. 2006, Woollett, Maguire, 2012) Therefore, comparing the taxi drivers, who must continuously re-navigate and calculate intricately mapped out routes, to bus drivers, who merely retrace a limited set of preset routes, shows that it is specifically the mapping activity that remodels and expands the hippocampus. Maguire confirms for animals and revolutionarily proves that for humans as well, that to modulate the hippocampus "the key factor seems to be utilizing a complex spatial representation over years of navigation." (Maguire et. al. 2006)

The clear growth of the hippocampi of London taxi drivers in response to their spatial mapping behaviors highlights that humans are indeed capable of modulating their own brains. People who spend years stressing their hippocampi will reliably enlarge them. The London taxi drivers study also shows that, surprisingly enough, changing one's own brain is really not that hard. This opens for consideration the reach of self-induced brain manipulation. To what extent can humans modulate their own brains, through what activities, and to what benefit?

The Relevance to Therapy

Answering these questions is of particular pertinence to psychologists, specifically those who practice therapy. This is because, "if psychotherapy is regarded as a form of learning, then the learning process that occurs in psychotherapy may produce alterations [in the brain]." (Gabbard, 2000). Researchers seek to highlight the physical, observable effects of therapy on the human brain to help prove the therapy's efficacy. And indeed, multiple fascinating observations have been made.

In 1992, a study contrasting different forms of treatment for depression found that "behavior therapy and fluoxetine [a common antidepressant] appear to produce similar decreases in cerebral metabolic rates in the head of the right caudate nucleus." (Gabbard, 2000). The caudate nucleus is part of the basal ganglia and responsible for "the acquisition of place-appropriate responses leading to habitual behavior," (Voermans et. al. 2004). While it does function in a memory system separate from the hippocampus, the two do have comparable enough roles that in the event of degeneration of one, the other can compensate (as detailed earlier in this paper). According to this study, "both memory systems support navigational memory, albeit based on the processing of different representations. It has been hypothesized that both systems work in parallel, receiving similar input information, but processing this information according to principles that emphasize different relationships among the elements of a given event or situation" (Voermans et. al. 2004). Importantly, the basal ganglia, like the hippocampus, does possess progenitor cells for growth by neurogenesis (Erikkson et. al. 1998).

The similarity between the roles of the basal ganglia and the hippocampus help the modulation of one stand in as evidence for the possibility of the modulation of the other. Similar functions means that similar activities will affect their size and shape. With the overwhelming evidence that this paper has examined for hippocampus-centric activities modulating the hippocampus, it follows that similar activities, only different in that they are reliant on the caudate, would modulate the caudate. If this is so then we can consider how the activities that the researchers found here to modulate the caudate, Behavior Therapy, might be similar to the activities that modulate the hippocampus (spatial memory and mapping behaviors).

Another research team comparing the effects of different mental health treatment forms showed that "cognitive behavioral therapy appears to cause biological changes in people with panic disorder." (Gabbard, 2000). These researchers first observed that individuals with panic disorders inappropriately release lactate in response to certain stimuli. This lactate then serves to trigger the panic attack. The researchers treated the individuals with CBT and tested the CBT's effectiveness by injecting them with the triggering lactate. The team saw that, after treatment, "the induction of panic by lactate... [was] effectively reversed through successful cognitive therapy. In other words, panic disorder sufferers in whom, before starting therapy, attacks were precipitated by injection of lactate no longer responded in that manner after therapy." (Shear et. al. 1991). While this study does not bring the physically observable effects of the therapy studied down to the level of the brain, it does provide another exhibit of therapy, an action, inducing physiologic, measurable effects.

A similar set of results, proving that performing the actions proscribed by therapy induces physiologic responses, comes from a research group who measured the variation of certain hormone levels of depressed patients in conjunction with CBT. They "observed that in a group of outpatients with mild major depression, responders to cognitive behavior therapy had significantly greater decreases in T4 levels and free T4 index than nonresponders" (Joffe et. al. 1996). The researchers propose that this is part of the whole "cascade of biological events that effect a therapeutic response in depression" (Joffe et. al. 1996). Here the physiological effects of therapy are found in hormone level variation, but it is assumed that digging a bit deeper would reveal modulation to the brain.

The Specific Effect of Cognitive Behavioral Therapy

Notably, these studies all tend to refer specifically, out of all the forms of therapy available, to Cognitive Behavioral Therapy (CBT). It seems that CBT is different from other forms of therapy and that it is especially effective in inducing measurable morphological brain change.

A practical guide for clinicians to employ CBT helps define this treatment method: "CBT is based on two central tenets: 1) our cognitions have a controlling influence on our emotions and behavior; and 2) how we act or behave can strongly affect our thought patterns and emotions" (Wright et. al. 2006). The cognitive portion of CBT works to resolve cognitive errors that contribute to an individual's disorder, such as overgeneralization and magnification, and the behavioral component consists of the patient learning and performing actual tasks such as breathing modification and journaling " (Wright et. al. 2006). CBT's in-practice structure consists of four basic steps that reflect these principles: 1. relabel unwanted thoughts as symptoms of a brain disorder, 2. reattribute these thoughts to the dysfunctional brain, 3. change behavioral responses even though the thoughts are still there, and 3. revalue the thoughts as less important (Beauregard, 2014). Based on the evidence thus far of actual behaviors modulating the brain center they rely on, it makes sense that the action centric, goal oriented CBT would be the type of therapy most likely to induce brain changes.

Dr. Aaron Beck, the founding father of CBT, stressed the importance of patient action and involvement in his or her own therapy. The structure of the patient - therapist relationship, termed "collaborative empiricism," expects the patient to work as an equal partner to the therapist in solving his or her problems. The patient is assigned behavioral tasks and homework assignments to personally, actively accomplish (Wright et. al. 2006). More than the therapy "being done" on the passive patient until the patient's problems are fixed, in the CBT model the patient is taught how to

remodel his or her own beliefs in conjunction with being told to perform self-driven actions. It is through fastidious participation and performance of these actions that the patient is "fixed."

Evidently, the actions proscribed by CBT rely on the hippocampus because, as this paper began to describe, multiple studies correlate the effectiveness of CBT with enlargement or modulation of the hippocampus. This relationship has been observed in patients treated with CBT for panic disorder (Beauregard, 2014), social phobia (Goldapple et. al. 2004), obsessive-compulsive disorder (Goldapple et. al. 2004), post-traumatic stress disorder (Levy-Gigi, Keri, 2014), spider phobia (Paquette et. al. 2003), and depression (DeRubeis et. al. 2008). And so, just as the London taxi drivers' spatial mapping behaviors modulated their hippocampi, the active CBT patient evidently relies on the hippocampus when he or she performs the CBT-assigned tasks and thereby enlarges his/her hippocampus.

CBT for Depression

An illustration of CBT's effect on the brain can be found in a clinical study comparing the effects of CBT and paroxetine (a standard antidepressant) on the depressed brain. Based on the premise established by multiple clinical trials "in patients with both mild and severe major depression consistently demonstrate similar rates of response to cognitive behavior therapy (CBT) and antidepressant pharmacotherapy," a team of researchers hypothesized that, while the observable effects of these two treatments are practically identical, their mechanisms of action are likely very different (Goldapple et. al. 2004). After administering a full course of CBT to a sample of depressed patients, the researchers imaged the patients' brains (Figure 5) and indeed found a pattern very distinct from that of paroxetine. They found that "areas of increased metabolism before to after treatment included the hippocampus and dorsal midcingulate" and that the changes effected by CBT were actually in the inverse direction of those caused by paroxetine (Goldapple et. al. 2004). CBT treatment effected "regional changes [that] involve sites similar, and in some cases identical, to those seen previously with paroxetine and other pharmacotherapies, but the changes were in the opposite direction." (Goldapple et. al. 2004). Where paroxetine decreased hippocampus size and connectivity, CBT enlarged it. Therefore, it is seen that modulating the hippocampus is a unique, effective method for treating depression that is distinctly accomplished by CBT. Notably, CBT was seen here to both expand and remodulate the hippocampus.

However, it seems that opposite conclusions were observed in a separate imaging study. Here, "MDD [Major Depressive Disorder] participants displayed a greater activation in the subgenual cingulate cortex, medial PFC, and left anterior hippocampus/amygdala before treatment, and a reduction in these brain regions after long-term psychodynamic therapy." (Beauregard, 2014). Essentially, the research team here saw therapeutic intervention shrink the hippocampus! A possible explanation for this opposite observation is the use of a different therapy, not CBT in particular, as intervention. Perhaps its mechanism is like that of paroxetine, which helps alleviate depression but via a pathway that modulates the brain into a pattern inverse to that of CBT (Goldapple et. al. 2004). Therefore, rather than confounding conclusions formed thus far, this contradictory observation can help reinforce the special effect CBT alone has on the hippocampus.

CBT for PTSD

A separate research team headed by Levy-Gigi examined the effects of CBT on the brains of patients suffering from PTSD. They found that "morphological changes associated with psychotherapy were confined to the hippocampal formation and cingulate cortex." (Levy-Gigi, Keri, 2014). PTSD is especially relevant as it has long been specifically correlated with smaller hippocampal size. Researchers in 1997 "showed that the left hippocampal volume in adults with post-traumatic stress disorder who had experienced childhood physical and sexual abuse was dramatically reduced when compared to that in matched controls." (Gabbard, 2000). Therefore a treatment that directly enlarges the hippocampus would likely be especially effective.

Indeed, Levi-Gigi's team reports that "the most noteworthy finding of this study was that clinical improvement during CBT in PTSD was associated with increased hippocampal size and elevated FKBP5 gene expression, a cellular regulator of the glucocorticoid receptor." (Levy-Gigi, Keri, 2014). First, confirmation of the way CBT enlarges the hippocampus is proffered. Second is the introduction of the gene FKBP5, a "regulator protein of the cortisol receptor and [since] abnormal cortisol secretion is linked to hippocampal atrophy, it is reasonable to hypothesize that the amelioration of FKBP5 gene expression had a causal role in the normalization of hippocampal volume." (Levy-Gigi, Keri, 2014). This hypothesis says that elevated levels of this particular gene, FKBP5, can be aligned with and seen as confirmation for hippocampal enlargement.

Levy-Gigi and her associates also returned to the previous discussion on what exactly is behind the hippocampal enlargement observed, considering how "possible mechanisms may be enhanced neurogenesis, increased neuronal size, and enrichment of dendritic arborization." (Levy-Gigi, Keri, 2014). According to the evidence examined previously, it is likely that the progenitor cells observed in the hippocampus, and so neurogenesis, is the mechanism behind the hippocampal growth observed here. Neuromodulation, or the reconnectivity and recharacterization of hippocampal cells, likely occurred as well.

CBT for Spider Phobia

Anxiety disorders, such as phobias, respond well to CBT intervention. This is because anxiety disorders typically include and/ or come from cognitive errors that CBT can specifically target and solve (Wright, 2006). One specific phobia studied in conjunction to CBT is spider phobia. The team behind the spider phobia study says that "although several psychological models have been proposed to explain the therapeutic effects of CBT, little is known regarding the neurobiological mechanisms underlying this form of psychotherapy." (Paquette et. al. 2003). To investigate this matter they administered CBT to a sample of spider phobic females, all of whom were deemed responders to this intervention. However, when the researchers examined the brains of their spider phobic subjects (via fMRI) before and after CBT, they found a decrease in hippocampus activity. Before intervention they found an overactivation of the hippocampus and after intervention they found this overactivity greatly decreased. This finding directly confounds the extensive research examined and discussed thus far. Therefore, the generalizability and validity of this study must be questioned.

The Connection Between Declarative Memory, the Hippocampus, and CBT

As laid out in the beginning of this paper, the hippocampus is considered to be the center of declarative memory, which is the collection of conscious memories people are capable of articulating. The foil to declarative memory is procedural memory, the contents of which are implicit, operating outside of conscious awareness (Gabbard, 2000). New research has begun to understand the effects of talk/ interpersonal therapy and psychoanalysis to be in the procedural, implicit realm. Sigmund Freud, father of psychoanalysis, himself alluded to implicit memory years before the concept was defined when he "stressed that what the patient does not remember will be repeated in the relationship between patient and analyst." This concept is defined as "transference," and in light of modern psychology can be seen as stemming from implicit memory (Gabbard, 2000). The patient in therapy will be implicitly affected by the therapist and his or her relationship to the therapist. Characteristic of this, he or she will not be able to explicitly articulate the effects of the psychoanalysis or psychotherapy even though he or she will exhibit behavioral change.

Illustrating this concept is the lament of psychiatrist Gabbard: "therapists are often disappointed when they see former patients and ask them what they feel was of most benefit to them during the years they were in psychotherapy. Much to the dismay of the therapist, patients often do not remember any of the psychodynamic formulations or interpretations that the therapist carefully constructed to provide insight. Instead, they remember a joke the therapist told, a belly laugh they shared, a moving moment of emotional connection, or a glance exchanged between therapist and patient when a special form of closeness was felt." (Gabbard, 2000).

Psychologist Lyons-Ruth interprets these moments in therapy as a form of "implicit relational knowing when something emotionally reparative transpires without involving the realm of insight or cognitive understanding." (Lyons-Ruth et. al. 1998). She and her colleagues believe such moments are a crucial part of the mode of therapeutic action. Alteration of implicit/ procedural memory and the manipulation of the manifestations of these types of non-declarative memories, such as transference, seems to be characteristic of all therapies besides for CBT.

CBT is unique in that it specifically targets explicit memory, rather than implicit memory. CBT does not attempt to grope its way through the murky depths of the subconscious, non-declarative, implicit realm. Rather, as illustrated above, CBT's two central focuses are on understanding and controlling cognition alongside altering behaviors in order to affect emotions and thoughts. Both these actions are necessarily declarative as they rely on the patient's explicit understanding, self-motivation, and complicity.

The hippocampus is the center of the declarative memory system and, stemming from this role, is its spatial mapping responsibilities. Therefore, the linkage between the identical effects of spatial memory/ mapping skills and CBT on the hippocampus is their reliance on declarative memory! Both make excessive use of the hippocampus and so enlarge it. The scatterhoarding squirrels, the homing pigeons exploring their barns, and the taxi drivers navigating London make use of the same exact memory modality and brain system as the traumatized, phobic, or depressed patient carrying out CBT-proscribed actions. Both groups over-rely on the hippocampus, in its declarative memory role, and so the same pattern of hippocampus enlargement emerges in both.

The diverse areas of research explored in this paper converge on the central point that exercising the hippocampus, via exaggerated practice of the skills and behaviors that it is responsible for, effects its measurable modulation and growth. The pointed use of the hippocampus's cognitive map function by the black-capped chickadees, the red-tailed squirrels, the homing pigeons, and the rats enlarged the hippocampus in each species. When the London taxi drivers exaggeratedly employed their parallel cognitive maps to navigate the city, they enlarged their hippocampi as well. Intensified use of the hippocampus in terms of its explicit memory responsibilities by CBT patients modulated the hippocampus along the very same lines. The search for an underlying feature to relate these actions leads to the very definition

of the hippocampus: the center of declarative memory. All of the parties discussed in this paper evidently over-employ declarative memory, and so the hippocampus.

Further Research and Conclusion

Based on the observations and correlations in this paper, further research could examine if or how other areas of the brain could be modulated. The declarative memory - hippocampal growth correlation is so clear and definitive that there must be similar trends in other areas of the brain. This paper has already observed that similar modulation is possible in the caudate nucleus. Perhaps identifying the specific skill that a different brain area is responsible for and then excessively practicing this skill would modulate or enlarge the corresponding brain area as well.

Further research could also examine whether the correlations in this paper could be looked at in reverse. Could invasively entering the brain and somehow forcibly enlarging the hippocampus effect an increase in spatial/mapping memory or explicit memory? And, assuming this enlargement were possible, could it be used as therapeutic intervention for the same patients that typically benefit from CBT?

Viewing the relationship in reverse has already been ventured towards by Maguire, the researcher who studied the hippocampal enlargement of London taxi drivers. She proposed "examination of the characteristics of those who succeed at taxi driver training, and [asking] whether innate pretraining cognitive factors and/or hippocampal volume are predictive of successful qualification." (Maguire et. al. 2006). In other words, do individuals with naturally larger or more malleable hippocampi, and so an inborn propensity for spatial memory, gravitate towards jobs that benefit from this characteristic, such as taxi driving?

The researchers who studied the effects of CBT on PTSD also mentioned viewing the correlation they observed in reverse. They proposed the "possibility that small hippocampal size is a premorbid vulnerability factor for PTSD" (Levy-Gigi, Keri 2014), looking at the hippocampus size first and the effects that follow after. If a smaller hippocampus could predispose an individual to disorders such as PTSD, then perhaps a larger than average hippocampus could protect them from this and other hippocampus-centric mental disorders. While still strictly conjecture, research on and validation of this theory might then lead to hippocampal enlargement becoming standard intervention for individuals deemed at risk for mental disorders correlated to the hippocampus. Having observed diverse correlations and multiple angles, this paper concludes with the vast potential for practical implications that may arise as researchers begin aligning and synthesizing some of these ideas.

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