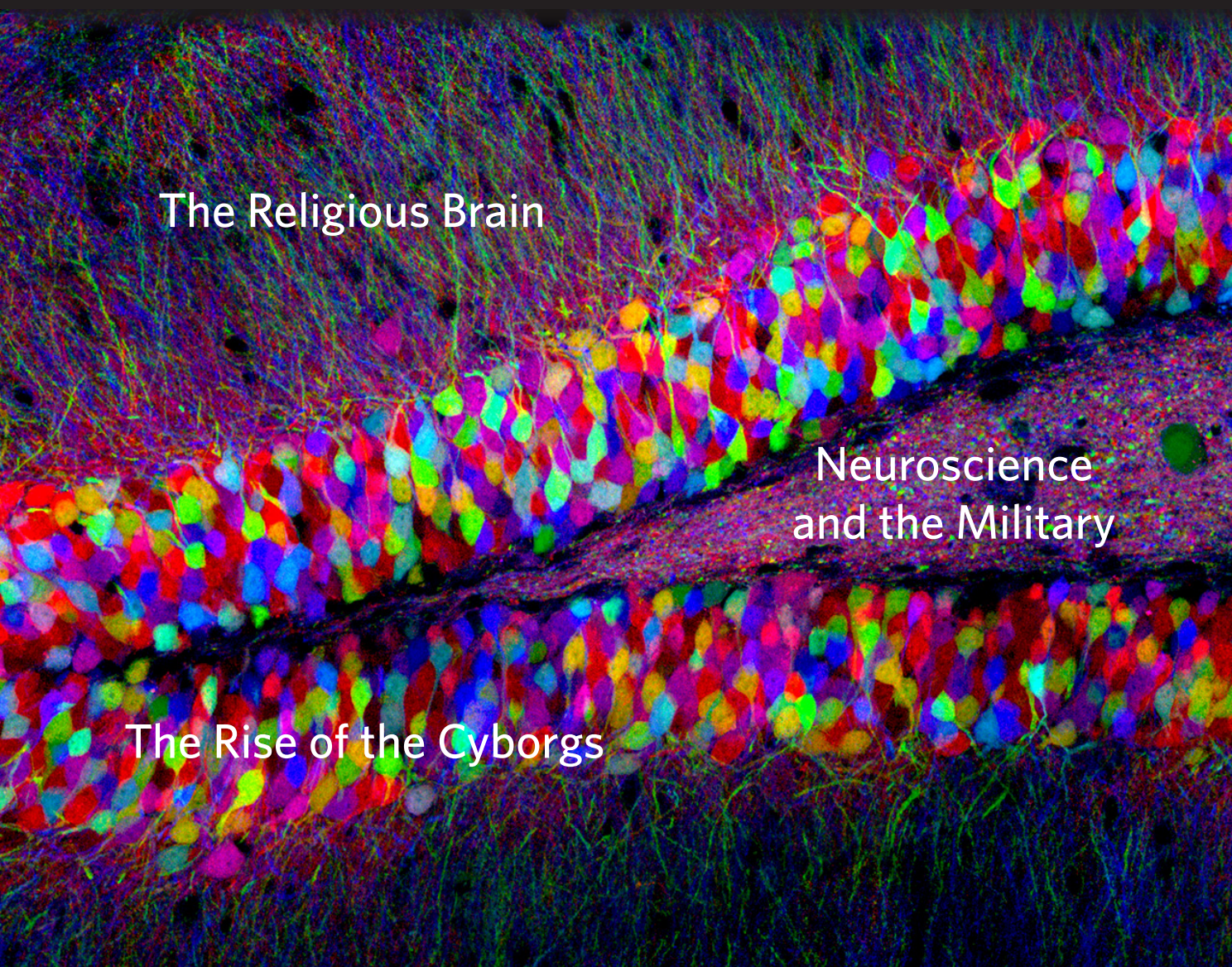
Spring 2010
Vol 1 Issue 2

thenerve

The Neuroanatomy of Homosexuality



Mind and Brain Society

The Mind and Brain Society (MBS; formerly known as the BU Organization for the Mind and Brain Sciences) was founded in the fall of 2008 in concert with BU's new Undergraduate Program in Neuroscience. The group aims to create a network for undergraduate students who wish to take an active role in current issues and research. MBS serves as a hub for not only Neuroscience majors, but all students interested in Psychology, Biology, Philosophy, Computer Science, etc. Our goal is to support an eager multidisciplinary undergraduate community with the conversations and resources fundamental to Neuroscience today.

Throughout the academic year, MBS hosts events spotlighting many different facets of Neuroscience. We hold discussion sessions during which we informally discuss a topic of interest over coffee; previous topics include "The Neuroscience of Religion" and "NeuroEthics." The group also hosts research presentations by BU professors and screenings of thought-provoking films containing neuroscience motifs.

Cover: Brainbow mouse hippocampus. Image by Tamily Weissman. The Brainbow mouse was produced by Livet J, Weissman TA, Kang H, Draft RW, Lu J, Bennis RA, Sanes JR, Lichtman JW. *Nature* (2007) 450:56-62.

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The U.S. media has been consumed by healthcare reform for the past year or so, arriving at a climax with the historic vote in the House of Representatives on March 21. Whether or not the new legislation will alleviate the country's problems remains to be seen. No matter what your opinion on the changes making their way through America's healthcare system, we cannot deny that they will have an impact on our community. Our hopes are that a new system will only enhance the neurological care for those around us. Here at The Nerve, we hope you will take a few minutes to forget about the politics and enjoy the science.

Having set out to conquer the world by means of studying abroad, our editorial team brings you the Second Issue from three continents, including Europe and South America. Our goal was to collect articles as far-reaching as our staff. From the relationship of the military with neuroscience to the neuroanatomy of homosexuality, we are confident you will find something inside to stimulate your brain.

This and other issues of The Nerve would not have been possible without the generous help of Howard Eichenbaum, Paul Lipton, Lindsey Clarkson, Denise Parisi, Zachary Bos, and Jarret Frank.

- Grigori Guitchounts and Kimberly LeVine
Editors-In-Chief

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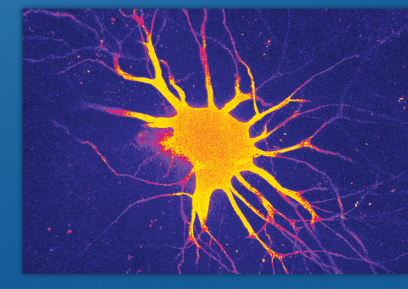

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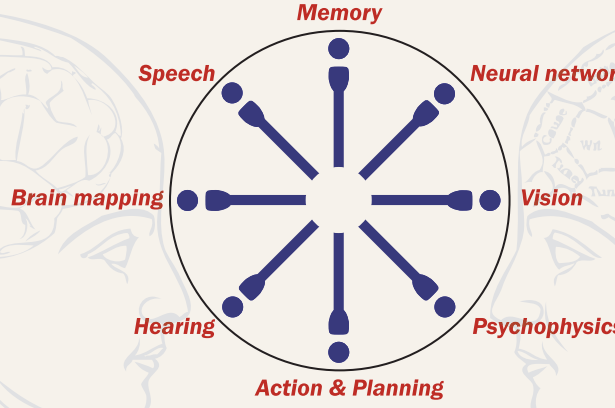
How does the brain give rise to the mind?



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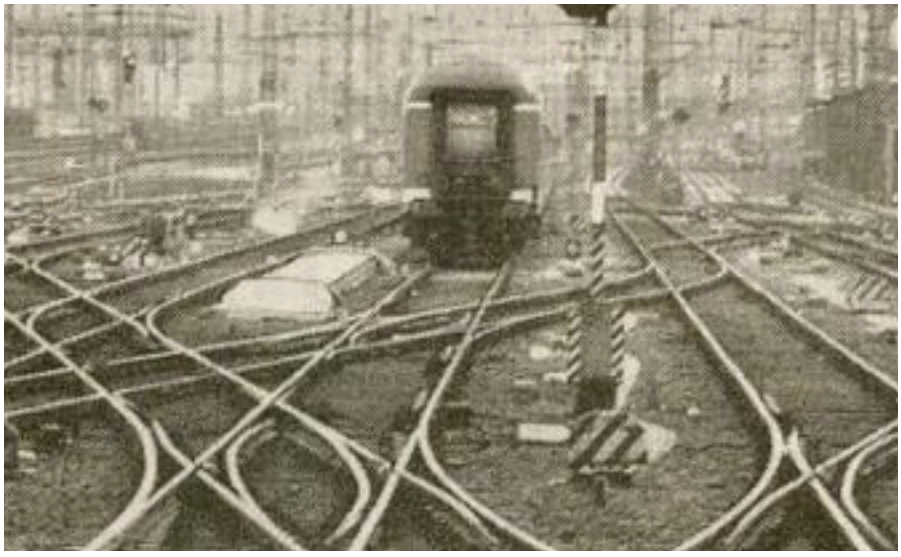
Vast Parallel Processing in a Retinal Interneuron



The eye is a truly wondrous processing organ composed of six primary cell types separated into two primary plexiform layers. While rods and cones, the actual light responsive cell types, are well characterized, horizontal and amacrine cells are significantly more complex in their activity and ability to modulate visual input. In their study, Grimes et al. examined one specific type of amacrine cells, the A17, and their morphological, biophysical, and synaptic properties as related to their feedback onto rod bipolar cells (RBCs); ultimately, concluding that, at least for the A17, amacrine cells are uniquely structured to create hundreds of parallel microcircuit feedback loops in order to provide an incredibly fine level of processing on the output of bipolar cells and the overall rod pathway, which is responsible for vision under low ambient light.

Both fluorescent and electron microscope imaging in combination with cell modeling studies suggested that each long, unbranching neurite of the A17 cell extending into the layer of RBCs is able to receive synaptic output and return appropriate processing largely independent of the activity at any but the most proximal parts of the cell, allowing for a single A17 cell to reciprocally modify hundreds of inputs with limited overlap to neighboring points of synaptic contact. Beyond these morphological features limiting the ability of electronic conductance, examination of both sodium and potassium channel response to injected current in A17 cells shows that these channels do not cause more than a transient depolarization of local portions of neurites in vitro, with little evidence to support cellular depolarization in vivo.

As such, this study's initial morphological data suggesting independent processing functions is lending significant credence. Further studies into calcium's activity within A17 cells shows that, even though transient intense Ca2+ activity can result in GABA release, even studies stimulating multiple Ca2+ channel patches along an A17 neurite could not experimentally propagate any electronic information beyond other synaptic contacts in the immediate vicinity, and only weakly even then.

Given that these A17 cells are able to receive and provide RBC contact-specific feedback at greater than 150 primarily independent synapses, the activity of this type of amacrine cell mimics the dendritic integration seen in cortical processing interneurons. The fine-tuning that has been studied and may be taken for granted in upper cognitive pathways seems to be mirrored even within the essentials of the visual pathway. This phenomena likely accounts for some of the fine visual acuity seen under low-light conditions that stimulate the RBCs and the ability to perceive subtle changes in light stimulus even when the magnitude of stimulus is considerably lower than normal visual parameters. Additionally, by condensing all the multitude of microfeedback circuits into a single cell, the visual system reduces the "wiring cost" necessary to maintain the fine level of feedback needed in the low-light rod pathway. The Grimes et al. study has laid important groundwork for finally piecing out the exact responsibilities of the modulatory pathways that allow for the incredible diversity of signals and visual discrimination seen in the stimulus-transducing portion of the optical pathway.

— Doug Hidlay

ORIGINAL PAPER: Grimes WN et al. Retinal Parallel Processors: More than 100 Independent Microcircuits Operate within a Single Interneuron. *Neuron*. 65, 873–885, 2010.

Mindblind Eyes in Asperger Syndrome

It is well known that autism spectrum disorders frequently plague sufferers with impairments in communication and social interaction. A popular hypothesis breaking into what underlies these impairments is that autistic children lack Theory of Mind (ToM), the ability to assign mental states to oneself or others; that is to say, one's ability to understand others' feelings or viewpoints based on the unique set of information available to one. In the Sally-Anne false-belief task (FBT), a popular test of the Theory of Mind (ToM) skill, children are asked to predict a girl's actions when she looks for a marble that has been moved from its usual location without her knowledge. Do children with Asperger syndrome understand Sally-Anne's mental state or are they unable to distinguish their own omniscience from Sally's misinformed view? Those with Asperger are, in fact, able to correctly predict Sally's action, confounding the mindblindess hypothesis supporting impairment in Theory of Mind.

Senju et al propose that Asperger patients have the ability to reason through false belief scenarios but nevertheless maintain an impairment assigning mental states. The study contrasts results between verbal and nonverbal forms of the false-belief task to trace the divergence of mindblindess between typically developing participants and those with Asperger Syndrome.

An earlier study by Southgate et al, using a paradigm similar to the Sally-Ann FBT, sheds light on the tendency of infants to not only look longer at unexpected events than at expected ones, but to make eye-movements toward expected events before they occur. Senju et al used this information to assess whether adults with Asperger syndrome can successfully assign a false belief as evidenced by anticipatory looking. As expected, neurotypical (i.e. those without Asperger's) adults and those with Asperger syndrome performed equally on the verbally instructed ToM tests (such as the Sally-Anne task). However on nonverbal ToM tests which measured looking bias, the Asperger group did not show the same significant level of bias toward the correct target as did neurotypical adults. The Asperger group's looking bias did not differ from zero, supporting the theory that they did not anticipate the impending movement and did not assign a false-belief to the character in the task.

The results show that adults with Asperger syndrome do not spontaneously predict others' actions in a nonverbal situation. This impairment characterizes mindblindess in autism spectrum disorder patients. Senju et al suggest that nonverbal mental state assignment skills require spontaneous encoding of socially relevant information, a skill that individuals with Asperger syndrome lack, which lends to difficulty with social interactions. On the other hand, the study proposes that it is possible to enhance explicit, verbal mental state assignment through compensatory learning.

— Kimberly LeVine

ORIGINAL PAPER: Senju A, Southgate V, White S, and Frith U. Mindblind Eyes: An Absence of Spontaneous Theory of Mind in Asperger Syndrome. *Science*. 325, 883-885. 2009.

Methylated Memories

Memory is certainly one of the greatest mysteries of neuroscience. How do we store information for long periods of time? How do we learn? Recent results published by Swati Gupta et al. of the Department of Neurobiology at the University of Alabama at Birmingham provide a good start to answering these questions. The study illuminates the role of genetics in neuroscience: regulation of gene expression proves important in the formation of long-term memories.

Epigenetics is the regulation of gene expression based on factors other than alterations in a DNA sequence: this regulation is largely reflective of environmental factors. Effects often occur after translation, once the gene has been transcribed into mRNA to be "read" by ribosomes, and a polypeptide chain has been assembled accordingly. Phosphate and acetyl groups are able to unwind DNA to expose histones, the proteins that DNA wraps around when it condenses to form chromatin. Once these histones are exposed, methylation can occur. Depending on which amino acid residues the methyl groups attach to, transcription can be either silenced or activated. Inducing or inhibiting methylation is how external factors can regulate the expression of genes.

Gupta's study examined methylation in the hippocampus of mice. This region of the brain is notable for its contribution to the formation of long-term memories: human patients with damage to this area generally have difficulty creating new ones. By looking at the methylation of H3 histones on various lysine residues in fear-conditioned mice, the study at the University of Alabama explored the effects of experience on epigenetics in the hippocampus during memory formation.

The mice used in the experiments were all young adult males of the same species. One experimental group underwent a process called fear-learning. These mice were brought into the laboratory thirty minutes before being placed in a training chamber. After two minutes in the chamber, they received electric shocks to their feet paired with a sound. The shocks occurred in sets of three, every two minutes. A second experimental group was content-exposed, meaning that they were put in the chamber for seven minutes and did not receive any shocks. Upon re-exposure to the chamber this group did not exhibit freezing behavior, indicating they had not developed a fear response to the chamber. A third group of mice were latent-inhibition plus fear-conditioned. Latent inhibition involves exposing a subject to a new situation for a long period of time (in this case, two hours) before beginning fear-conditioning by introducing the unconditioned stimulus, the foot shocks (as experienced by the fear-conditioned animals). This group ensured that associative learning was taking place: when they were reintroduced to the training chamber 24 hours later, freezing behavior was observed even though they were not shocked upon re-entering the chamber. A control group received no experimental treatment.

After the mice were trained, they were watched for freezing behavior when presented with the conditioned stimulus: the training chamber and the sound paired with the shocks.

Once behavioral testing was complete, the CA1 area was removed from the hippocampus of each mouse. Antibodies were used to separate DNA from chromatin, and PCR was used to amplify and analyze the samples.

Samples that were observed an hour after conditioning took place showed an increase in transcription-activating H3K4 trimethylation in the mice that had been contextually fear-conditioned as opposed to the mice who had only been context-conditioned. This observation links the methylation to associative learning processes. The H3K9 dimethylation that was shown increased in both the contextual fear-conditioned mice as well as in the context-conditioned mice an hour after training. This transcription-silencing methylation must be important to fear learning as well as context learning. In looking at the mouse brains 24 hours after training, it was found that both kinds of methylation are reversible: amounts of methylation decreased.

Another finding that is supportive of the idea that methylation of histones aids long-term memory formation is the importance of two genes, Mll and eed. These two genes are essential to the synthesis of H3K4-specific methyltransferase, an enzyme that methylates this particular histone. Heterozygote Mll mice showed stronger freezing behavior than eed mice: this is because Mll is specific to H3K4 methyltransferase and eed is to methyltransferases in general. Mll is particularly essential to the methylation process observed. As long as mice were heterozygous or homozygous dominant for Mll and eed, they learned and remembered normally.

In another experiment, inhibition of HDAC (histone deacetylases), with sodium butyrate (NaB) was found to decrease methylation on H3K9 histones. In other words, if the histones were lacking in acetyl groups because of HDAC suppression, less methylation occurred: a link between hippocampal acetylation and methylation.

H3K4 methylation increased specifically around certain promoter regions on particular genes, exhibiting the regulation of methylation involved in fear conditioning. In general, fear conditioning tended to demonstrate an increase in methylated DNA. This methylation seems to serve as a signal for gene transcription.

So how is all this genetic information useful to our brains? According to Gupta's paper, studies have shown that histone methylation levels in the hippocampus may be able to help doctors identify schizophrenia earlier. Demethylase enzymes are being isolated, and their inhibition or upregulation could be used as treatments for many neurologic diseases. Epigenetics is proving to be a useful tool in deciphering how our brains work, and how to fix them when they don't!

— Natalie Banacos

ORIGINAL PAPER: Gupta S et al. Histone Methylation Regulates Memory Formation. *The Journal of Neuroscience*. 30(10):3589 –3599. 2010.

Decreased Risk of Dementia is Associated with CETP Polymorphism

Dementia is debilitating to those affected; it is a major characteristic of many neurological diseases, such as Alzheimer's disease. In fact, the prevalence of dementia is increasing as the population ages, resulting in public health and economic burdens. However, dementia does not affect all patients in the same manner. In fact, some patients enjoy a slower or lesser cognitive decline than others, much of it determined by genetics. Sanders, Wang , Katz, and colleagues have investigated a gene polymorphism in cholesteryl ester transfer protein (CETP), which may be associated with a lesser and slower memory loss/decline as well as a lower risk of dementia.

Previously, other researchers have documented that the CETP polymorphisms has been associated with longevity and lower cardiovascular risk, especially in samples of Ashkenazi Jews that had higher percentages of centenarians with the polymorphism than controls. CETP is a protein that is involved in central nervous system cholesterol homeostasis; thus, the polymorphism results in a lower concentration in serum, increased HDL levels, and HDL/LDL particle sizes. All of these are posited to play a role in cardiovascular protection.

In the Ashkenazi population, researchers have also found the homozygous polymorphism at a 5-fold higher rate in 75- to 85-year-old individuals without dementia compared to those with dementia. These studies purport a protective association between these CETP polymorphisms and decreased dementia. However, CETP polymorphism studies on more general populations have not previously demonstrated any cognitive benefits, possibly because of the limited

time frame they encompassed.

Thus, Sanders, et al. looked at the single-nucleotide polymorphism (SNP) at CETP codon 405, where an isoleucine is changed to a valine, and focused on the cognitive effects over time. To test their hypothesis that this polymorphism would be associated with lower memory decline and lower risk of dementia, they conducted a longitudinal prospective cohort study that incorporated 70+-year-old community-dwelling adults without dementia at baseline, who were registered with the Einstein Aging Study. In it, they investigated associations between the CETP polymorphism genotype and longitudinal memory performance and risk for dementia or Alzheimer's Disease.

Using the Free and Cued Selective Reminding Test (FCSRT), Sanders and colleagues assessed memory loss over time. The FCSRT is a test where learning conditions are controlled by having subjects search a card containing four pictures of items that correspond to unique category cues. After these items are identified, researchers test immediate cued recall and eventually conduct three test trials consisting of free recall, followed by cued recall. Sanders and colleagues ascertained that memory declined in polymorphism homozygotes by a rate 51% slower than in the control group. The homozygotes also had lower risk of both dementia and AD.

These results may help scientists and doctors not only find possible venues for treatment (i.e. CETP inhibitors, etc), but also it may lead to greater understanding of the etiology of dementia. Alzheimer's may soon be more treatable than previously anticipated.

— Neil Datta

ORIGINAL PAPER: Sanders AE, et al. Association of a functional polymorphism in the cholesteryl ester transfer protein (CETP) gene with memory decline and incidence of dementia. *JAMA*. 303(2):150-158. 2010.

Neuronal Transplantation Induces Plasticity in Visual Cortex

Normal neural development features critical periods during which maximal learning occurs in a sensory modality or neural system. The most commonly studied critical periods are those for visual perception and language acquisition. The former was reported in the 1960's by David Hubel and Torsten Wiesel, who performed a series of groundbreaking experiments that earned them the Nobel Prize in medicine.

During the critical period of visual perception, both eyes must be open and receiving meaningful input in order to be functional later in life. Occlusion of one eye (Monocular Deprivation, MD) during the critical period induces rapid reorganization in visual cortex that leads to the takeover of cortical 'real estate' by the non-deprived eye's axons, leaving the animal blind in the occluded eye. Dogma has it that unsuccessful learning during the critical period (as in monocular deprivation) cannot be reversed later in life; once the animal is blind in the deprived eye, nothing may fix that.

Derek Southwell and colleagues at UCSF show that this is not necessarily the case. In a paper published in Science in February, they report that transplantation of inhibitory neurons into mouse visual cortex after the critical period is over reactivates it, allowing vast reorganization.

After the critical period, monocular deprivation does nothing to hinder vision or reorganize cortex; animals wearing eye patches for several days can still see well after the patch is taken off. Southwell capitalized on this fact to test whether neuronal transplantation affects visual cortex during MD post critical period. Indeed, MD 33-35 days after transplantation induced a shift in ocular dominance columns just as it does during the regular critical period. Transplantation had the strongest effect when the donor cells reached the age at which the regular critical period occurs, regardless of the host's age.

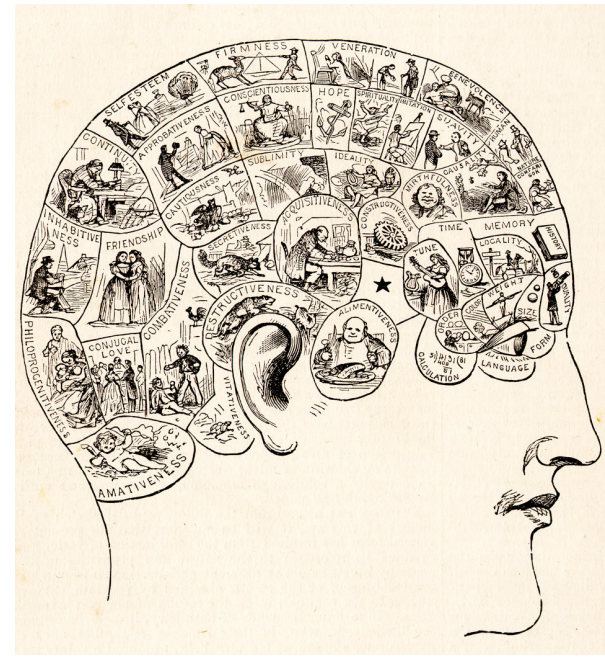
Furthermore, the transplanted cells migrated into all layers of host visual cortex and developed morphologies of mature inhibitory neurons with reciprocal synaptic connections. And even though transplanted neurons' synaptic inputs were only one-third as strong as those in native synapses, as measured by excitatory post-synaptic potentials, they were more numerous.

These results are promising to the field of regenerative medicine. Perhaps in the future, we will be able to reverse seemingly permanent neurological conditions by introducing new cells into neural networks and jump-starting neuroplasticity.

— G. Guitchounts

ORIGINAL PAPER: Southwell DG, et al. Cortical Plasticity Induced by Inhibitory Neuron Transplantation. *Science*. 327: 1145-1148. 2010.

Research finds neurons drive behavior



Daniel Huber and colleagues reported in a paper in Nature their research on the link between the activities of specific groups of neurons in the primary somatosensory cortex and perceptual and cognitive functions in mice. The primary goal in conducting this research was to develop an alternative to the method of electrical microstimulation in order to isolate groups of neurons and study their activity in vivo.

The drawback of electrical microstimulation is that the accuracy at which axons are excited is typically poor. Alternatively, through the use of photostimulation, in which a light-gated algal channel channelrhodopsin-2 (ChR2) was introduced into the barrel cortex pyramidal neurons of mice, the discrimination between cells is far greater, and a considerably lower number of neurons required stimulation in order to produce robust behavior. ChR2 photostimulation in vivo reliably generated stimulus-locked action potentials at frequencies up to 50 Hz. An untrained group of mice was capable of detecting brief trains of action potentials (five light pulses, 1ms, 20 Hz). After training, however, mice could detect a photostimulus firing a single action potential in approximately 300 neurons. Even fewer neurons (approximately 60) were required for longer stimuli (five action potentials, 250 ms).

To conduct this research, in utero electroportation was used to introduce ChR2 fused to a green fluorescent protein (GFP) (ChR2-GFP) together with a red fluorescent cytosolic marker (RFP) into neocortical pyramidal neurons. The responses of ChR2-GFP-expressing neurons to photostimulation in anaesthetized mice were characterized, and recordings were gathered from red fluorescent neurons using two-photon targeted loose-patch recordings. Photostimuli consisted of light pulses produced by a blue light-mitting diode (LED, 470 nm) glued to the mouse's head (the researchers made sure the mice could not see when the LED was on or off). At maximum light intensities, about half of the patched red neurons responded reliably with at most one action potential. An increase of the photostimulation duration beyond 10 ms did not reveal additional responsive neurons.

The relation between photostimulus intensity and the probability of spiking ChR2-GFP-expressing neurons was then determined, and it was found that with decreasing light intensity, neurons abruptly switched from firing action potentials with high probability to firing no action potentials at all. It was confirmed that ChR2 can transduce photostimuli into precisely timed spike trains in vivo.

To test whether awake mice could learn to report photostimulation of layer 2/3 pyramidal neurons in the barrel cortex, light pulses were delivered to ChR2-GFP-expressing neurons in freely moving animals. The mice were temporarily connected to an LED controller and trained to associate photostimulation of CHR2-GFP expressing neurons with water reward on one of two choice ports. After four to seven training sessions, mice were capable of reliably reporting photostimulation by choosing the correct port in the presence or absence of stimulation, unlike the control mice without electroporated neurons, which performed at chance levels even after 25 training sessions.

The results of these experiments demonstrate that photostimulation of layer 2/3 neurons can drive robust behavior. These findings are significant in that they provide a far more accurate method of studying the circuit basis of perception and cognition in vivo.

— Lauren Joseph

ORIGINAL PAPER: Daniel Huber et al. Sparse optical microstimulation in barrel cortex drives learned behavior in freely moving mice. *Nature*. 451:61-64. 2008.

ARTICLES

The Rise of the Cyborgs

By Darrien Garay

cyborg

Cyborg. It's a word that calls to mind images of a RoboCop-like organism clanking around in some far off future. However, our notions about the reality of cyborgs may be obsolete. Successful clinical research has taken giant leaps forward in the intimate fusing of brain and machine. Take for example the story of Erik Ramsey.

On the evening of November 5, 1999 Erik was involved in a traffic accident that left him riddled with severe internal trauma. Erik's injuries resulted in a stroke that damaged his brainstem[1]. Due to this stroke, Erik developed a neurological condition known as Locked-in Syndrome. Locked-in patients are completely paralyzed and can move only their eyes[2]. However, they maintain conscious awareness, can reason, and sense every pain or discomfort.

Erik's story could have ended when he was 16, essentially incarcerated within his own body, but technological advances and tremendous determination are writing a new chapter, one of hope. Five years after the accident, Erik volunteered for an experimental speech-research program, a decision that would lead to the implantation of mechanical devices directly into his brain[1].

"is it really possible to liberate the mind from the confines of the body?"

When Brains and Machines Can Chat

The device implanted within Erik's brain is part of a brain-machine interface (BMI). BMI, also known as brain-computer interface or neural interface system, is an emerging branch of neuroscience that seeks to overcome the "limitations of our bodies by forming a direct interaction between the brain and the outside world."[3]

BMIs can be divided into two major categories: those that induce desired brain activity or those that record brain activity.

Cochlear implants are one example of a BMI which induces desired patterns of neural activity. A processor above the outer ear receives incoming sounds and translates them into digital signals. These signals are then transmitted through the skin and skull to a micro-

"locked-in patients are completely paralyzed and can move only their eyes"

electrode array implanted directly onto the auditory nerve. The array stimulates the auditory nerve, bypassing inner ear dysfunctions that cause the deafness. According to the FDA, as of April, 2009; 188,000 people have received cochlear implant surgery worldwide[4].

BMIs of the second class, those that record neural activity, are being tested as augmentation systems for patients suffering from various degrees of paralysis. These systems circumvent limb paralysis, connecting the brain's output fibers directly to machine effectors. The machine then executes the mental commands the patient's muscles can no longer follow.

But is it really possible to liberate the mind from the confines of the body?

Monkey Think, Robot Do

Dr. Nicolelis and his colleagues at Duke University were able to successfully harness a monkey's brain impulses to command a robot, half a world away, to walk[5].

First, researchers implanted recording electrodes into the motor cortex of Idoya, a monkey trained to walk on a treadmill. Neurons in motor cortex command muscle activity necessary for movements. The firing patterns recorded from an area of her motor cortex that controls the legs were then fed into a computer that translated them into a digital output.

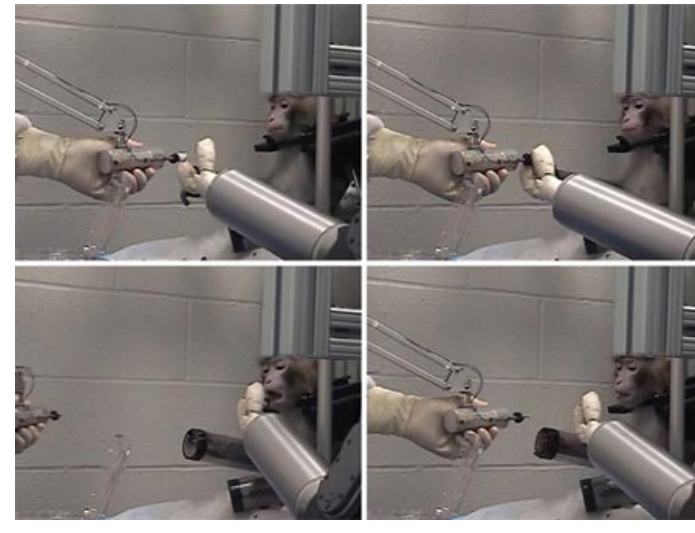
Next, the computer receiving Idoya's brain activity was connected via the internet to a humanoid robot, known as CB (short for Computational Brain), in Kyoto, Japan. CB was specifically designed to mimic bipedal locomotion and could easily walk, jump, and squat.

Her brain now wirelessly connected to the robot's limbs, Idoya was again placed onto the treadmill. In front of the treadmill was a screen that presented live video of CB for Idoya to watch as she moved.

As the treadmill was switched on, Idoya began to walk - her motor neurons fired – and CB came to life. His robotic legs moved in almost perfect synchrony to her gait. As the researchers had hoped, the neural signals recorded from Idoya's brain orchestrated CB's strides.

Idoya was even able to keep the robot walking when she had stopped walking herself. The visual feedback, provided by the screen, allowed just the thought of walking to successfully control the robot's limbs.

"We have shown that you can take signals across the planet in the same time scale that a biological system works. Here the target happens to be a robot. It could be a crane. Or any tool of any size or magnitude. The body does not have a monopoly for enacting the desires of the brain," said Dr. Nicolelis[6].



A Voice from the Future

When Erik Ramsey was approached by Dr. Phillip Kennedy, chief scientist at Neural Signals Inc[1], to participate in an experimental surgery and research program, he consented with a flick of his eyes.

During the ten hour surgical procedure, a "neurotrophic electrode" was placed within Erik's speech-motor area[7]. The speech-motor area coordinates the muscles of the jaw, tongue, and throat that are necessary for the production of speech. The tip of the recording electrode was placed 5mm into Erik's cortex. The outer end was attached to an FM transmitter which could wirelessly relay the activity of the region's neurons to an external decoder.

After successful implantation, the neural signals of Erik's speech-motor area could be precisely recorded and translated into a digital signal. The Neural Signals team then reached out to Dr. Frank Guenther of Boston University.

Dr. Guenther had dedicated a majority of his research career to the development of an accurate mathematical representation of the neural signals associated with speech production. His expertise on the brain interactions necessary for speech production was of paramount importance in the creation of algorithms and software capable of interpreting neural activity in Erik's brain.

"We can decode intended sound directly from the premotor cortex [where the speech-motor area is found], rather than having to decode intended muscle activity. This suggests that when you talk to yourself in your head, your premotor cortical neurons are representing the sound that would come out of your mouth if you were actually speaking the words. Furthermore, we can tap into this 'inner speech signal' and send it out of a computer speaker, thereby allowing paralyzed individuals to regain speech capabilities," Dr. Guenther told me in an e-mail.

Currently, Erik is able to use the "speech synthesis" system to produce vowel sounds in real-time[8]. Erik is presented with a target sound, such as OO (as in hoot) and A (as in hot), and instructed to attempt to move his tongue and jaw as if he were actually producing the sound. This imagined movement activates his speech-motor area. The system then decodes his neural activity and generates the sound he is attempting to make. After training, Erik is able to produce the target vowel sounds with an 89% accuracy.

The next step for Erik and the researchers is the production of consonants; the ultimate goal is words. Each milestone requires the development of new speech processors and decoding algorithms.

Erik and patients like him are living proof of the emerging coalescence of man and machine. Have we reached a new plateau in the evolution of humanity? Think about this the next time you use your iPhone to find your way around town or your Nike+ to track your workout progress.

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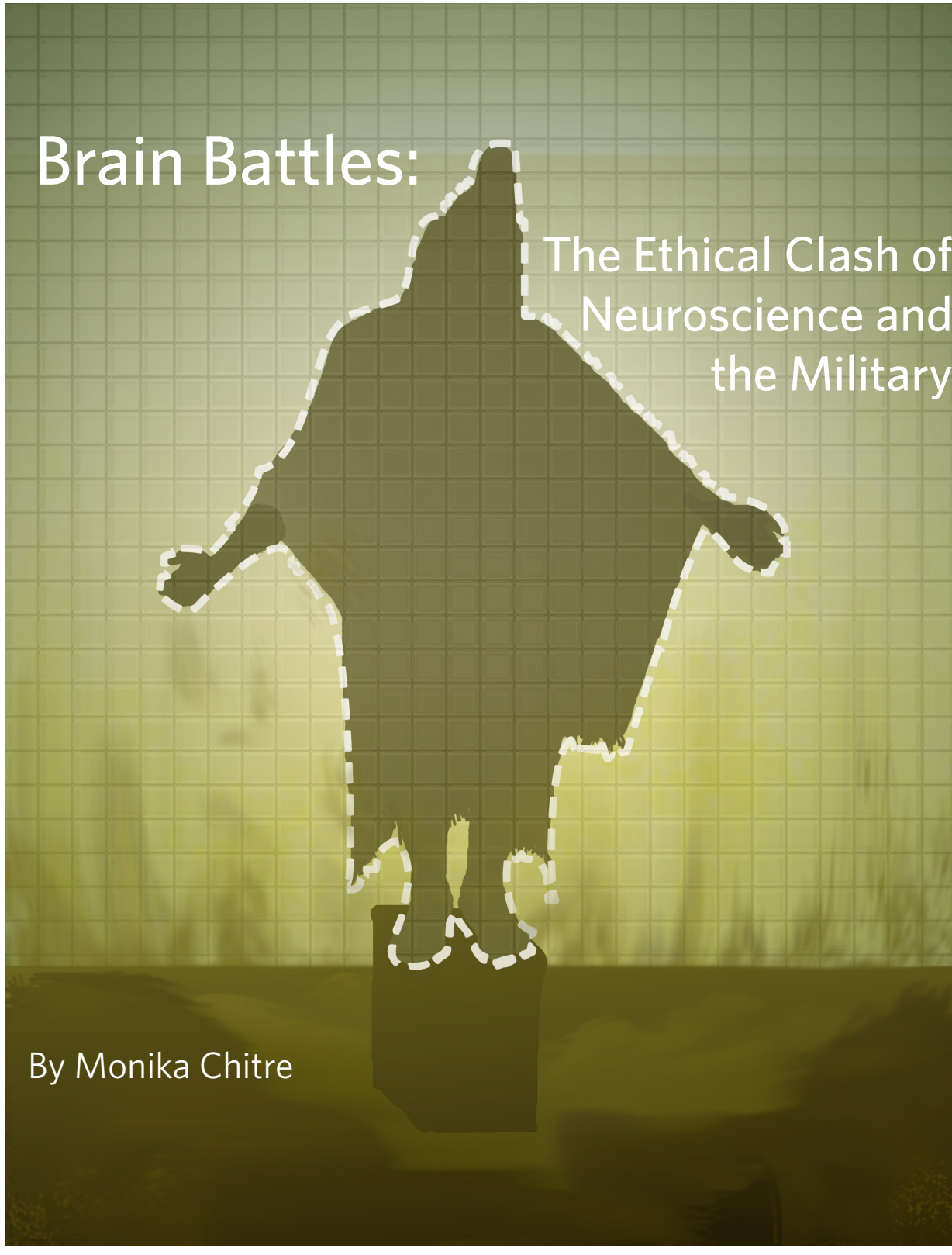


Brain Battles:

The Ethical Clash of Neuroscience and the Military

By Monika Chitre

In 1997, a group of people were told a story and shown a slideshow about a series of events. In the middle of the story, a horrific car accident was described, but the beginning and ending portion of the story were emotionally neutral in context. One third of the group was given a placebo one hour before the story was told. One third of the group did not receive any drugs. And the last third received propranolol – a beta-adrenergic blocker typically used to decrease the effects of hypertension. A week later, the subjects who were given the placebo or no drugs at all remembered the emotional portion – the car accident – of the story well. However, those who received the propanolol scored lower on the memory test than any of the other participants[1].

When American soldiers leave the country for deployment, they undergo a certain amount of mental stress that most civilians will never have to endure. The days are long and physically exhausting. Many soldiers must cope with the fact that they have killed human beings. Some soldiers may even have to interrogate prisoners and essentially torture them to draw more information out of them. Five percent of American males and ten percent of American females experience post-traumatic stress disorder (PTSD), and these percentages are even higher among high-risk populations like war veterans[2].

The military has maintained a discrete relationship with the mind and brain sciences since the 1950's. Dr. Jonathan Moreno, a professor at University of Pennsylvania and the author of the 2006 book Mind Wars, talks about how his father tested LSD for the military[3]. Over one third of psychologists received funding from the government in hopes of finding a use for their research in the military. During the 1950's and beyond, psychologists developed interrogation techniques that involved psychological torture and humiliation[3]. In the 21st century, the intimate relationship between the mind and brain sciences and the military was touched upon when the American Psychological Association refused to comment on the torture scandal that took place at the Iraqi prison Abu Ghraib[3].

Currently, the military has shown interest in the development of a drug that would dampen consolidation of emotional memories in soldiers. While most of the research since the 1960's has focused on drugs that enhance cognition by acting on dopaminergic pathways, this field has also turned out to be the most controversial. Should one have the ability to take pills that would expand his working memory and learning while increasing productivity? Would these pills be available equally to everyone, regardless of socioeconomic status? Or would those who are already high achievers simply propel themselves forward in a vicious feed-forward cycle? These questions do not even touch on the concern of where society would be headed if such drugs were on the market. On the other hand, a smaller effort has been put into the development of agents that can interfere with memory formation.

The primary role suggested for such a drug would involve patients who suffer from PTSD, which is extremely prevalent in veterans[9]. In 2002, a study was conducted with PTSD patients involving propranalol. The patients were given the drug in addition to talk therapy over the course of three months. Initially, little difference in the patient's psychiatric evaluations was shown between the placebo and propranalol groups, but a significant change occurred at the three-month follow-up. 43% of the placebo recipients responded to trigger stimuli (recording of the patient talking about the traumatic event), while none of the propranalol subjects responded physiologically. Although the data was not robust, it was apparent that such a drug could have a significant attenuation effect on those suffering from PTSD[4].

In Mind Wars, Moreno mentioned that the use of this drug could be taken a step further. In-

"neuroscientists can change the way America fights wars"

stead of giving the drug to dampen the effects of PTSD, the drug could be administered as a preventative measure. Soldiers can take the drug before they go to battle or interrogate a detainee. After taking the drug, they would not maintain feelings of guilt or distress after they kill an enemy or torture a prisoner[3]. On the other end of interrogation, oxytocin could also be used to increase the amount of trust the prisoner has in the interrogator, so he may give up more information easily[5]. Importantly, propranolol only the attenuates the emotional component of memories, not the memory itself; thus, the soldiers taking propranolol would remember everything that happened, but those memories would have no emotional value[10].

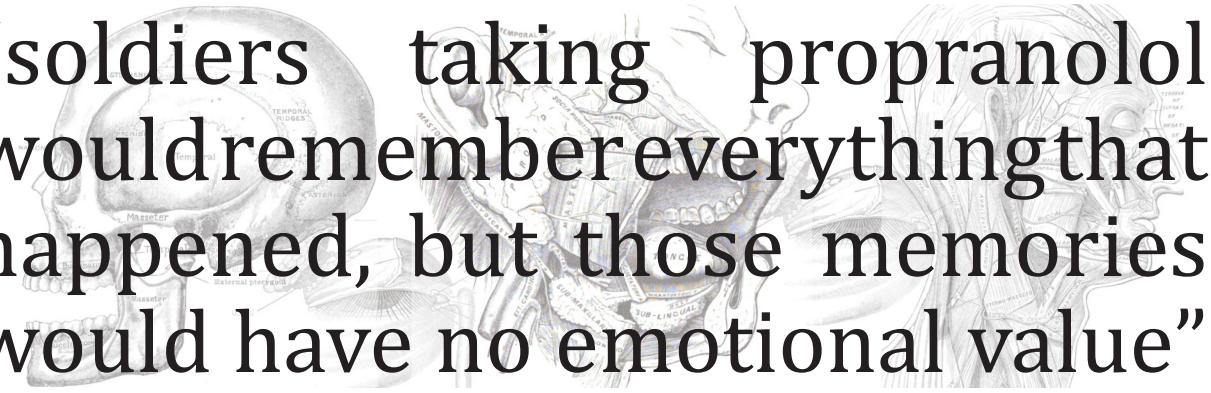
Though beta-blockers seem like a good idea in theory, the state of American interrogation techniques allows the question of ethics to arise. Such questions came to a head after the Abu Ghraib torture scandal in 2004. Once the information was exposed to the public, the American military panicked and scrambled to find a source to blame. It was not clear if the scandal occurred simply because of a few intrinsically evil individuals, the environment, or the people who create the environment itself. Dr. Philip Zimbardo – famous for his Stanford prison experiment in 1971 – researched the event extensively. He concluded that most (if not all) individuals are capable of treating others the way the soldiers treated the prisoners at Abu Ghraib because of the system in which an individual participates[6].

"If you put good apples in a bad situation, you'll get bad apples," said Zimbardo in an attempt to explain an individual's capacity for evil in an interview with the New York Times[6].

However, neuroscientists fail to realize that the products of their research can and most likely will be abused in the military. In Mind Wars, Moreno comments that his neuroscientist colleagues cancel seminars on the ethics of advances in neuroscience because only a handful of people plan to attend[3]. The National Academy of Sciences did not recommend that the military take more interest in neuroscience until May of 2009[7]. In comparison to the physicists of the 1950's who were hired specifically to create atomic bombs for the military, neuroscientists have not come to understand the importance of their research to the government as quickly as they should have[3].

Such ignorance may impede neuroscientists' research from being used ethically. In the 1950's, Einstein and a panel of high-profile American physicists wrote the Russell-Einstein Manifesto to voice the concerns and consequences that come with atomic bombs. Many of the Manhattan Project physicists grew sober after the atomic bombs they created were actually used. They intimately understood all of the dangerous after-effects that these bombs would cause the world if countries continued to use these weapons extensively. Such awareness does not exist in the neuroscience community yet, especially because the line between offensive and defensive use of neuroscience is clouded[3].

In the late 1980's and early 1990's, the Soviet Union came under fire from the United States and Britain because of the research they were conducting on dangerous biological substances like smallpox. Their work was being done behind a curtain because they were using this research exclusively to fine-tune bioterrorist techniques for the Soviet military. Once the USSR fell, the secrets came out, and the research was stopped. In the United States, it has been decided that any research on biological compounds must be limited so that it can only be used defensively by the American military. Unlike bioterrorism, neuroscience can easily be used offensively and defensively. In the case of interrogation, psychological



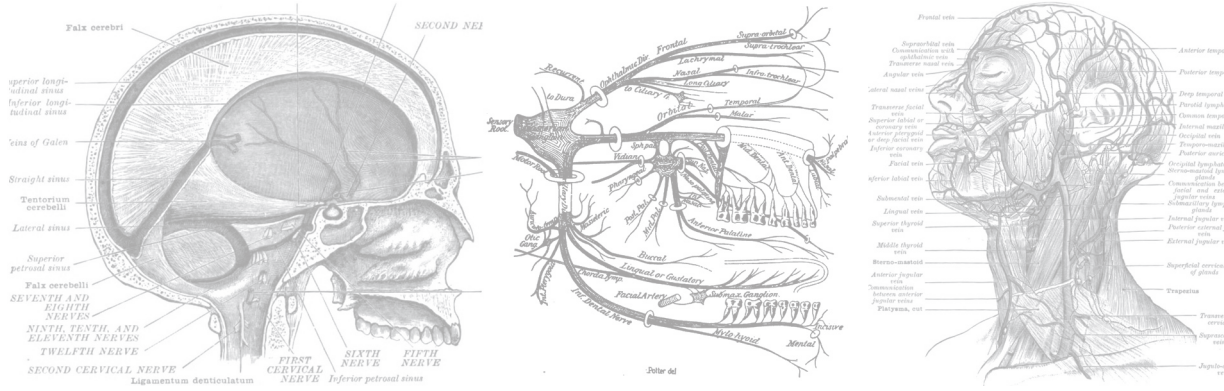
"soldiers taking propranolol would remember everything that happened, but those memories would have no emotional value"

torture and humiliation tactics are used commonly, and it is questionable if this use is purely defensive[3]. With the advent of drugs like propranalol, the results could be even worse.

Abu Ghraib happened without any drug intervention. The soldiers who exhibited extreme sadistic tendencies by physically and sexually abusing their prisoners did not need drugs to numb their emotions because the environment and the system that created the environment easily pushed them into being monsters[6]. A drug with intensified effects of propranalol would most likely make interrogation even worse. If soldiers cannot feel the emotional horrors they create and fail to feel guilty about the things they do, scandals worse than Abu Ghraib could happen.

Although such a drug could prove very useful for defensive tactics and treatment of PTSD, the military should also use neuroscience and social sciences to create new techniques for interrogation. Matthew Alexander, an interrogator responsible for taking down Zarqawi's forces in 2006, commented in an article to the Washington Post that he could not stand what was going on in Iraq. Alexander goes on to explain that the reason he was successful in subduing Zarqawi was because he used his own brand of interrogation technique that capitalized on cultivating trust in the detainee. One detainee told Alexander that the reason he gave Alexander information was because he defied the stereotype of the American military by not torturing him. This article, written in 2008, claims that few changes have taken place in the military's interrogation techniques despite the success that Alexander brought to the mission in Iraq[8].

The relationship between neuroscience and military will never disappear. However, neuroscientists can take advantage of their ever-growing ties with the military to ensure that their research won't be abused by the government. If neuroscientists take a more active role in execution of their research in the military, they could essentially change the way America fights wars.



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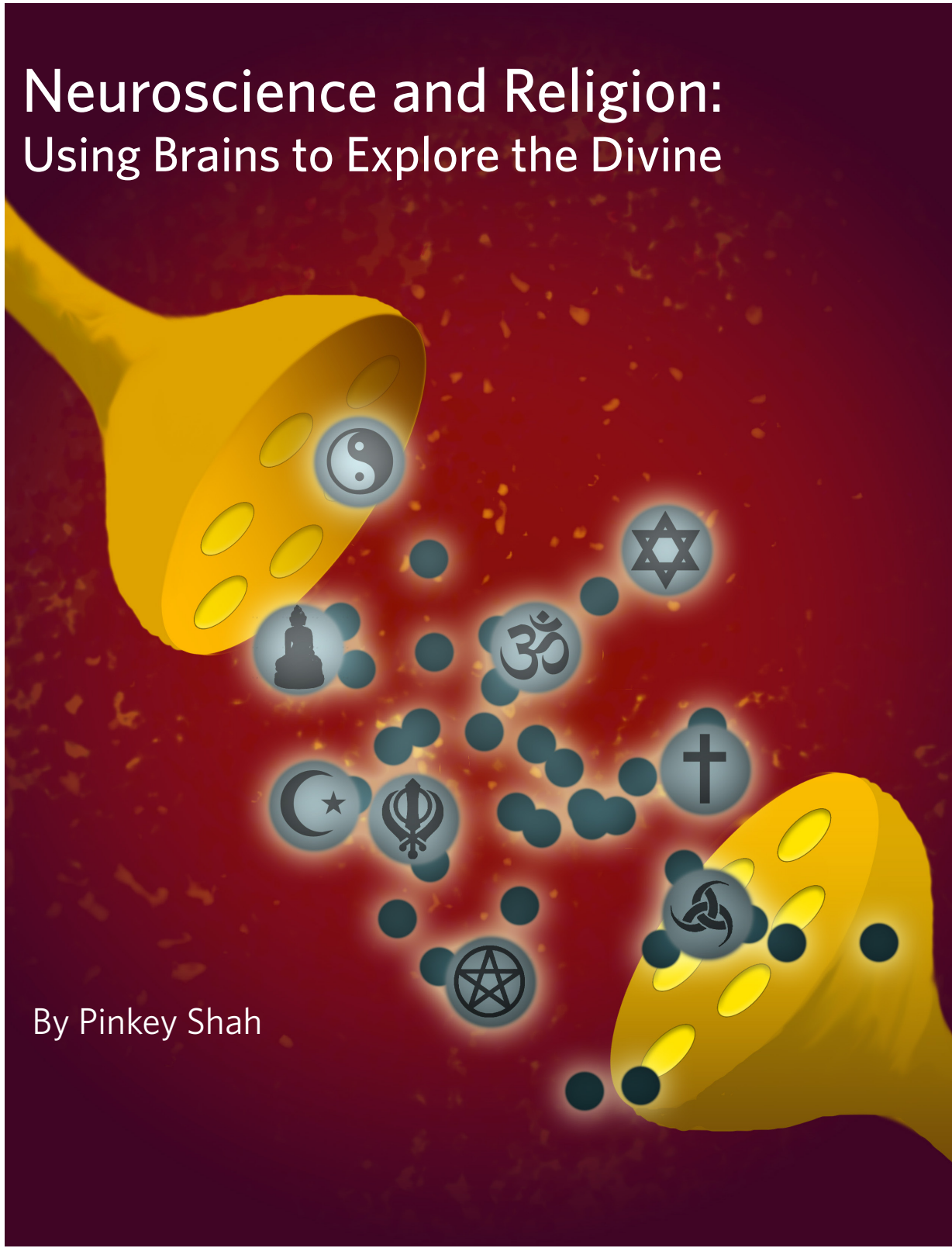
Neuroscience and Religion:
Using Brains to Explore the Divine



By Pinkey Shah

Jewish philosopher Martin Buber said that "[M]an cannot approach the divine by reaching beyond the human: he can approach it through becoming human. To become human is what he, the individual man, has been created for."[1] Buber's is just one of many voices trying to determine the origin and the purposes of religion. Buber believes that understanding religion is understanding oneself. His vague words make it difficult to discern whether he is challenging religious zealots by arguing that their ideas cannot possibly reach beyond the scope of the human mind, or whether he is actually praising religion for its essential simplicity and attractive way of life. Regardless, many theologists and philosophers agree with Buber's principal argument regarding the reflection of human nature in religious beliefs.

To discuss "religion" as a phenomenon, one must clarify the boundaries of the term. The broadest definition of religion is a set of beliefs shared by a common people. In many cases, these belief systems seek to explain the nature of existence[12]. The large percentage of Americans that report a belief in some sort of religion demonstrates the appeal of the varying religions. Statistics have suggested that as many as ninety-six percent of Americans believe in some form of a god or universal spirit [8]. Many religious groups share three primary features: a belief in an afterlife, rituals and demonstrations of faith, and an attribution of events to greater significance than the apparent mundane causes and ramifications[9].

To some, religion offers emotional and mental stability transcendent of simple human interactions and mentalities. Both tranquility from feeling personal "closeness" to the divine as well as the fear of divine retribution are reinforcements of the magnificence and security of a higher power[3]. Rites, rituals, or prayers may allow individuals to influence their position in this greater scheme and in turn create an environment conducive towards personal growth and happiness. This appeal of religion offers a concrete sense of purpose and an overarching "universal plan"[8] which provides a measure of security in an otherwise unclear world. Accordingly, many religious followers welcome the notions of "destiny" and even the "soul," which carries their essential being onward after death. These beliefs can largely determine the conduct of many people. The shared experiences like-minded believers take part in create an important sense of communal unity, and both scientific and anecdotal evidence have linked faith, religion, and spirituality to both physical and emotional well-being.

While many view religion as a system that supports happiness and comfort even after death, the institution is not without its opponents; after all, countless wars and atrocious crimes have been committed in the name of God, the Crusades being just one example. One prominent opponent of religion was psychoanalyst Sigmund Freud, who regarded religion as a compensatory mechanism for society's inability to maintain order and achieve productivity. His stance states that humans naturally behave in a destructive and chaotic manner when they lack a governing central power. As a result, religions aim to establish an appropriate code of conduct. Freud calls human nature's need for religion to maintain society the "father-complex". As a helpless child looks to his father for love and protection, an individual who fears his own fate looks to God for protection from life's perils. Freud argues that religion also breeds conformity in its followers through its promises of reward in exchange for general compliance [4]. This model of the Western world's interactions between society and religion held true until the early seventeenth century when scientific advances began to challenge religious doctrine on a significant scale.

The Galileo Affair, perhaps the most well-known clash of religious and scientific authorities in the West, began in 1610 after Galileo published Sidereus Nuncius (Starry Messenger). The paper contained observations Galileo made via telescope that supported the theory of a heliocentric model of the universe. The heliocentric theory was originally proposed by Copernicus and argued that the Earth and the planets revolve around the Sun while the Sun is stationary at the universe's center. This idea was in clear contrast with the Catholic Church and its beliefs concerning a geocentric universe, a theory proposed by Ptolemy and supported by the Christian canon. Geocentrism argues that the Earth is the center of the universe and all of the heavenly bodies revolve around the Earth. This belief centered around the importance of Earth in the Bible as well as several scriptural passages that made reference to Earth's apparent fixed state. Unable to prevent the spread of Galileo's findings, church officials allowed heliocentrism to be taught as a hypothesis only in scientific circles, while preventing its spread to general populace in an attempt to prevent discord within the Christian community. In

"an important ramification of our pattern-seeking is the inevitable search for understanding of the human existence and explanations for unsolved problems"

the end though, Galileo was put on trial in 1633 and was found guilty of heresy for his claim against the teachings of the Catholic Church and the Holy Bible[2].

Neuroscience has taken an interest in examining man's relationship to religion through the brain given its apparent role as the "bridge between the physical and the imaginative."[1] A neuroscientist might say that lower neural networks process external and internal stimuli and modulate simple, instinctive behavior, while the higher ones, such as the frontal lobes, provide self-awareness and the great range of thought that separates man from other animals. It is necessary then, to build the model of the higher-lower functions from a basic level to discuss religion's complex relationship with human cognition.

To provide a brief overview of the relevant brain structures, the six-layers of cells associated with sensory perception, motor command and planning, spatial reasoning, conscious thought, and language is called the neocortex. This feature is evolutionarily the newest and contains the most "higher-order" functions. The frontal lobe, located right behind the forehead, is responsible for most abstract thought such as the recognition of cause-effect relationships, distinguishing "good" from "bad", and essential logic and reasoning skills.. Other parts of the neocortex include the parietal lobe in the superior and posterior portion of the brain, the temporal lobes on the sides of the brain, and the occipital lobes in the farthest back portion of the brain. Lower level brain structures include the midbrain, cerebellum, and brain stem. The midbrain contains the limbic system, which is evolutionarily older than the neocortex and sits between the neocortex and the brain stem and is responsible for much of emotion and memory [1].

Investigations of the neuroscience of religion often logically focus on the limbic system due to the strong association of religion with emotions and emotional memory. "Sacred emotions" describe genuine emotions associated with religious commitment and result from consistent exposure to religious settings. Simple gratitude is defined as "emotional appreciation and thankfulness for favors received." A "sacred" form of gratitude may result from religiously-inspired importance of gratitude for everyday items and privileges that might be otherwise taken for granted, such as food, clothing, and shelter. This heightened sense of gratitude may promote positive emotions, resulting in increased enthusiasm and energy. From a medical perspective, the chemicals responsible for the positive feelings associated with gratitude may alter functions as essential as pulse, blood pressure, and even muscle tone. Gratitude and many other emotions all show varying kinds of widespread effects on man's autonomic nervous system. [11]

Plenty of scientific speculation argues that genetic information guiding religious behavior exists and that when these genes are expressed one tends to exhibit religious behaviors[10]. Some have even claimed the search for a "God gene" based on the apparent conservation of a parent's religious commitments in his children. A child, for example, whose father serves as a pastor, will likely grow up in a religious setting. Now, this child may voluntarily, or perhaps involuntarily, share the same beliefs as his father, and the question of "nature versus nurture," arises[10]. The hypothesized "God gene" would include inherited genetic information that predisposes individuals to believe in a higher power. This hypothesis was formulated by geneticist Dean Hamer who offers four major pieces of evidence to support his theory, the most relevant of which is the discovery of a gene known as VMAT2. This gene codes for a transporter of monoamine neurotransmitters in the brain and this transporter alters critical brain chemistry, which demonstrates itself ultimately in behavior. Hamer called attention to the gene when he found that it was a common element in the DNA of over 1000 individuals claiming to be devoutly religious. The data is still out on how strong a connection exists between VMAT2 and faith, but Hamer does not expect to see a direct link between his findings and spirituality; rather, he believes his work is a step towards finding the neurological pathway connecting the human intellect and investment in religion[5].

Many scientists have turned toward studies of the brain in action rather than trying to identify genes that correspond to religious piety, in order to examine the neural roots of religion. The field of

brain mapping has grown rapidly as technology allows incredibly clear studies of brain chemistry and electrical signaling. The ultimate goal is to establish a clear connection between precise areas of the brain and how they influence the workings of human consciousness. Perhaps if the neural center for "anger" as an emotional phenomenon were to be located and changed so as to remain inactive, one could prevent the emotion, serving as the ultimate anger-management program. In regards to studies of religious experience, scientific evidence gathered at the University of California in San Diego points to an area in the temporal lobe, though not a region traditionally associated predominantly with emotion, that produces "intense feelings of spiritual transcendence combined with a sense of mystical presence." One neuroscientist, Michael Persinger of Laurentian University, was able to reproduce these feelings in individuals with no reported religious devotion by stimulating the appropriate area within the temporal lobe. Many participants claimed feeling a greater "presence" and, in one such experiment, a participant reported "[seeing] Christ in the strobe" light flashing in front of him as this brain region was stimulated[3].

The human brain may be, above all else, a pattern-seeking entity. We feel compelled to finish musical scales; feel uneasy listening to random noise; and see wholesome shapes when looking at partially occluded objects. But an important ramification of our pattern-seeking is the inevitable search for understanding of the human existence and explanations for unsolved problems. This may be in part responsible for the universality of religion in human culture and in turn may have aided science's rise to predominance in the Western world. Science concerns itself with experimental data and theory while religion claims authority for the supramundane concepts considered beyond the scope of man[8]. If an explanation for some problem isn't evident, God must be responsible. Religious belief cannot be confined to the expression of a single gene, but rather exists as a consequence of some level of human nature, the need to explain the inexplicable[7]. As scientific explanations of the universe, man, and even religion spread, religions evolve in their own way to continually offer support in avenues in which they claim science lacks authority. Freud believed that scientific discovery has caused religion to lose much of its influence, despite the ever-growing religious population[4]. Psychology and neuroscience have attempted to examine the origins of religion and its complex role in understanding the human condition. Ideally, neuroscientists hope to establish a clear biological explanation for the rise and perseverance of religion as a universal phenomenon throughout history.

Looking ahead, one wonders how religion and man will interact as science solves more and more of the universe that long needed religious faith to explicate. When individuals feel the need to seek guidance, will they consult religious authorities or scientific ones? As neuroscience examines religion more carefully, will people share Freud's view of religion as a flimsy construct more and more? The incredible longevity of religious behavior suggests a functional permanence to its existence in society and that it may very well never disappear from its prominent position in everyday life. Elucidation of the neural bases of religious belief promises only to explain why people tend to be religious. Figuring out why and how the brain makes one believe in a god does not demean that belief in any way; nor does it prove that God doesn't exist. Perhaps the most pressing question is how politicians and the public will respond to such research and whether scientists will be supported in their quests.

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Depression have you in a funk? Try the Special K Challenge.

By Aisha Sohail and Jeff Wessell

Introduction

In high school, they warned us of the dangers of date rape drugs such as Rohypnol, GHB and Ketamine. But current studies demonstrating the clinical uses of these once illicit drugs shed light for their uses as pharmacotheraputics. Rohypnol, or roofies, has been shown to be a potent hypnotic and is used in foreign countries to treat patients with severe insomnia. GHB is now FDA-approved to treat patients with narcolepsy. But what may be most intriguing is that Ketamine (aka Special K) has gone through several clinical trials that implicate it as a powerful antidepressant, working especially well in patients with treatment-resistant depression.

Traditional Antidepressants

Currently there are three main classes of antidepressant treatments that are prescribed to patients with major depressive disorder (MDD). MDD is a disorder characterized by overall low mood and can be accompanied by a lack of interest or pleasure, and low self esteem. The three classes of treatments - Monoamine Oxidase Inhibitors (MAOIs), Tricyclics, and Selective Serotonin Reuptake Inhibitors (SSRIs) – share a common final pathway; they were designed to increase levels of neurotransmitters available at synaptic junctions because for years, "low levels of neurotransmitters" has been the hallmark of depression. However, recent research shows that the story is not that simple.

Individuals with depression have a decreased volume in their prefrontal cortex which is accompanied by neuronal atrophy. Until recently, this neuronal degeneration was believed to be irreversible and untreatable. New studies have proved that neurogenesis, a process of new neuronal generation and growth, can occur in mature brains. All of the current forms of antidepressant treatment indirectly cause neurogenesis by elevating synaptic neurotransmitters. For instance, SSRIs selectively block reuptake of serotonin (5HT) thus increasing the amount of 5HT in the synapse. The elevated amounts of 5HT cause a cascade of postsynaptic activity beginning with elevating levels of cAMP, an important intracellular second messenger. Elevated levels of cAMP in turn increase levels of intracellular PKA, which in turn increases levels of CREB. This process is not merely a domino effect, but involves various regulatory factors between each step. Ultimately CREB, a transcription factor, binds to a region of DNA inside the cell and increases Brain-Derived Neurotrophic Factor (BDNF). BDNF is a neurotrophin involved in promotion of neurogenesis, differentiation of new neurons and synapses, and neuronal growth.

The BDNF hypothesis of depression is rationalized by hippocampal neuronal atrophy and death. The hippocampus is believed to play a significant role in emotional control,[1] therefore adverse neuronal changes can account for mood disorders. Decreased neurotrophin levels are correlated with a lack of neurogenesis in a given brain region. Thus, current antidepressants fit the BDNF hypothesis of depression by increasing neurotrophin levels and eventually promoting neurogenesis. Clinical evidence in support of the BDNF hypothesis has been presented by Chen et al using immunohistochemistry to stain for BDNF levels in post-mortem patients with mood disorders who were either treated or untreated with antidepressants.[2] Subjects with mood disorders on antidepressants showed increased levels of BDNF in regions of the hippocampus compared to non-medicated individuals with mood disorders.

Current antidepressants do not effect a change in individuals immediately; patients must be taking the medication for 2-4 weeks before full therapeutic effects are attained. In a study performed by Wang et al, chronic fluoxetine (Prozac, an SSRI) administration to male mice demonstrated an increase in dendritic arborization, an indicator of neuronal activity and proliferation.[3] Only chronic fluoxetine produced such results after 3-4 weeks, suggesting that it takes time for the neuroplastic changes and increased neuronal complexity to take place. This result complements the time necessary for the medication to enact its behavioral effects in humans. It is assumed that this delay period is one in which downstream effects required to produce neuroplastic changes and neurogenesis occur, suggesting that therapeutic effects cannot be attained in a short period of time.

Evidence for Ketamine as a potent antidepressant

Zarate, Singh, and colleagues (2006) found a robust, rapid (hours), and relatively sustained (1 week) response to a single dose of the NMDA antagonist ketamine in patients with treatment-resistant MDD; subjects infused with ketamine showed significant improvements on a depression rating scale

test compared to those infused with placebo.

These results are remarkable considering ketamine's short half-life of only 2 hours. It is unlikely that ketamine's euphoric effects were mistaken for its antidepressant properties because ketamine's antidepressant effects last for up to 1 week. These effects also cannot be attributed to the placebo effect, as various analyses showed the significance of ketamine over placebo, and the effect sizes of this study were very large at day 1 and moderate to large at day 7 post-administration. Similar results have been replicated in mouse models.[4]

Mechanisms of Ketamine's antidepressant action

Ketamine binds to the NMDA receptor with an affinity that is much higher for the NMDA site than other sites; blocking opiate, cholinergic, or other monoamine receptors does not interfere with ketamine's behavioral effects,[5] suggesting that its behavioral effects are probably mediated by via the NMDA receptor. In addition to being a noncompetitive NMDA antagonist, ketamine also produces a presynaptic release of glutamate, which is apparently essential to its antidepressant action.[6] The rapid antidepressant effects of ketamine could be due to an increase in glutamatergic throughput due to the increase in ionotropic glutamate AMPA receptors relative to ionotropic glutamate NMDA receptors. NMDA receptors are permeable to Ca2+ ions and Na+/K+ ions, whereas AMPA receptors are permeable to only Na+/K+ ions. NMDA receptors have a magnesium block mechanism such that they are not activated until membrane has been depolarized via AMPA current

"results from ketamine promise to revolutionize depression treatment"

If NMDA receptors are blocked by Ketamine, glutamate throughput is forced to prefer AMPA receptors over NMDA receptors. In other words, glutamate released from a synapse will activate mostly AMPA receptors. This finding is consistent with the observation that post-mortem studies of depressed patients confirm decreased levels of metabotropic glutamate receptors mGluR2 and mGluR3, which are primarily responsible for decreasing NMDA receptor activity.[7]

In addition, studies with an AMPA receptor antagonist, NBQX, also demonstrate the need for increased AMPA receptor throughput for ketamine's antidepressant actions. The Forced Swim Test (FST) is a paradigm to measure depression in which immobility (swimming) time correlates well with depressive symptoms in mice. When NBQX was administered to mice before FST, there was no significant change in immobility time compared to placebo; however, when NBQX was administered immediately prior to ketamine administration, it abolished the decrease in immobility time.[8] Common treatments with standard antidepressants have also been shown to enhance AMPA receptor surface levels.[9] This period of latency necessary to achieve antidepressant effects with standard agents may represent the time necessary to exert direct modulatory effects on AMPA receptors. These observations suggest that ketamine's antidepressant properties may be modulated by increased AMPA receptor throughput.

Not only does ketamine work rapidly, but it also has sustained effects that can be explained by AMPA-related neuroplastic changes. AMPA potentiation in ketamine's antidepressant action is consistent with the observation that AMPA may promote increased neuronal survival, attenuate apoptosis, and prevent synaptic deterioration produced by deafferentation[10,11,12]. AMPA receptor activation increases BDNF expression.[13] In one study, AMPA stimulation in hippocampal slice cultures caused the selective activation of MAPK through the upstream activator MAPK kinase (MEK). Inhibition of either component of the AMPA-MAPK pathway increased cellular damage due to serum deprivation, suggesting that this pathway facilitates compensatory signals in response to injury. Likewise, AMPA potentiation with ampakine CX516 enhanced MAPK activation and reduced synaptic and neuronal degeneration resulting from excitotoxic episodes.[14] Moreover, AMPA receptor activation has been shown to increase BDNF mRNA in a manner dependent upon MAPK signaling; and BDNF-induced cell survival has been shown to require the MAPK signaling pathway in neuronal cultures deprived of survival factors[15.16].

Traditional antidepressants and glutamatergic antidepressants are thought to act via a similar pathway in the brain. The traditional antidepressants change levels of synaptic neurotransmitters to effect a change in intracellular cAMP, PKA, CREB, and ultimately BDNF. Glutamatergic antidepressants en-

hance glutamatergic throughput by upregulating the number of AMPA receptors with respect to NMDA receptors, increasing the MAPK intracellular signaling pathway. The effect is that neuronal apoptosis is attenuated and levels of BDNF are increased, promoting overall neuronal health.

Results from ketamine, and soon perhaps other non-traditional antidepression drugs, promise to revolutionize depression treatment. Perhaps in the near future, ketamine therapy may defeat the chronic blues that is depression. Whether or not depression is a phenomenon that should be eradicated is another question.

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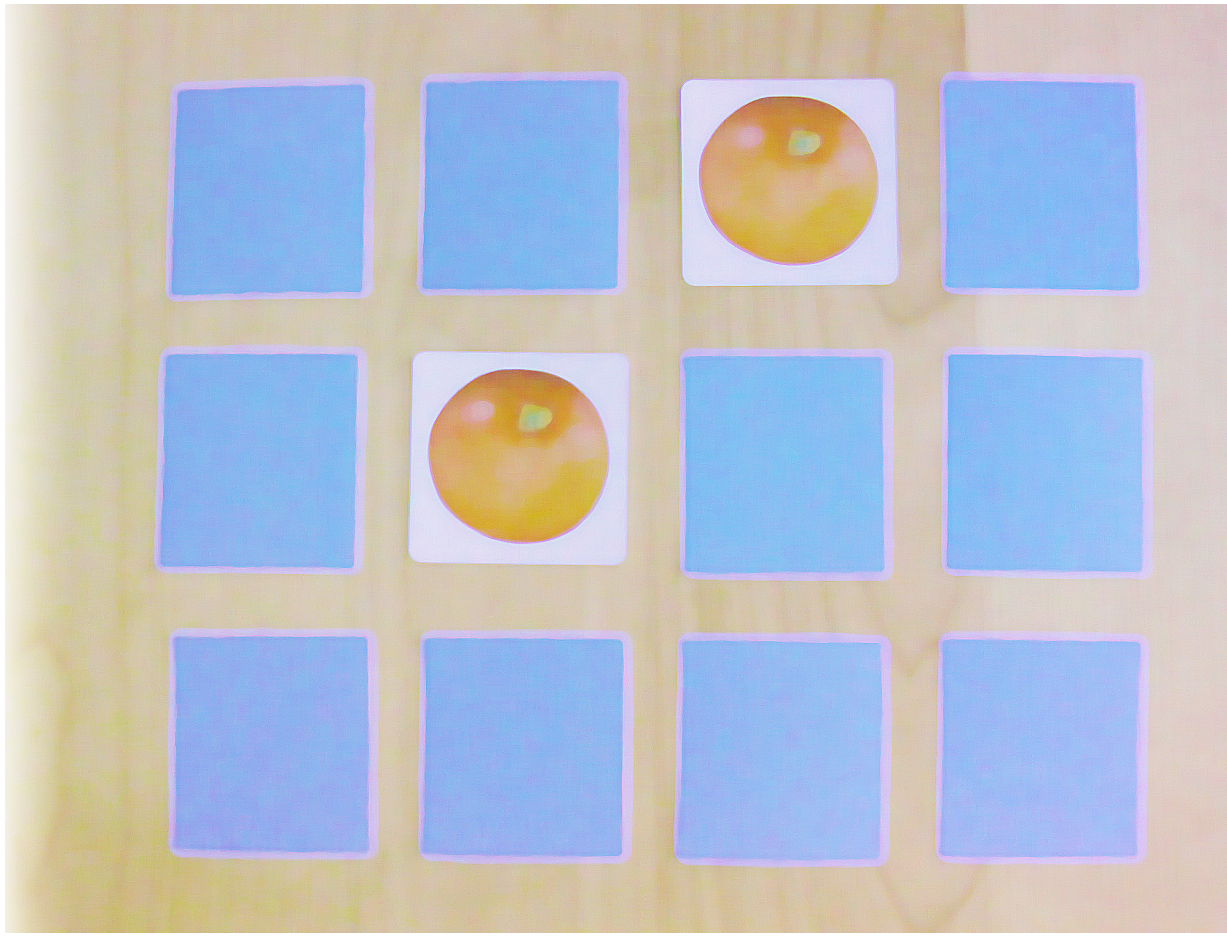

Recognition Memory
An Analysis of Two Prominent Theories

By Danielle Miller

REVIEWS

INTRODUCTION

Recognition memory is a particular aspect of memory that provides the ability for an individual to identify a previously encountered stimulus. There are two prominent theories as to how recognition memory operates. One theory proposes that there are two distinct processes involved in the recognition of a stimulus, called recollection and familiarity[1]. Another theory, however, denies the independence of the two processes within recognition memory. In this theory, familiarity is primarily thought of as a weak memory, whereas recollection is considered to be a type of strong memory[2].

This paper aims to take a closer look at both theories by exploring evidence that supports each one. A deeper evaluation of the dual process model and single process model will be made in order to explore all aspects of recognition memory. The paper will provide the reader with a background sufficient for understanding all aspects that are currently proposed about recognition memory.

RECOLLECTION AND FAMILIARITY AS TWO DISTINCT PROCESSES

In one theory of recognition memory, recollection and familiarity are seen as independent processes. In this particular theory, recollection is the process that recovers specific details about an event, whereas familiarity involves a sense of the experience but lacks details. Recollection and familiarity can be displayed as two separate processes with evidence from recognition tests, receiver operating characteristics (ROC) curves, amnesic patients, and fMRI studies. Data supports that recollection and familiarity occur in two separate areas of the brain and that their usage and function are different; depending on the task at hand, each brain region may be recruited or manipulated differently. According to the proposal, both are housed within the medial temporal lobe (MTL) structures but recollection is dependent on the hippocampus, and familiarity relies on the perirhinal cortex[1].

Evidence from Recognition Tests

One way in which recollection and familiarity differ is in the application and availability of the processes. Familiarity typically becomes available more quickly than recollection and is usually the first process that is engaged in recognizing a stimulus1. Subjects do very well in discriminating between two items to determine which one was previously encountered and which one was not. Yet, when subjects need to remember much more details in order to discriminate between the two objects (i.e the spatial associations with the objects) performance is reduced, suggesting that familiarity is engaged and used effectively in making discriminations between encountered and non encountered items, but recollection must be engaged for further processing of differences[3].

The amount of time allotted to an individual who is recognizing a stimulus affects performance. In one experiment, participants were advised to reject highly familiar items4. Participants at first accept the highly familiar items but then begin to reject as time goes on. This illustrates the distinction between familiarity and recollection. At first recognition memory employs familiarity, which is a rapid, readily available process used for fast responses and then switches to recollection, which is a much slower process that allows for correct responses when given longer time1. Thus, at first, those participants used familiarity and accepted the items, which was an incorrect response; recollection was employed only after familiarity, allowing for a correct response of rejected items.

Evidence from ROC

More experimental results that support the dual process theory is the data collected from ROC curves. ROC's involve collecting recognition confidence responses and then relating the proportion of correct recognitions (the hit rate) to the proportion of incorrect recognitions (the false alarm rate)[5]. The shape of ROC can thereby support the existence of two processes. Since recollection supports high-confidence responses, a measurement of recollection can be obtained by the asymmetry of the ROC curve; in contrast, familiarity can be measured by the degree of curvilinearity[5].

In animal models, ROC's can be manipulated to show the affects that lesions have on recognition memory. In normal rats, the ROC curve has both an asymmetrical and curvilinear aspect to it, representing the fact that the rats use both recollection and familiarity in recognition. In rats with hippocampal damage, there is a loss of the asymmetry, which suggests that recollection (represented by asymmetry) is supported by the hippocampus. Since the curvilinear portion of the curve is still intact, familiarity appears not to be affected by hippocampal damage6. It is evident that this deficit in recollection is not due to the loss of memory strength, because an increase of delay (which causes a weakened memory) leads to a loss of curvilinearity and retention of recollection[1].

The dual process model but not the single process model can readily explain the data from another study. In this experiment rats were trained using the ROC paradigm. Rats that had hippocampal lesions produced an ROC curve without asymmetry but maintained the curvilinear aspect of it[7]. This means that rats with lesions to the hippocampus lost recollection processes but kept the process of familiarity. In contrast, control subjects that had an intact hippocampus primarily relied on recollection, producing a more asymmetrical curve[7]. This reliance on recollection for normal rats was most likely due to the fact that the rats were exposed to the same odors and mediums for multiple pairings, providing a more concrete association with the stimulus. Thus this study supports the dual process model; it effectively shows that recollection and familiarity are dissociable and differentially affected by hippocampal damage[7]. The maintenance of familiarity in rats with hippocampal lesions suggests that the hippocampus is not equally involved in recollection and familiarity as the single process model proposes.

While ROC data support the idea that familiarity and recollection are two independent processes within recognition memory, brain studies of humans and animals also provide further insight to this theory. In these studies, the region that each process is thought to involve is investigated more closely.

Evidence from Brain Studies

In some cases, damage to the MTL structures can cause amnesia. Amnesiacs have severely impaired episodic memory, which is the type of memory function that relates to the specific events in an individual's life. The MTL includes the hippocampal formation, entorhinal, perirhinal, and parahippocampal cortices[8]. Bolstering the theory that familiarity and recollection are two separate processes, these studies show that recollection is supported by the hippocampus, whereas familiarity is heavily dependent on the perirhinal cortex[9]. Therefore, according to this theory, amnesiacs with concentrated damage in the hippocampal area should show impaired recollection whereas familiarity should be relatively intact.

Amnesic patients with extensive MTL damage will have higher deficits in recollection with less damage to the familiarity process[10]. Since both processes are not equally impaired following such damage, it appears that recognition is not a unified memory system located in the MTL. Instead, recollection is dependent on the hippocampus and familiarity on the perirhinal cortex, which is in the surrounding parahipppocampal region[9]. This supports the idea that recognition consists of two processes that are heavily implicated in two different areas of the brain.

A case study of patient YR, who had selective bilateral damage to the hippocampus, demonstrates impairment of recollection with intact familiarity[11]. Patient YR was impaired at association memory for different items, a task mediated by the hippocampus, but had intact familiarity recognition between items[11]. Because this study shows selective hippocampal damage resulting in impaired recollection with intact familiarity, the dual process model is supported.

Another patient KN, who also had damage to the hippocampal region with sparing of the perirhinal cortex, showed impaired recollection and preserved familiarity[12]. Experimenters used the remember/know procedure, which requires an individual to declare if an item can be recalled with specific details or if it is known that the item appeared but there are no

details surrounding the event[13], as well as ROC analysis, both of which suggest a deficit in recollection. This also supports the dissociation between recollection and familiarity.

There have also been studies where the perirhinal cortex has appeared necessary for normal familiarity function. Patient NB, who received a surgical resection of the left anterior temporal lobe structures including the perirhinal cortex but sparing the hippocampus, showed impairment on familiarity tasks but normal function on recollection tasks[14]. NB was tested using remember/ know, which is a procedure that requires subjects to claim whether they remember or know (the word feels familiar) a word from a list that was previously presented, and ROC paradigms. This supports the idea that the perirhinal cortex is implicated in the familiarity process. This evidence supports the theory that recollection and familiarity are two separate processes occurring in different regions of the MTL structures.

> "separation of location of the processes implicates the dual process model as a key player in recognition"

In hypoxic patients, in whom the hippocampus is largely damaged due to a lack of oxygen, there are some differences in deficits between recall and familiarity[15]. In some studies recollection was severely damaged in hypoxic patients and familiarity was normal[16]. Yet, some studies fail to report such a severe difference in deficit[17]. The reason that the deficit is not as selective to one process may be due to peripheral damage in the surrounding areas of the hippocampus, which could then affect familiarity.

In animal studies, in which the lesions can be more selective, there has been a correlation between selective hippocampus damage and impaired recall. Using ROC analysis, rats with hippocampal damage had impaired recollection and, in some cases, enhanced familiarity[18]. Normal rats used recollection for tasks whereas rats with hippocampal lesions relied on familiarity. This provides more concrete evidence that selective damage to the hippocampus does cause a deficit in recollection while sparing familiarity.

Evidence from fMRI Studies

Some studies have focused on recording the activation of certain brain areas while a participant is doing a task using functional MRI. In recognition memory tasks, individuals use tasks that employ both recall and familiarity. One particular task that is commonly used is the remember/ know task.

Using fMRI during the remember/ know task, experimenters examine the brain regions that are activated during the encoding and retrieval of remembered or known items. Across different techniques, hippocampal activation is higher for those items that are remembered (recollected) than those that are familiar1. Only recollected responses produced activity in the hippocampus noticeably different than not remembered items; familiar responses, however, did not produce significant activity in the hippocampus relative to unfamiliar items[19]. There was, however, encoding activity in the anterior parahippocampal gyrus, primarily the perirhinal cortex, for familiar items[20]. No other MTL structure was significantly activated for familiar items; recollected items did not produce activity in this region.

RECOGNITION AS A SINGLE PROCESS

Another theory proposes that recognition memory is composed of a single process, therefore denying the independence of the two processes within recognition memory. It is thought that there are not two separate and distinct processes, but rather that recollection and familiarity support strong and weak memories respectively[2]. This theory claims that there is not a difference in location between the elements of recognition memory, but rather that recollection and familiarity occur both in the hippocampus and in the perirhinal cortex collectively[2]. Evidence that supports this theory includes amnesia studies, ROC, fMRI studies, and single cell recording. These studies point to a uniform process for recognition memory that only differs in the strength of the memory.

Evidence from Amnesic Patients

A study of 56 hypoxic patients strongly suggests that recognition memory is a singular process. In this particular study, in which the lesions appeared limited to the hippocampus, 55 of the patients had impairments in both recall and familiarity[21]. Hippocampal damage that results in a loss of both recall and familiarity suggests that the two processes are in fact not separate and occur in the same location of the brain.

Another study which involved six patients who had bilateral hippocampal damage resulted in an equal impairment of recall and familiarity[22]. This provides evidence against separate processes, as it appears that both are located in the same areas of the brain. The single process theory can be supported further with ROC curves that outline the memory system's usage of strong and weak memories.

Evidence from ROC

ROC curves can be interpreted as a representation of memory strength. ROC involvement of confidence levels reflects the strength of the memory, or the certainty of having previously viewed a particular item[2]. Asymmetrical curves reflect strong memories and curvilinearity reflects weak memories[23]. This implies that the ROC curves without asymmetry (only curvilinearity) produced by brains with hippocampal lesions reflect an individual's reliance on a weak memory as opposed to an entirely different process.

According to the single process theory, stronger memories result in a higher curve than weaker memories. In one study, once the overall memory strength was similar in patients with lesions in the hippocampus to the control, the graph of the ROC was asymmetric (strong memory) and matched the control ROC[24]. This indicates that even in the absence of the hippocampus, the curves can obtain asymmetry, suggesting that recollection is a type of strong memory.

Evidence from fMRI studies

While ROC curves are helpful in the analysis of memory strength in recognition memory, fMRI's are useful in determining specific brain areas that are functioning during a particular task. In the remember/know task, studies have determined that recollection is impaired more than familiarity in patients with hippocampal lesions. It must be recognized, however, that this requires an assumption that the task is testing recollection and familiarity specifically[2].

In an fMRI study recording brain activation of MTL structures in individuals, activity in the right perirhinal cortex and bilateral hippocampus increased as a function of increased memory strength, regardless if the memory was recollected or familiar[25]. When source memory success, or successful recollection, was held constant, activity in the hippocampus was still noted, suggesting that hippocampal activation occurred without recollection and was reliant more on familiarity based memories[25]. This supports the theory that familiarity and recollection do not exist as separate processes but overlap in similar brain regions. It also suggests that MTL activity occurs as a result of memory strength and is not based on the type of memory encoded. However, the study only examined recollection of the originating source of the information. Therefore, it may very well be likely that other types of recollection are separate processes from familiarity. Since the researchers only examined recollection in the form of source memory, it cannot be claimed that all types of recollection overlap with familiarity in brain regions.

Evidence from Single Cell Recordings

The recordings of single cell neurons appear to be much better for detecting the differences in memory strength. Hippocampal neurons of epileptic patients were recorded while the patients were asked to make discriminations between old and new items. It was observed that certain neurons fired when new items were presented and other neurons fired when old items were; those that fired to the old items increased firing even when the recollection of the location of the item failed, suggesting that the hippocampus was involved in item recognition even when recollection was absent[26]. Hippocampal activation during item recognition suggests a single process occurring, which involves both recollection and familiarity. However, the neurons firing in the absence of recollection may also point to a different conclusion; these particular neurons seem to fire for all remembered items, and therefore, may not be encoding for any specific memory[1]. Thus, the firing of these neurons may not mean that memory is occurring as one process. The perirhinal cortex also shows no distinction in processes. In recordings of the perirhinal cortex, there appears to be

no difference in the encodings of items that will later be strongly remembered as opposed to those that are weakly remembered[2].

CONCLUSIONS

Recognition memory is described by two major theories: one pertaining to a dual process that involves a strong dissociation between recollection and familiarity and another that involves a single process that describes a distinction between strong and weak memories. The dual process theory accounts for the data obtained from both human and animal studies, whereas the single process model cannot fully explain some data obtained from studies.

Selective hippocampal lesions affect specific processes (recollection) within recognition memory. Specific losses of certain processes suggest that there are two processes, which are localized in different areas of the brain. Separation of location of the processes implicates the dual process model as a key player in recognition memory.

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The Neuroanatomy of Homosexuality

By Claire Bryson

REVIEWS

The anterior hypothalamus of the human brain is sexually dimorphic and has been investigated for dimorphism with regards to sexual orientation through examination of postmortem brains of homosexual males, heterosexual males, and heterosexual females. Studies examining the interstitial nuclei of the anterior hypothalamus[3] and the anterior commisure[4] have shown correlation to sexually-orientated dimorphism. Through further research, a relationship between the development of these sexually dimorphic regions and steroid hormone levels has been established. Though neither consequence nor causation can be definitively demonstrated from this research, its implications are suggestive of the early differentiation of human sexual orientation and its origins spanning neurobiology and endocrinology.

Sexual orientation has long been a topic of controversy and debate in social, political, and scientific circles. In the last twenty years, scientific efforts have examined the biology of this phenomenon. Most of this research has focused on the anterior hypothalamus and the preoptic area (POA) within the larger hypothalamic region. Historically, these areas have shown a relationship to male sexual behavior.[1] More recent research has elucidated differences in the anterior hypothalamus and its endocrinological functions between heterosexual males and homosexual males. In the current literature, there is little doubt that these areas of the brain are sexually dimorphic; however, debate still exists regarding how these differences affect sexual orientation.

"there is little doubt that these areas of the brain are sexually dimorphic; however, debate still exists regarding how these differences affect sexual orientation"

To understand male sexual orientation as a phenomenon, familiarity with the development of male fetuses must be discussed. Gender is determined by the activity of a lone pair of sex chromosomes passed on by the parents. Initially, the gonads are indistinct and can develop as either testes or ovaries. In males, the testis determination factor (TDF) gene, when expressed properly, causes testicles to develop, while in absence of its function, ovaries will develop.[2] After this stage, the testes and their specific hormonal secretions direct the organization of the rest of the body, including the brain, which also develops either masculine or feminine traits. As seen from the process, humans begin as "female," so to speak, and develop the male characteristics. Thus, hormonal secretions are both important and delicate in male development, depending largely on the androgenic, or masculinizing, steroid hormone testosterone.[2] This molecule functions as a "pro-hormone" to masculinize the brain during development.[2] Studies examine the occurence of this neuronal patterning according to gender and its prevalence in homosexual men in attempts to determine whether sexually dimorphic areas of the brain are affected by, or even correlate to, the sexual orientation of males.

In a key article, Simon LeVay presented the difference in hypothalamic structure between heterosexual and homosexual men[3]. Cited by a majority of articles in the field, LeVay's hypothesis and study was expository and led to extensive additional research. LeVay argued that the hypothalamus held the the key to sexual orientation. He cited that, in male monkeys, lesions in this region impair heterosexual behavior without eliminating sexual drive[3]. LeVay investigated two specific small groups of neurons, the interstitial nuclei of the anterior hypothalamus 2 and 3 (INAH 2 and 3). He hypothesized that one or both of these nuclei would exhibit size dimorphism with sexual orientation, not just with gender as had been previously examined[3]. Because INAH had already been observed to be more than twice as large in heterosexual men than women, LeVay extrapolated that INAH 2 and/or 3 would be large in individuals sexually oriented towards women (heterosexual men and homosexual women) and small in individuals sexually oriented

towards men (heterosexual women and homosexual men). Because brains of homosexual women were not available, only the brains of homosexual men were examined. And although most of the homosexual male samples were from post mortem AIDS patients, this had no effect on the results; comparison of heterosexual men who died of AIDS with homosexual men who died of AIDS still showed the difference in INAH3 nuclei. Furthermore, the variance of subjects by age was eliminated by age-matching study groups.

LeVay's research found that INAH 3 did exhibit the hypothesized sexually-oriented dimorphism[3]. In accordance with his hypothesis, the volume of the nucleus was more than twice as large in heterosexual males as in homosexual males, a statistically significant result[3]. Given the double blind-procedure, no bias could exist, and no statistical difference was found when comparing brains of heterosexual males who died from AIDS to other brains of heterosexual males. Ultimately, homosexual men and heterosexual women both had smaller volumes of INAH 3 compared to that of heterosexual men, supporting LeVay's arguments on the nature of INAH 3[3].

The applications of this discovery are limited by the inability to determine causation. Because of the postmortem nature of the experiment, it was impossible to gain detailed insight into all subjects' sexualities. This limits the ability to show correlation between brain structure and the diversity of sexual behavior. Additonally, "exceptions" to the rules do exist; homosexual males with INAH 3 regions sized appropriately to heterosexual males were observed, suggesting that INAH 3 alone does not necessarily affect sexuality. Clearly, there are further unidentified variables which impede the ability to identify the dimorphism of INAH 3 as cause or consequence of sexual orientation. Regardless, sexual orientation has a demonstrated biological correlation to some extent, which necessitates further in-depth research.

Laura S. Allen and Roger A. Gorski studied sexual dimorphism in the anterior commisure (AC) of the human brain, a fiber bundle that is sexually dimorphic but not directly related to reproductive function[4]. Their study, similar to LeVay's, examined volumetric differences between homosexual males and heterosexuals of both genders and used age-matching and double-blind procedures to elminate variance and bias[4]. The AC in homosexual men was found to be 34% larger on average than that of heterosexual men and 18% larger than that of heterosexual women[4]. When adjusted for individual brain mass, the AC of homosexual men was 36% larger than heterosexual men and 5.9% greater than heterosexual women. heterosexual women had an AC 28.4% greater than heterosexual males[4].

The functional significance of the size of the AC is unknown, but it shows clear sexual dimorphism and experimentally determined sexual-orientation dimorphism, similar to the INAH 3 area. Little research has examined these differences in humans, but studies on animals have shown that they arise in the perinatal organism[2]. Given the results regarding both INAH 3 and AC correlation to sexual orientation, the understanding that no single brain structure correlates to sexual orientation carries weight. The apparent interconnected nature of varying brain regions suggests that factors operating early in development differentiate on the basis of gender and sexual orientation within sexually dimorphic structures and brain function in a cumulative manner[2]. Exploring which specific factors influence which kind of development requires an endocrinologic approach alongside traditional neurobiological studies.

The endocrinologic approach examines the role of sex hormones in sexual orientation. In mammalian models, like in humans, an androgen masculinizes the developing genitalia and then the brain as well[1]. The question is whether or not these fetal androgens alone also 'masculinize' the brain or if there are further key players in development such as neurotransmitters or neurodevelopmental factors.

Conflicting studies have suggested that boys may turn out homosexual as a result of lower-than-normal fetal androgen, from higher-than-normal levels, or for reasons having nothing to do with androgens, with no study appearing more conclusive than the rest[1]. However, through studies of sheep, Roselli et al.[5] have some evidence that male-oriented rams receive lower-than-normal androgen stimulation of the brain. Since testing in rats has suggested that estrogen may affect the volume of the ovine sexually dimorphic nucleus (oSDN), this effect was then studied in rams to explain the minority of males which display a preference for mating with other males over females[5]. It was found that male-oriented rams did in fact have a smaller nucleus in this brain region than female-oriented rams[5]. These observations lend strong support to the importance of the anterior hypothalamus's influence on sexual orientation in males[5]. The enzyme aromatase converts androgens like testosterone into estrogens and plays a crucial role in the masculine development of the rat SDN-POA, masculinizing the rat brain and

"the apparent interconnected nature of varying brain regions suggests that factors operating early in development differentiate on the basis of gender and sexual orientation within sexually dimorphic structures and brain function in a cumulative manner"

leading to masculine behavior[1]. These results show a relationship between steroid hormones, oSDN morphology, and the resulting sexual orientation in rams. With such progress using with rams as a mammalian model, researchers may be able to draw implications about human sexual orientation.

Before being applied to humans, research must determine more precisely how steroid hormones and the related biology affect the size of the oSDN. Does the level of aromatase activity determine oSDN size, or does oSDN size determine the level of aromatase? If aromatase effects in the POA are responsible for the size of the oSDN and the size of the oSDN is in turn responsible for sexual preference, then interfering with hypothalamic aromatase in developing rams may reliably shrink the oSDN and produce male-oriented rams[5]. This demonstration would be suggestive of a causal relationship between steroid action, hypothalamic morphology, and sexual preference in sheep[5]. By extension, this demonstration could also suggest that steroid hormones affect the human hypothalamus to influence sexual orientation. Studies investigating this effect would further emphasize the critical biology of sexual orientation and eliminate the social argument of "choosing" one's sexuality.

There is still significant research that needs to be done before anything truly conclusive can be reached. First of all, these studies lack homosexual female subjects. Due to the prevalence of AIDS among the homosexual male community, records of sexual orientation allow for postmortem analysis of their brains. This is not the case for homosexual women, as a population that has not been as affected by AIDS. A longitudinal study would be required to track homosexual women to ultimately allow for post mortem analysis on the sexually dimorphic nucleus areas of the hypothalamus. Longitudinal studies could also examine varying levels of steroid hormones throughout development. There has been speculation that homosexual men in general have a lower age at puberty, perhaps due to variations in hormone levels[6]. In general, future research could also focus on the relationship between steroid hormones and development of the SDN in the hypothalamus. Related topics of study remain largely unexplored in humans, such as the preliminary studies of pheromone sensitivity based on individual's sexual orientation [7].

The question of human bisexuality remains. What biological evidence could be shown in such an individual? It could prove enlightening to thoroughly examine the brain of a bisexual person and find differences from both homosexual and heterosexual individuals. Still, correlating neurobiological and endocrinological dimorphism cannot argue causation without further experimentation in animal models. Additionally, separating environmental influences like factors during gestation from purely genetic ones may not be possible. Therefore, the interaction and communication between various fields of research on this topic will be critical to future success. A concerted effort between disparate methodologies of investigation may provide the key for advances in the years to come, and, regardless of their results, the research itself will no doubt have profound implications in society.

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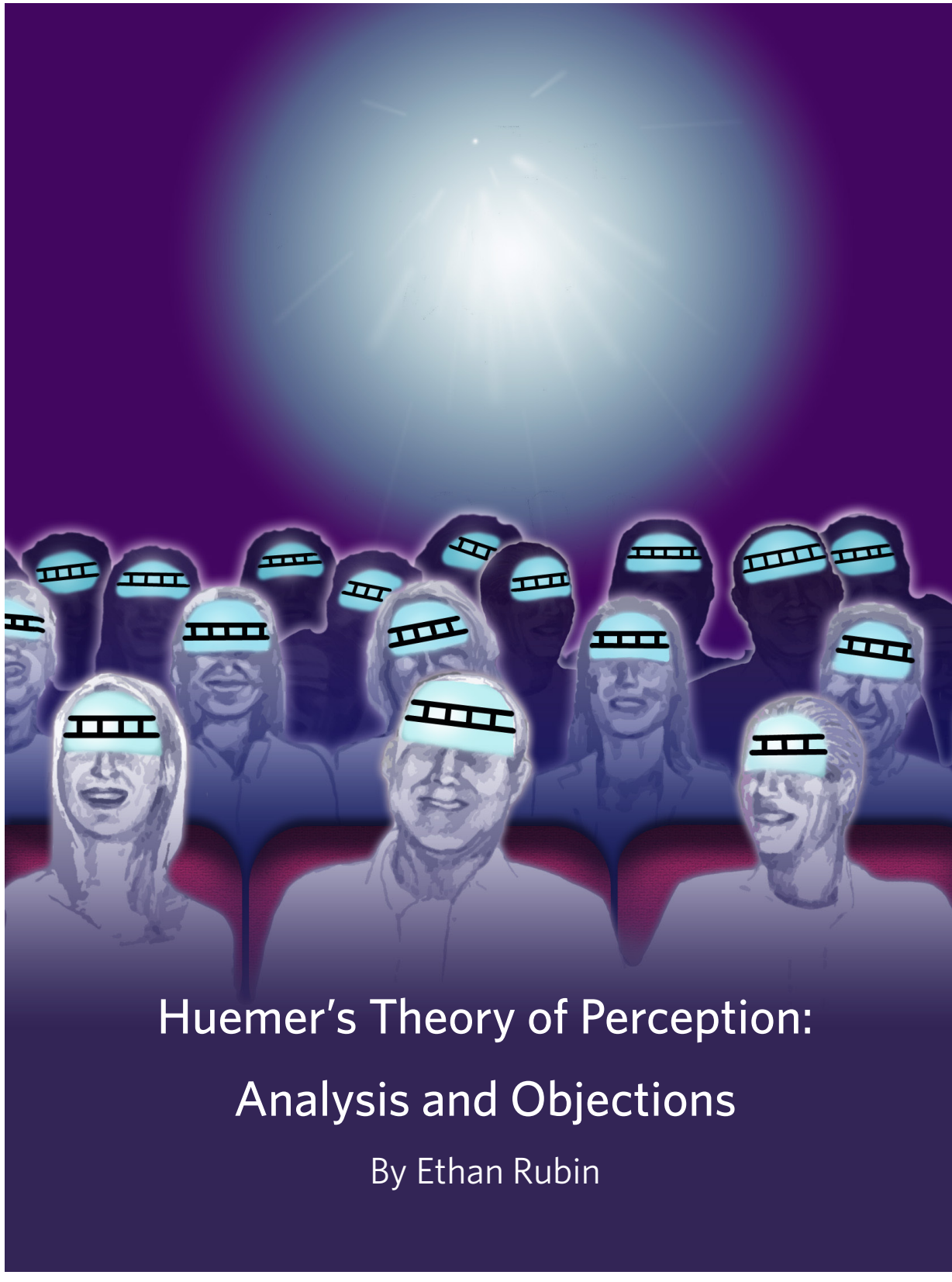

Huemer's Theory of Perception: Analysis and Objections

By Ethan Rubin

REVIEWS

In his book Skepticism and the Veil of Perception, Michael Huemer lays out an account of perception that supports a version of direct realism. He states two main theses: that perception is direct awareness of external reality, and that it leads to non-inferential knowledge of that reality. The second claim requires that the first be adequately defended, which is the goal of Chapter IV in particular. In this paper, I intend to map out Huemer's argument and assess its strengths and weaknesses; each section explaining a key point in his theory. After it has been explained, I will bring up objections to certain aspects of the theory as they appear in the text, and consider the most promising defenses against them.

Awareness requires an apprehension and a non-accidental correspondence between apprehension and object

Huemer's first task is to clarify his claim regarding direct awareness. He uses the term "awareness" in a technical sense, as the relation between one who is aware and the object of which he is aware. This establishes that one must be aware of something – if there is no object present, then there cannot be actual awareness. This excludes cases of hallucination from awareness.

Huemer claims that awareness must include a state of apprehension. He defines this term as a mental state of assertive representation. Not all mental states, he claims, have representational content (the example he uses is the sensation of tickling). Thoughts, desires, and perceptions, however, do have representation content, but represent their objects in different ways. Apprehensions are characterized by actualized representation, meaning that they represent their objects as being the case. He calls this characteristic the apprehension's assertiveness. Apprehension, therefore, must represent an object as actually existing, as opposed to representing it as a possibility or command.

Huemer also requires that the apprehension of an object at least roughly correspond to the nature of the object. He calls this "satisfying the content of the representation". By accepting the possibility of some deviation, he allows for certain common illusions, such as the appearance of a bent stick in the water. The correspondence between the awareness of the stick and the stick itself is close enough that the viewer can correctly identify it and describe it with reasonable accuracy. If the stick were perceived as a different object, such as a green kitten, there would not be enough correspondence between the apprehension and its object to consider the relationship awareness.

Huemer also stipulates that the correspondence between apprehension and its object cannot be accidental, stating that "the apprehension must have been formed in such a way, and under such conditions, as to make its correspondence with reality probable". For instance, if one were to hallucinate a particular scene while that scene coincidentally occurs elsewhere, he or she cannot be said to be aware of that event. Note that this scenario is unsatisfactory even if the correspondence is perfect. This sort of example highlights two problems with accidental correspondence: the apprehension is not of the true object, and the observer does not have sufficient reasons to believe that it is.

Direct awareness is unmediated

Huemer's theory hinges on the difference between direct and indirect awareness. In indirect awareness, he states, one's awareness is of x, but only by means of his awareness of something else. When driving a car, for instance, one is aware of the amount of gas left in the tank. This awareness is

indirect because it is based on the driver's awareness of the indicator needle on the dashboard, which he or she expects to reflect the amount of gas in the tank. Direct awareness, by contrast, is unmediated by such a secondary awareness. In order to be indirectly aware of something, one must first have a direct awareness of something else. Indirect awareness is a causal and logical relationship – one is led to reach the second awareness by a logical connection between it and the first. As such, it transmits the authority of the direct awareness to the indirect. This requires that direct awareness refer reliably to external reality.

Three Elements of Perception: a Perceptual Experience, an Object of Perception and a Causal Relationship

Having laid the foundation for his theory, Huemer turns to an analysis of perception. He identifies three major components of perception, each structured similarly to awareness. First, there is a purely internal mental state, which he calls the perceptual experience. Second, there is an object of perception, which is external and at least roughly satisfies the content of the experience. Third, there is a causal relationship between the two. The absence of any of these elements disqualifies the event in question from being perception.

The perceptual experience differs from perception as a whole in that it does not necessarily entail an external object. Because the experience is internal, it is not necessary that it be accompanied by an object. This is how Huemer accounts for hallucination. A perceptual experience does occur in hallucination, but there is no external object present. The perceptual experience still occurs because on an internal level, hallucinations are indistinguishable from genuine perception. This implies that they share a common mental state and that internal experiences should be recognized as separate from external objects of perception.

As in awareness, the object of perception must meet a standard of resemblance to the content of the perceptual experience. This standard allows for some discrepancies, but only to a point: when the experience represents the object as being fundamentally different than it is in reality, it can no longer be called perception. The content satisfaction criterion is present in other representations as well. A painting, for example, can diverge from its subject's appearance to a certain extent, but at some point it can no longer be considered a painting of that subject.

Huemer recognizes another sort of perceptual error that must be explained. It is possible to perceive an object in a manner that corresponds to the actual nature of the object and still mistake it for something other than it is. For instance, one might see a coil of rope and mistake it for a snake. To resolve this, Huemer introduces the notion of primary versus secondary perception. In secondary perception, the object is perceived by virtue of another perception: perceiving the coil of rope or the snake involves the same primary perception, as the same image is seen in both cases. The difference lies in the secondary perception, in which that same image is taken to be of different objects. The coil of rope is therefore seen as a snake. This sort of error is only admissible to a point, much like the case of illusion in primary perceptions. A mistaken secondary perception only arises from a primary perception that has a reasonable resemblance to the secondary perception; a coil of rope does have some visual resemblance to a snake. If someone were to mistake the coil of rope for a bear, there is a more serious error at work.

Finally, there must be a connection between the internal experience and the external object. Huemer proposes that the object must have caused the perceptual experience if the experience is of the object, thereby excluding coincidental correspondence. This causal relationship also must be direct; Huemer excludes what he calls deviant causal chains. If you were to have an accurate perceptual experience, but only because someone with the appropriate knowledge implanted the perception in your mind, it is true in a sense that the presence of the object caused the perceptual experience. The causal chain, however, has an intermediary link and is not perception.

Three Elements of Perceptual Experience: Sensory Qualia, Representational Content and Forcefulness

Huemer proceeds to subdivide the first component of perception, perceptual experience, into three features. He claims that a perceptual experience always has sensory qualia, which are defined as "what it is like" to have the experience. It also must have representational content, and that content must have forcefulness – the characteristic of seeming present and real. These components are notably similar to those of awareness.

According to Huemer, all experiences are accom-

panied by qualia; sensory qualia are those that correspond to perceptual experiences, as opposed to emotional or imaginative experiences. Qualia exist over and above representational contents, and are ineffable in that they cannot be explained to someone who has never had a comparable experience. Someone who was born deaf, for example, cannot understand what it is like to hear. This ineffability is not mystical or metaphysical, nor does it apply to common experiences and normal perceivers – two people with unimpaired hearing can describe sounds to each other effectively.

"...we have knowledge via perception, which is not the same as saying that all perceptual experiences constitute knowledge."

On Huemer's theory, perceptual experiences also involve representational content. He explains that "things appearing to be a certain way is not some further consequence of your experience; things appear a certain way by virtue of your having the perceptual experience itself". This assertion challenges theories of perception that ascribe appearances to an act of interpretation that takes place after the perceptual experience. For Huemer, representational content is an essential part of the experience. Consider the bent stick illusion: the stick is not interpreted as being bent. On the contrary, the experience represents it as being bent and the viewer interprets this appearance as an illusion. If interpretation determined the object's appearance, the illusion would only occur if the perceiver believes the stick is bent. But no normal perceiver would argue that the stick is bent, despite the fact that it appears to be so. The temptation to say the stick is bent is based on how the stick looks. Hence, this appearance must be an integral part of perceptual experience and independent from interpretation.

Representational content is crucial to learning because it represents the object of perception as something that actually exists. This evokes Huemer's description of assertiveness – a perceptual experience represents its content as actualized, or as being the case. It follows is that representational content is propositional. A perceptual experience expresses the proposition "it is true that object X is before me," which is a precondition for reaching conclusions regarding that object. This proposition leans on another, namely that "it is true that my perceptual experience portrays the external world with satisfactory accuracy."

Huemer is careful to point out, however, that propositional content does not necessarily imply conceptual content. Conceptual content, unlike representational content, is not an intrinsic property of an experience. A perception is the same whether the perceiver has concepts for all the objects, for only some of them, or for none at all. In fact, we cannot have enough concepts to address the nuance and variability of experience. For example, the concept "red" is insufficient to differentiate between the many shades of red that we perceive as being distinct. The use of demonstratives can address them because it has a pointing function, saying "I see it is that, or thus and so." This pointing does have propositional content, i.e. "it is true that I am perceiving that object, which is that way," but the perceiver does not have concepts for "that object" or "that way."

By rejecting the necessity of conceptual content, Huemer is not rejecting the possibility of conceptual content. He agrees that conceptual content exists and is capable of affecting perceptual experience. His point is that perceptual experiences can occur without conceptual content, implying that conceptual content is not an intrinsic or essential component of perception. He refers here to Wittgenstein's ambiguous "duck-rabbit". He admits that if one has the concepts of duck and of rabbit, the picture has the conceptual content of both duck and rabbit. If one only has the concept of duck, however, the picture will not have the conceptual content of rabbit. If the viewer does not have either concept, the picture has no conceptual content, but the viewer still has a perceptual experience. Perceptual experience can be altered by the inclusion of concepts, but it does not have to be conceptualized and does not depend on conceptual content.

The propositional, assertive nature of perceptual experience leads Huemer to his discussion of forcefulness. He begins by asking how imagining and perceiv-

ing differ. The two can have the same content – if one imagines a duck or sees one, the content is a duck in both cases. One possible difference is that a perceptual experience has more detail and precision than an imaginative one, but this difference can be overcome by focus and training, or by a photographic memory. Detail, therefore, cannot be the fundamental distinguishing factor between the two. No one confuses imagining with perceiving, because the latter represents its content as being actualized, whereas the former does not. Huemer calls this difference forcefulness. This should not be confused with Hume's concept of vivacity, which is more like the difference in detail that Huemer considers and discards. Hume's vivacity is merely a question of faintness or vividness, while Huemer's forcefulness contains an element of being present.

Why This Is Direct Realism

One could support the majority of Huemer's claims and still be a proponent of indirect realism by arguing that perception makes us aware of mental states that become knowledge by a secondary, non-perceptual process. Huemer, however, insists that we are directly aware of more than just mental states and that his theory of perception satisfies his definition of direct awareness. As he explained earlier, awareness consists of an apprehension, or assertive mental representation. His description of perceptual experiences accords with the definition of apprehension: perceptual experiences have forcefulness (making them assertive), qualia (making them mental) and representational content.

Huemer's theory fits the definition of direct awareness by stipulating a causal connection between the perceptual experience and the object of perception. Saying that awareness must be of something is equivalent to saying that it must be caused by its object. Therefore, asking what a perception is awareness of is also asking what causes the perceptual experience. Huemer maintains that only physical facts can satisfy the contents of perception and therefore must be their source. It makes no sense to say that mental states cause perceptual experiences because the contents of perceptual experiences are not present in mental states; mental states do not have the properties, such as shape, color and texture, which form the contents of perceptual experiences. He rejects brain states for the same reason; normal perceivers do not have the perceptual experience of synapses firing. Perceptual experience cannot be caused by mental or brain states because they do not bear resemblance to its contents. The visual (or auditory, olfactory, etc.) experience is first and foremost of the object one is experiencing.

Based on these arguments, Huemer concludes that perceptual experiences are directly caused by physical objects that have the attributes that the experience represents them as having. According to Huemer, it follows that "In the primary sense of 'aware'… we are directly aware of the fact that there are objects with those colors and shapes". That is, because our perceptual experiences are direct, the knowledge we gain from them is also direct. He attributes the opposing argument, which holds that knowledge of external objects is indirect because it is based on perceptual experiences, to a confusion between the object of awareness and the vehicle of awareness. This is clarified by the following analogy: one must use an axe to chop wood. He is not, however, chopping the axe, but is chopping the wood by using the axe – the wood is the object of the chopping and the axe is the vehicle, or means, of the chopping. Applying this to perception, the perceptual experience is the metaphorical axe that "chops" external objects. We cannot perceive an object without having a perceptual experience that represents it to us, but that experience is only a tool. The awareness is directly of the objects by means of perception, just as wood is chopped by the man using the axe.

To put it another way, we do not perceive our perceptual experiences. If awareness were based on perceptual experience, we would have awareness of external objects by perceiving experiences, but this is not the case. We perceive external objects by having perceptual experiences, not by perceiving perceptual experiences. The same goes for awareness: our awareness does not arise from being aware of an apprehension, but simply by having an apprehension. Perceiving perceptual experience or being aware of apprehensions requires a second order act in which one turns his attention to processes that occur whether or not he reflects on them. This is an extra step, requiring introspection and deliberate effort, not a constitutive element of perception.

Objection 1: How to Recognize Knowledge

Huemer fails to account for a practical problem in his theory. He admits that one must be capable of handling certain mishaps that tend to befall perception from time to time, but does not make any conclusive statements about how this is to be done. Hallucination and correctness by coincidence are problems that he needs to address more thoroughly.

His definition of awareness stipulates that it is a relationship and therefore must be of something. This condition excludes hallucination from awareness because one cannot have a relationship with something that does not exist. There is an obvious external difference between awareness and hallucination that makes them fundamentally distinct, but this does not suit Huemer's project. Since he is describing awareness phenomenologically, from the inside, he must account for how the perceiver himself understands his mental states. It makes sense to say that one cannot have a relation with a nonexistent object, but if he feels like he is in a state of awareness and cannot differentiate between his hallucination and a real object, it is unclear how the distinction is salient.

Huemer does admit that there is some irregularity in perception. His position is that we have knowledge via perception, which is not the same as saying that all perceptual experiences constitute knowledge. Even so, the fact that we cannot tell the difference between awareness and hallucination is problematic because it impedes knowing which experiences lead to knowledge. Huemer could argue that one is inclined to judge that an experience is hallucinatory when it does not accord with his expectations of reality, correcting for errors in perception after the fact, but this raises two problems. First, it is only a plausible solution if the hallucination is recognizably outlandish and depicts an "object" whose existence is improbable enough to make the hallucinator disregard his perceptual experience – remember that the mental state is the same in both perception and hallucination, the only difference being the presence or absence of the object. It is not implausible that one could have a mundane hallucination of an unsurprising object, or even an existing object that he had accurately perceived before. There would be no cause for suspicion and he would accept the hallucination as awareness. Second, inserting an act of judgment in the case of hallucination would leave Huemer open to the objection that such an act of judgment takes place in other cases as well. The mental state involved in hallucination is the same as that involved in perception – if hallucination is subject to review over and above the experience itself, normal perception must be subject to the same process of judgment. The inclusion of judgment in this context begins to stray dangerously close to indirect realism, which Huemer wants to avoid.

Similar arguments can be made regarding Huemer's demand for a direct causal connection between apprehension or perceptual experience and the object represented. The distinction he makes between an acceptable connection and an accidental or deviant one is once again external rather than internal. One example he uses of accidental correctness is that of calling a friend. *After the phone rings multiple times, one may conclude that the friend is not home. However, one could unknowingly have dialed the wrong number and not actually tested whether the friend was home or not. The conclusion may still be correct by coincidence and, by asking the friend whether he was home at the time, he can come to know that his conclusion was correct, and yet this does not qualify as awareness. The reasons why it cannot be awareness are clear to the third party reading the example, but the person in the example has no access to those reasons. There is no way for him to verify the relationship between his experience and his apparent knowledge.

A deviant causal chain presents the same problem. In Huemer's example, someone has a perceptual experience of a cup. A scientist has implanted an exact copy of the perceptual experience caused by the cup in the would-be observer's brain, with the result that the experience does correspond with the object it represents. The cup caused a perceptual experience in that it caused the scientist to implant that specific experience, but the subject cannot be said to have perceived the cup because the causal connection is too far removed. The reader has no trouble understanding why this is not perception, but the deceived character in the example cannot reach the same understanding. In light of these examples, causal connection seems like a dubious criterion. If one cannot distinguish between the causal chain of a genuine apprehension and that of an "apprehension" based on coincidence or deception, then one cannot use causal connection as a standard for accepting or rejecting his own experiences. It seems that Huemer owes us a better solution to the internal problems of recognizing knowledge.

Objection 2: Where to Draw the Lines

Huemer is satisfied with some ambiguities that should make the reader wary. By making provisions for rough correspondence between a perceptual experience and its object but disqualifying those that do not correspond enough, he commits himself to a spectrum that covers the entire range between exact resemblance and complete disjunction. At some point in this spectrum, experience ceases to be perception and becomes hallucination. Most readers would ask Huemer to indicate where this point lies. It is easy to make an absurd example that highlights the difference between the extremes – compare seeing a stick in water that appears bent and seeing a stick in the water that appears to be a green kitten. The closer we come to the middle of the spectrum, however, the more difficult it is to distinguish – compare seeing a stick in water that appears bent and seeing a stick in water that appears slightly more bent than the optical phenomenon accounts for. How much more bent can the stick appear before one is no longer perceiving the stick?

Huemer might respond that the spectrum is ambiguous by nature and that distinctions must address the case at hand and its context. This may be true, but there must be some general standard in place by which to make the distinctions in each case. Even if it highlights a vague section of the spectrum as the area in which experience begins to lose legitimacy, there should be some kind of criterion. Saying that acceptable cases "roughly satisfy" the representation and unacceptable ones "diverge radically" tells us very little about what qualifies and what does not. Despite the intrinsic fuzziness of the correspondence condition, Huemer could stand to do a better job of defining the spectrum and identifying the boundaries of perception.

He falls prey to the same pitfall in describing the deviant causal chain. He states that the causal connection between perceptual experience and its object must be close enough that the object directly causes the experience, but "directly" does not specify what qualifies. I had to suppress laughter upon reading the sentence, "I shan't enter into the question of how exactly one might define 'deviant causal chain'…." Huemer identifies direct causal connection as an essential component of perception, in whose absence perception cannot occur at all. A deviant causal chain precludes direct causal connection, meaning that the experience in question is not perception. Seeing as this is central to his theory, how can Huemer justify glossing over what a deviant causal chain is? He is obligated to specify what is deviant and what is direct – saying that the deviant chain is "convoluted and abnormal" replaces "deviant" with synonyms and does nothing to pin down what it means.

This problem could also be addressed by appealing to case-by-case decisions. For the most part, what Huemer means by a deviant causal chain is understood despite the absence of a precise definition. The objection incites a sort of Wittgensteinian reply, as in "you know what I mean, this is perfectly clear to you when the case arises." This solution works better here than it would for the previous objection. The resemblance condition must allow for a range of illusions and imprecisions, whereas the causal connection is a stricter requirement. The presence of virtually any intermediate cause between the experience and its object is sufficient to disqualify the causal chain, which makes it much easier to consider a case and decide that the relationship is not direct.

Objection 3: Unnecessary Components of Perceptual Experience

Huemer's analysis of perceptual experience does a good job of analyzing the various features that are present, but his insistence that they are separate entities may be misled. He claims that sensory qualia, representational content and forcefulness are all different components of a perceptual experience. Upon consideration, however, it seems that they are inextricably linked and cannot be disjoined. Rather than split up perceptual experience into three elements, it would be more accurate to speak of it as a single entity with features that account for its particular nature. Forcefulness, for instance, can be considered an element of representational content, as it is essential to and inseparable from perceptual experience. Without forcefulness, the experience is no longer a perceptual one: it is an imagination or a memory. This is because forcefulness is a feature of how the object of perception is represented to the perceiver, namely as being present. But Huemer had posited assertiveness long before he introduced forcefulness. Assertiveness is an essential aspect of representational content and lends immediacy to experience; seeing as assertiveness does the same work as forcefulness, there is no reason to tack forcefulness onto the end of the theory.

Sensory qualia are the most dubious of the components Huemer identifies. He begins his discussion with the disclaimer that their ineffability is not mysterious and must not be mistaken for "a resort to obscurantism and mysticism". This is not, however, the strongest objection against qualia. Even having accepted their ineffability as a characteristic of experience, the existence of qualia still seems superfluous. Because perceptual experiences are internal, as Huemer states, qualia could just as easily be an intrinsic characteristic of perceptual experiences without being a separate class of mental entities.

Huemer's point is that the representational content and the object that satisfies it are the same, but because there is some difference between the object and the experience, some "what it is like" to experience the object, qualia must exist. The function he attributes to qualia, however, can easily be included in the notion of representational content. Representational content represents an object as being a certain way to the perceiver. This is an aspect of his internal mental state and as such has the same ineffability as qualia; it represents the object as being "this way." As it represents the object to the perceiver, the perceiver experiences the representational content. How is this different from qualia, "what it is like" to perceive an object? The distinction implies that representational content is a component of perceptual experience that is not experienced in any particular way, which is absurd – "what it is like" for one to have a perceptual experience is what it is like to have its object represented to him. How else could representational content possibly function? There is no way that content could be represented to the perceiver except by his experiencing it, nor is there anything outside of his experience that he is aware of when he perceives something. The nature of representational content thus neutralizes the need for qualia to explain experience.

Huemer's explanation of the difference between red and red* (the quale) is based on a confusion. He states that "…red* is a property of experience, whereas red … is a property of physical objects". It is correct to separate these as properties of two different types, but the way in which he speaks of them is misleading. Red as a property of physical objects is not a color, but rather the tendency to reflect certain wavelengths of light. Color, on the other hand, is an experienced property. It would be more logical for red* to refer to the physical property of reflecting light and for red to indicate the color that is experienced. From this perspective, it is unnecessary to posit the existence of qualia because we no longer have the sense that the color we experience is something strange and illegitimate that must be explained away.

Upon asking whether there is any reason for qualia to exist or if they serve any purpose, Huemer exhibits more unintentional humor by responding "I do not know the answer to this", yet still insisting that they must exist. He offers two potential answers, neither of which is very convincing. First, he claims that the information obtained through perceptual experiences could not be represented without qualia. The very fact that he uses the word "represented" betrays his argument. He asks how we could perceive red without qualia and swiftly concludes that it is impossible, but it is perfectly plausible that we perceive red by way of representational content, which represents the object as being red, and therefore have no reason to posit qualia. Second, he asserts that qualia serve a conative function, expressing the pain or pleasure of an experience. There is no obvious reason why representational content should not perform this function as well, representing a warm experience as pleasant or a red experience as striking. He argues that qualia "simultaneously give us information about the world and give us emotional reactions or desires. Those two functions are integrated into the same experience, rather than being functions of two separate states or events". It is the purpose of representational content to give us information about the world; if the two functions are integrated, it makes more sense to simply assign them to representational content and discard qualia as redundant.

Objection 4: Sense Data and Representationalism

When he explains how his theory is a form of direct realism, Huemer makes a dangerous statement: "We might also be said to be aware (directly and primarily) of the colors and shapes of the (facing surfaces of) physical objects around us, since that could also be described as what satisfies the content of a state representing there to be objects of those colors and shapes". Although he describes this view as if it were only a trivial variation of his previous claim, it opens the door to a host of opposing theories that he wants to avoid. In particular, it allows for the possibility of a sense datum theory, which in turn implies representationalism.

He ends this section by saying "We must therefore conclude that direct realism is true". This conclusion

follows from his original claim that we are directly aware of the existence of objects, but it does not follow from the sense datum theory he implies in his second claim. According to the latter theory, we are directly aware of sense data, not objects. In order to have awareness of objects, one must undergo a non-perceptual process of judgment, forming a theory that infers the existence of objects from the sense data. Therefore, sense data do "satisfy the content of a state representing there to be objects", but they do not do so directly because the state is based on the sense data. By admitting the plausibility of this view, Huemer is in danger of committing himself to indirect realism.

The axe and wood analogy Huemer provides is clever and useful, but it does not grant him immunity from sense datum theory either. He intends the physical objects to be the "wood" and perceptual experience the "axe", but the analogy works equally well if we replace "physical objects" with "sense data." The argument would go as follows: We use perceptual experience as a tool that enables us to perceive sense data directly. As a consequence, we are aware of physical objects only indirectly. Huemer could object that sense data are also vehicles of perception, but his analogy betrays him again. If perceptual experience is the vehicle of perception, sense data must be the objects of perception. Once the sense data have been perceived, the analogy repeats: sense data become the vehicle by which we become aware of physical objects. At this point, however, awareness has already become indirect. In order to use them as means, one must first obtain the sense data as objects. When used as means, they are not vehicles of perception but rather of judgment – all the necessary perception has already occurred. Physical facts, in turn, become the objects of judgment and are thus distanced from the direct relationship with perception that Huemer wants to maintain.

Conclusion

For the most part, Huemer's theory is plausible and supports his theses. Objections one through three do have some validity but are not strong enough to falsify his system in general. Some can be defended against, while others can be reconciled to his account with only minor revisions. Of the first three, objection three is the most radical, but Huemer could address it easily. Neither the existence of qualia nor the independence of forcefulness is so central to his argument that his theory would be irreparably damaged by removing them, and all the phenomena they explain could be preserved in the updated account.

Objection four, if correct, deals a heavy blow to Huemer's original theses. Sense datum theory would rewrite his first thesis to say that perception is direct awareness of sense data. The second thesis would then have to be revised to say that we have indirect, inferential knowledge of the external world as a result of the sense data gathered by perception. Although Huemer only becomes explicitly vulnerable to sense datum theory at the end of the chapter, the rest of his account would not need extensive alteration to accommodate sense data.

If we replace his references to physical objects with references to sense data, we arrive at the following theory: perception consists of an internal mental state, an object that produces sense data in the perceiver, and a causal relationship between the mental state and the sense data. The internal mental state consists of the experiences of perceiving sense data (whether or not these are called qualia), whose contents represent patches of color as immediately present (whether or not this is called forcefulness). Therefore, perception is direct awareness of sense data, which leads to indirect knowledge of the external world by a process of judgment.

This is by far the greatest threat to Huemer's project – it challenges his central theses without contradicting the majority of his theory, making it difficult for him to argue against. One defense Huemer could mount is that we are not aware of any process of judgment between perception and awareness. If sense data require judgment to be seen as objects, why do we see objects in the world without having to reflect on them first? The task of filling the breaches in this theory, however, lies with Huemer himself.

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OPINION

Homemade Terror

"Fear is a tyrant and a despot, more terrible than the rack, more potent than the snake." ~ Edgar Wallace

"People react to fear, not love; they don't teach that in Sunday school, but it's true." ~ Richard M. Nixon

Who can forget the emotions that burst from the American psyche in the period following September 11, 2001? Bewilderment, despair, outrage, and a profound sorrow gripped our collective consciousness as we watched the symbols of our country crumble in dust clouds that only temporarily obscured the grim reality that waited to be unearthed. As America reeled from this traumatic blow, one reaction lingered like the scent of rotted meat. We became a nation united in fear.

The media splashed images, of snarling faces pledging our destruction, upon our mental canvases in what seemed like a nonstop delude. In the weeks following 9/11, we suffered from a campaign of terror launched not from overseas but from within our own borders. How much of this fear saturation was used to further economic and political agendas? Fear sells, and no one knows this fact better than media corporations and politicians. The Patriot Act, signed by President George W. Bush October 26, 2001, legalized roving wire taps, greater access to individuals' private records, and "sneak & peak" warrants. Most were willing to accept these policies, as long as they guaranteed their families could sleep safe from the ever present specter of terrorism.

On March 20, 2003 a Coalition force headed by the United States and England began an aptly named "Shock and Awe" bombing of Baghdad. These explosions heralded an invasion and eventual occupation that will continue into the foreseeable future. In the months of debate leading to the first strike, phrases such as Al-Qaeda and weapons of mass destruction were showered upon the American public. These buzzwords in conjunction with the color-coded terror threat levels, enacted March 11, 2002, pushed American anxiety into a post 9/11 frenzy.

A radio address given by President George W. Bush on March 22, 2003 proclaimed the following, "The people of the United States and our friends and allies will not live at the mercy of an outlaw regime that threatens the peace with weapons of mass murder. Now that conflict has come, the only way to limit its duration is to apply decisive force. This will not be a campaign of half-measures. It is a fight for the security of our nation and the peace of the world, and we will accept no outcome but victory."

America was ready to initiate war to secure the peace. But as allegations of deliberate twisting of information mounted, support for the war plummeted. According to a CBS News/New York Times poll the percentage of Americans who thought the "war with Iraq was worth the loss of American life and other costs of attacking" dropped

from 46% on August, 2003 to 24% on September, 2009. When the fear dissipated so did America's disregard for the costs of war.

What is it about fear that allows it to so drastically influence our thoughts and actions? Discoveries in Cognitive Neuroscience may hold some of the answers.

One of the most provocative findings is that emotional stimuli are processed automatically and subconsciously. Research by Dr. Kevin Ochsner and colleagues has found that emotional stimuli masked from conscious perception still resulted in an increased autonomic response (i.e. increased heart and respiration rate) and amygdala activation. The amygdala is an almond-shaped collection of nuclei found within the medial temporal lobe. The amygdala is thought to evolutionarily predate brain regions such as the neocortex (whose size and complexity separates human cognition from other animals'). From an evolutionary point of view, organisms that have an immediate and reflexive reaction to fearful stimuli (such as the odor of a predator) are more likely to escape threatening situations, and therefore more 'fit' than those who don't.

Images that inspire fear, such as the flaming collapse of the Twin Towers and Osama Bin Laden with threats streaming from his lips, can influence our behavior even when were not consciously paying attention to them. Think back to the months and years following 9/11 or to the period leading up to the invasion of Iraq. The media was pervaded with images and stories of terror. How much did this bombardment dictate our willingness to establish "the security of our nation" no matter the cost?

Luckily, there is research into how people cope with fear and anxiety. The consensus emerging from the literature is that the best strategy for regulating anxiety is reappraisal. Emotional states stem from our evaluation of an emotional situation's context and elements as they directly relate to us. Shark attacks are more fear inducing than car accidents because of the way we gauge the scenarios. By cognitively changing the way we interpret a situation, we can actively alter the way we feel about it.

Imagine you're about to deliver a speech in front of an audience (public speaking may be one of our biggest fears). You can feel your anxiety rise and heart race as you envision possibilities of failure and embarrassment. One way many combat this negative affect is through reappraisal. They tell themselves that they're not nervous - they're excited and that this excitement will lead to a better performance. They remind themselves that they have felt this way before and have still delivered. Reappraisal has been found to be more effective than both suppression and acceptance in regulating the negative aspects of fear.

If more people had stepped back and revaluated the information that was used to justify the invasion of Iraq, war may have been avoided. Maybe not. Either way, I am wary of those who would manipulate my innate fear response to influence my thoughts and behaviors. Are you?

— Darrien Garay

> "What is needed, rather than running away or controlling or suppressing or any other resistance, is understanding fear; that means, watch it, learn about it, come directly into contact with it. We are to learn about fear, not how to escape from it."
>
> ~ Jiddu Krishnamurti

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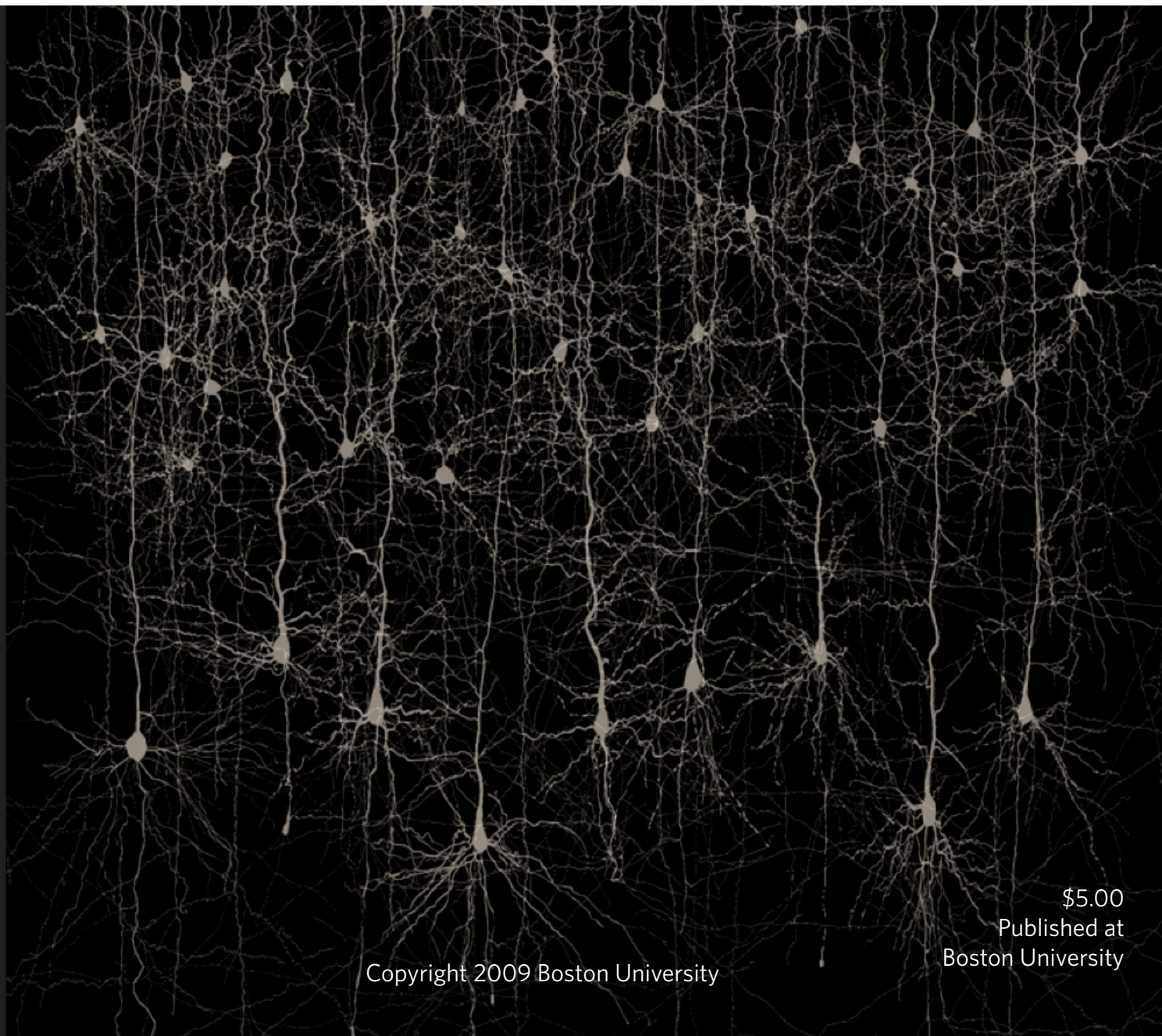

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