COLUMBIA SCIENCE REVIEW

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Demystifying Autism Spectrum Disorders Morbidity, Misconceptions, and Modern Diagnostics

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The Columbia Science Review strives to increase knowledge and awareness of science and technology within the Columbia community by presenting engaging and informative articles, in forms such as:

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Demystifying Autism Spectrum Disorders



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Be Careful What You Eat



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Cocktail Science 04 18 The Grand Feast of the Microglia

Front cover illustrated by Allison Cohen.

Cocktail Science



ard to focus on classes after | Thanksgiving? Then get a small green plant. A study conducted by Professor Tøve Fjeld at the Agricultural University of Norway found that workers who had plants on their desks were more productive and satisfied with their colleagues and employers than workers who didn't. Researchers believe this effect is due to chromotherapy, also known as color and light therapy. In another study, children who spent their breaks in a green and natural environment surrounded by trees and grass were happier and scored slightly better on tests than children who spent their breaks in other environments. These two plants should help students to be more productive:

- Rosmarinus: an evergreen perennial herb with a distinct smell that can wake up a student who has a homework assignment due tomorrow. To get the most of its smell, students can break off and guickly rub a small piece of it in both hands, and then inhale the aroma from their palms.
- Zamioculcas: also known as Zanzibar gem, it is another convenient perennial plant for students. It does not need much water because its roots retain moisture for a long time. Thus, it will not die, even if students forget to water it during finals.



emale choice, the process by which females choose mates, has been a controversial issue since Darwin's The Descent of Man and Selection in Relation to Sex. Primatologists have tried to explain why female primates mate with many males, instead of mating with the most genetically desirable. After all, there are many risks associated with promiscuous mating. The hypothesis that female primates mate promiscuously to prevent infanticide has the most support. In 2004, scientists Jerry Wolff and David Macdonald conducted a survey of 133 mammalian species. In 80% of these mammals, if the offspring of a female were killed, she would enter the estrous, or a fertile phase, thereby increasing her fitness. Promiscuous mating occurred in 62% of the primate species predicted to be susceptible to infanticide. According to anthropologist Sarah Hrdy, infanticide has been observed in 34 different primate species. When females mate promiscuously, they confuse paternity of the infant, while males are less likely to harm an infant if there is a chance that he sired it. For example, Japanese macaques were eight times more likely to attack an infant if they had not mated with the mother, than if they had. As psychologist James Kimmel remarks, "Among the primates, parenting behavior by males is rare...because primate mothers generally will not allow males to get very close to their newborn. The males of many primate species have been known to harm infants."



in medicine.



Dersonalized medicine, the concept that drug therapies should be tailored to patients' genetic or environmental conditions, has been receiving much attention from medical researchers and drug companies in recent years. Many of the technologies used in personalized drug research are tools developed by systems biologists for analyzing the available data on biological networks. In particular, systems biology applied to drug research considers disease as a defect that is amplified throughout a series of biological networks which include things like proteins, reactions, and chemical factors, all of which are interconnected. This concept of examining biological networks, rather than individual molecular interactions, stands in contrast to the traditional empirical approach used in drug development. As Professor van der Greef describes it, systems biology "aims to understand both the connectivity and interdependency of individual components within a dynamic and nonlinear system, as well as the properties that emerge at certain organizational levels." In a sense, physicians have long been personalizing medicine on a patient-by-patient basis. Indeed, all medical traditions have an inherent element of personalization that stems from the intimate nature of the physician-patient relationship. If anything, the new field of systems pharmacology is simply the application of a recent trend in biology towards a personalization process that has been occurring for quite some time

ice have been given the key to sustaining youthful memory by means of their own vital fluid. Researchers at Stanford University have demonstrated that infusing the blood of young mice into the brains of old mice can counter the agerelated effects of cognitive decline. This effect is believed to be related to the altered expression of several hundred genes involved in the cellular mechanisms behind learning and memory, as well as the appearance and strengthening of neural connections in areas of the brain where new connections are not usually formed. When subjected to tests of memory, the mice that received young blood significantly outperformed those that received old blood. While these mice provide compelling evidence for the connection between young blood and vigorous memory, the cause of this phenomenon within the sanguine fountain of youth itself remains a mystery.

Alexis Tchaconas Illustrations by Allison Cohen and Esha Maharishi

Demystifying Autism Spectrum Disorders: Morbidity, Misconceptions, and Modern Diagnostics

among children: more children are diagnosed with in the field in which he coined the term 'autism'. to simply as 'autism'), rarely do people stop and of ASDs is relatively new, ASDs have become in-Consequently, these overlooked details have led in this short time. In the sea of speculation and undevelopmental disorders, 'autism' as a developmen- claims backed by empirical evidence.

 Λ utism spectrum disorders (ASDs) are currently tal disorder only quite recently came into being in \square the most prevalent developmental disorders 1943, following Leo Kanner's pioneering publication ASDs each year than AIDS, cancer, and diabetes The pattern of incidence, however, suggests that combined. While almost everyone has heard about these disorders have gone unnoticed prior to their ASDs in the media over the past few years (referred formal identification. While the formal definition consider the historical evolution it has undergone. creasingly complex, widespread and misunderstood to the misconceptions that cloud understanding of known pathogenesis, a true understanding of ASDs the disorder and its prevalence. Despite the wide- is impeded by myth and misunderstanding. Perhaps spread acknowledgement of ASDs today as neuro- it is time to distinguish fact from fiction by pursuing

ASDs, synonymous with pervasive developmental studies used to back the statistics vary in sample disorders (PDDs), encompass a group of neurodevelsize and controlled parameters. The CDC says, "The opmental disorders organized as a spectrum, with complex nature of these disorders, coupled with a each ASD characterized by varying degrees of diflack of biological markers for diagnosis and changes ficulty with social interaction, communication (verbal in clinical definitions over time, creates challenges and non-verbal), and unusual, repetitive behaviors. in monitoring the prevalence of ASDs." A closer It is commonly thought that ASDs are emotional examination of the current diagnostic criteria that or mental health illnesses, but ASDs are biological classify certain behaviors as characteristic of each disorders affecting brain growth and development. ASD reveals the often overlooked, yet potentially There is truly no 'typical' ASD; the disorders are as exacerbating component of rising ASD prevalence: diverse as the population that they affect, ranging that autism is not necessarily more prevalent now widely in symptomatology and levels of functionthan before, but rather is identified more frequentality. Some incorrectly assume that individuals with ly. The combination of broadening the definition of ASDs cannot have social relationships, but one must ASDs, expanding the spectrum, and earlier diagnoses might account for these astronomical statisremember that at the high-functioning end of the spectrum is Asperger's Syndrome, an ASD in which tics: ASDs have become 10 times more prevalent people affected have normal development aside over the past decade, affecting 1 in 1000 children from sustained impairment in social interaction and (2000) to affecting 1 in 88 children today. repetitive behavioral patterns. At the other end of Biological research revealed that males and sibthe spectrum is Autistic Disorder, which includes in- lings of those with the disorder have a greater sustellectual disability, abnormal cognitive skills, and a ceptibility to develop an ASD. Thus, scientists have range of behavioral symptoms including hyperactivconsidered a genetic link to ASDs as the most promity, short attention span, and impulsivity. Upon anaising potential cause of the disorder. Environmental lyzing the worldwide population affected by ASDs, factors have also been implicated in ASD pathogenno correlation was found between ASDs and socioesis, the most popular theory pointing to the vaccine preservative thimerosal (a mercury derivative). economic factors, race, or ethnicity. Children diagnosed with an ASD have up to a 30% comorbidity The vaccine theory, however, has been widely disrate, and by adulthood often develop disorders such pelled as a myth because the use of thimerosalas epileptic seizures, Tourette syndrome, Fragile X free vaccines in the past decade has not correlated syndrome, and attention deficit disorder, among othwith a decrease in ASD prevalence. Unaffectionate ers. These observations suggest that more complex and unemotional mothers have also been a susfactors are influencing the incidence of ASDs, which pected environmental factor, as Dr. Bruno Bettel-

cannot be observed superficially. heim memorably referred to them as "refrigerator What exactly causes ASDs? That remains a mys- mothers" in the 1940s. The refrigerator mother thetery, but the statistics indicate prevalence of ASDs ory has since been rejected by doctors, who have has dramatically increased over the past decade. dissociated parenting from a child's ASD diagnosis. Currently, ASDs affect 1 in 88 children and are four The susceptibility to ASDs generally appears to be times higher in males than in females (1 in 54 boys strongly predetermined by a child's genetics more affected), as determined by an Autism and Develthan anything, with an overall heritability of 90%. opmental Disabilities Monitoring (ADDM) Network In fact, pediatric guidelines suggest that children population study. While the public is generally displaying the diagnostic criteria for an ASD be tested for genetic abnormalities, with a chromosomal aware that the prevalence of ASDs is escalating each year from media coverage, these numbers are microarray analysis (CMA) that detects clinically rarely explained or put in context. It is even more significant chromosomal abnormalities, and a DNA important to note that the definition of ASDs conanalysis for Fragile X syndrome (accounting for approximately 2% of ASD cases). The environment is tinues to include more symptoms and characteristic traits, a trend paralleling the increase in the dislikely involved in autism via epigenetics, or external order's incidence itself. Consequently, it is illogical factors that cause heritable changes in gene functo qualify the rise in ASDs as an "epidemic" when tion for regulating brain growth and neuronal comthe criteria for ASDs constantly expand, and the munication.

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Considering no medical test exists to diagnose ASDs, most diagnostic tests rely on parent reports and common "signs" of ASDs that specialists can recognize, including a lack of social or emotional reciimpaired use of nonverbal behaviors (eye contact, facial expression, body postures and gestures), and some degree of an intellectual disability. Diagnoses are subject to a medical professional's evaluation, and the family's recognition of these symptoms in the first place. A child's diagnosis starts in the household, then moves to the child's pediatrician, and is finalized through referrals to specialists for each symptom, including a speech pathologist for communication (to distinguish between typical and autistic speech), a psychologist for repetitive behaviors (evaluated via parent surveys and observations), and a behaviorist for socialization (who uses observational learning). For a medical opinion, psychiatrists, neurologists and developmental-behavioral pediatricians are often consulted to give the corresponding ASD affecting the child.

circumference (due to consistently larger head size among children with ASDs than controls) or perform an electroencephalogram (EEG) to detect abnormal brain waves, but both of these techniques are not recommended as routine screening tools unless the child presents dysmorphic traits or seizures. Neurologists and pediatricians often order a metabolic work-up, including urine and blood panels for heavy metal levels, organic acids, and celiac antibodies, to determine whether a metabolic disorder (biological errors in amino acid, carbohydrate, purine, peptide, and mitochondrial metabolism) is the cause of an ASD. Since metabolic disorders are at the core of an ASD in less than 5% of all cases, extensive metabolic testing is not recommended for standard practice unless physical abnormalities are observed. Unfortunately, clinical experience suggests some neurologists and pediatricians order EEGs and other methods not recommended for routine ASD evaluation-perhaps in the interest of thoroughness and because of medical-legal concerns or other nonclinical considerations.

Since a singly effective treatment technique for ASDs has yet to be identified, some parents pursue complementary and alternative (CAM) therapies to treat a child on the spectrum, using nonconventional "natural" methods such as modified diets (i.e. gluten-free, casein-free), food supplements (i.e. omega-3 fatty acids), and special exercises (i.e. yoga and tai chi). While these methods are easily accessible procity, stereotyped and repetitive use of language, and perhaps more psychologically comforting for parents given these therapies' less invasive nature, there is currently no scientific evidence to support the efficacy of nonconventional therapies. Thus, the majority of therapies used are those deemed conventional, or backed by years of research/implementation and physician recommendation, which include educational techniques (i.e. Applied Behavior Analysis), sensory therapies (i.e. art and music), and medications (i.e. Adderall and Clonidine).

Current research suggests that ASD diagnosis and treatment can begin as early as when the child is six months old. The formal diagnosis of autism cannot be confidently made until a child is two years old, but identifying autistic tendencies (i.e. fixation with objects, no eye contact, and delayed language formation) from as early as when the child is six months final, holistic evaluation of the symptoms and the old may be an important first step to slow (or potentially stop) the development of ASDs. A recent Neurologists will often measure a child's head study published in the journal Pediatrics is the first

to provide data supporting the assumption that the earlier the intervention, the less severe the autism. Psychologists Sally Rogers, Geraldine Dawson, and colleagues developed the Early Start Denver Model (ESDM) in 2009, a novel developmental-behavioral intervention which was the first method to proactively target children that are "at risk" for developing an ASD. The ESDM is an accessible therapeutic method done entirely in the household, with families observing their child's everyday behaviors, which could reveal a predisposition for an ASD (as per exhibiting behaviors within the diagnostic criteria). The pioneering study tested two groups of children with ASDs of comparable initial severity over two years, treating one group with ESDM, and the other (control group) with typical community interventions (i.e. speech and language therapy, occupational therapy). Children in the ESDM group exhibited significant improvements in IQ, cognitive ability, and adaptive behavior over the two years of intervention based on these measures, when compared with the control group (which displayed more severe delays in adaptive behavior than their ESDM-treated counterparts). Following the two-year evaluation, children in the ESDM group were significantly more likely to improve

Until the cause(s) of ASDs are identified via empiritheir diagnosis from autistic disorder to the milder cal evidence and specific methods are developed to PDD-NOS, compared to the children in the control target these causes, early diagnostics are the most group. If replications of this experiment yield similar effective means of tackling ASDs. In the meantime, results, the ESDM may very well be the future of it is important to sort through the out-of-context detecting and treating autism. framing effects from media portrayal of ASDs that By implementing a method of early intervention have detracted from a true understanding of these prior to a formal diagnosis of autism, a child at risk extremely diverse, yet interrelated disorders. In the for developing an ASD may improve in basic cognitive coming years, continued ASD research efforts will functions and have a decreased chance of developing hopefully reconcile the competing genetic and enan ASD. In fact, according to Professor David Manvironmental theories of ASD etiology, armed with more longitudinal data and empirical evidence. With this knowledge, the increased prevalence of ASDs can become more representative of actual incidences rather than merely expanded classification criteria. Given the continued increase in ASD prevalence, it is likely that ASDs were always present at such a high rate, but went unnoticed until changing times and lifestyles amplified ASD phenotypes, and consequently our interest in them. Sustained scientific investigations of ASDs are crucial in understanding the spectrum of implications that lie ahead, from the economic pressures of rising treatment expenses, to necessary changes in social dynamics at schools and in the workplace to accommodate individuals with ASDs. 🕸

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dell, proactive therapies could be "preventing a certain proportion of autism from ever emerging." Such an idea dispels another common misconception: that a child once on the autism spectrum will always be on the spectrum. If a child displays autistic tendencies during the diagnostic frame prior to three years of age, children can very likely fall off the spectrum if these tendencies are directly targeted via early intervention

Did Fermat Ever Prove His Last Theorem?

Joanna Diane Caytas Illustration by Allison Cohen



n 1637, Pierre de Fermat scribbled in there exists a solution (x,y,z), and to find L the margin of Diophantus' Arithmetica a way to produce another solution (x',y',z')what later became known as Fermat's Last from (x,y,z), with x',y',z' positive and z' < z. Theorem

"It is impossible to separate a cube solutions: $(x_1, y_1, z_2), (x_2, y_2, z_2), \dots, (x_r, y_r)$ into two cubes, or a fourth power into z)... with $z_1>z_2>z_3>...>z>...$ However, since two fourth powers, or in general, any each z is a positive integer, this list must power higher than the second, into two end and thus cannot be infinite. This is a *like powers. I have discovered a truly* contradiction, and hence there is no such marvelous proof of this, which this margin solution. is too narrow to contain."

Or, equivalently: There do not exist Diophantine equation (in which the only positive integers a, b, and c such that a^n + allowed solutions are integers) $x^{4+}y^{4}=z^2$ $b^n = c^n$ for any integer n greater than two. has no pairwise coprime solutions (i.e.,

However, the name Fermat's Last solutions where the greatest common Theorem is quite misleading for two divisor of each pair of x, y, z is 1). The proof reasons. Firstly, it was certainly not the last is as follows: of Fermat's theorems, as he had a fruitful career lasting another 28 years. It wasn't coprime solution (x,y,z) to the equation even the last statement Fermat wrote in $x^{4}+y^{4}=z^{2}$. If we let $a=x^{2}$, $b=y^{2}$, c=z, then it's the margins of Arithmetica. Secondly, easy to see that $a^{2+}b^{2} = x^{4+}y^{4} = z^{2} = c^{2}$, Fermat's Last Theorem was no theorem i.e. $a^{2+}b^{2}=c^{2}$, and hence (a,b,c) is a primitive at all. Since its statement lacked any Pythagorean triple. By the properties proof, it was merely a conjecture. This was of Pythagorean triples, necessarily a=st, consistent with Fermat's annoying habit $b=(s^2-t^2)/2$, $c=(s^2+t^2)/2$ for some odd of not providing proofs for his statements integers s and t (relatively prime) and but instead sending them as challenges to s>t>0. Since s and t are both odd, $a=x^2=st$ is his colleagues. It became known as the an odd square, which has the property that "last" one because its generalized proof $st \equiv 1 \pmod{4}$, i.e. $s \equiv t \pmod{4}$. had escaped mathematicians for a full (From $b = y^2 = (s^2 - t^2)/2$, we get 358 years.

But could Fermat actually have found a being odd numbers, then $(s-t) \equiv O \pmod{4}$, valid proof of his statement?

The original statement of Fermat's only 2 as a common even factor.) Thus, Last Theorem was handwritten next to (s+t)=2z, for some odd number z. From a problem based on the Pythagorean $s \equiv t \pmod{4}$ we know that 4 divides Theorem. Perhaps significantly, while (s-t), but we also know that $(s-t)(s+t)=2\gamma^2$. Fermat challenged other mathematicians For this to work, we need $s+t=2u^2$ and to prove his theorem for cases of n=3 and $s=t=4v^2$ for some relatively prime integers n=4, he never again mentioned a general u, 2v. From this we obtain $s=u^2+2v^2$ and statement "for any integer value of n $t=u^2-2v^2$, which gives us $x^2=st=u^4-4v^4$, i.e., greater than two." In fact, the n=4 case $x^{2}+4v^{4}=u^{4}$. can be deduced from the only surviving Now, we repeat the process: let A=x, proof known to be written by Fermat $B=2v^2$, $C=u^2$. Then $A^2+B^2=x^2+4v^4=u^4=C^2$, himself. Using his own method of infinite so (A,B,C) is again a primitive Pythagorean descent, Fermat showed that the area of triple. Therefore, we can find odd integers a right triangle with integer sides can never S and T that are relatively prime such that equal the square of an integer. In modern x=A=ST, $2v^2=B=(S^2-T^2)/2$, $u^2=C=(S^2+T^2)/2$, notation, this is equivalent to showing that so that $4v^2=S^2-T^2=(S-T)(S+T)$. Thus, the equation $x^{4}+y^{4}=z^{2}$ has no solutions in $S+T=2X^{2}$ and $S-T=2Y^{2}$ for some X, Y. positive integers x, y, and z.

The idea of the proof is to assume that Substituting and solving for u^2 , we obtain

Iterating, we obtain an infinite number of

With more details, we can say that the

Let's assume that we have a pairwise

 $2y^2 = (s-t)(s+t)$. Since $s \equiv t \pmod{4}$ with s,t $(s+t) \equiv 2 \pmod{4}$, so (s-t) and (s+t) can have

From this we obtain $S=X^2+Y^2$ and $T=X^2-Y^2$.

 $u^2=(S^2+T^2)/2 = X^4+Y^4$. And with that, we in positive integers. Euler proved this $a^{4}+b^{4}=c^{4}$ can be written as $a^{4}+b^{4}=(c^{2})^{2}$.)

here to prove this special case of his Last for every n>2. In 1955, Yutaka Taniyama Theorem, involves simple techniques. This and Goro Shimura worked on elliptic is not surprising as during Fermat's lifetime, curves ("doughnut-shaped" curves of the even basic calculus was only just about form $y^2 = x^3 + ax + b$, with *a*,*b* constant) and to be invented. René Descartes developed modular forms (special objects displaying analytic geometry in his 1637 treatise La extremely high symmetry and complexity). Géométrie, in which he also introduced Further developed by André Weil, the algebraic notation. Évariste Galois, born 1971 Shimura-Taniyama-Weil Conjecture in 1811, laid the foundations of abstract (better known as the Taniyama-Shimura algebra, Galois theory and group theory, Conjecture) linked elliptic curves with the night before his 1832 death in a duel. modular forms: all elliptic curves over While Fermat communicated regularly Q (the field of rational numbers) can be with mathematicians of his time, he based parametrized by modular functions and his studies on the works of the ancient be said to be modular. More formally, the Greeks and of François Viète, the creator Taniyama-Shimura Conjecture says that of New Algebra, who had only introduced given an elliptic curve $y^2=Ax^3+Bx^2+Cx+D$ some basic algebraic notations to simplify over Q, there exist nonconstant modular mathematics, such as using letters as functions f(z), q(z) of the same level parameters in equations. Viète did not yet N such that $f(z)^2 = A q(z)^3 + B q(z)^2 + Q(z)^3$ use the multiplication sign or the equality C q(z) + D. In 1985, Gerhard Frey made sign. No wonder, then, that the original a connection between the Taniyamastatement of Fermat's Last Theorem was Shimura Conjecture and Fermat's Last descriptive rather than symbolic.

apparatus available to Fermat, later to the Conjecture. In particular, Frey mathematicians tried to prove his deceptively showed that if $a^{p+b^p=c^p}$ is a solution to simple statement for years with no success. Fermat's Last Theorem, the associated After 200 years, all but one of Fermat's Frey curve is $y^2 = x(x-a^p)(x+b^p)$, with a,b,c as conjectures were proven, and in some cases nonzero relatively prime integers and p as disproven, mostly by Leonhard Euler. Only an odd prime. This would form a special Fermat's Last Theorem remained elusive semistable elliptic curve over the rational because mathematics still lacked adequate numbers Q which could not possibly be tools. But with continued evolution in the modular. Therefore, if the Taniyamafield of number theory, scholars were able Shimura Conjecture could be proven, then to chip away at his general statement by all elliptic curves over Q must be modular, proving more special cases.

the equation $x^{p+}y^{p=}z^{p}$ has no solution Theorem.

have found a new solution (X, Y, u) to the for p=3, Dirichlet and Legendre for p=5, equation $x^{4+}y^{4}=z^{2}$. Substituting back our and Sophie Germain for a few special variables, we find that $z=(s^2+t^2)/2=u^4+4v^4$, cases of p. After the establishment of hence u < z, as required. (The statement the Wolfskehl Prize in 1908, interest in proven above, "the equation $x^4+y^4=z^2$ has Fermat's Last Theorem was spurred to the no solutions in positive integers x, y, and extent that over a thousand false proofs z," is stronger than Fermat's Last Theorem were produced within four years. By 1993, for the case n=4, since the solution (a,b,c), using computers, Fermat's Last Theorem was shown to be true for $n \le 4,000,000$. Fermat's method of infinite descent, used But there was still no general proof Theorem: a counterexample to Fermat's Realizing the limited mathematical Theorem would be a counterexample and hence, there could not possibly For example, the n=4 case settles the exist a counterexample to Fermat's Last cases for *n* divisible by 4, i.e., 4/*n*. Also, Theorem. In other words, any proof for since *n* can be factored into primes, it is the Taniyama-Shimura Conjecture would enough to show that for each prime p>2, equate to a proof for Fermat's Last

Until then, Fermat's Last Theorem had pages worth of conference proceedings. not been considered an important problem Nonetheless, it was still not possible to by modern mathematicians. However, include all the results employed in Wiles' the link between the Taniyama-Shimura proof, many of which required entire Conjecture and Fermat's Last Theorem separate books for explanation. However, showed that the latter was not merely the 600-page publication included some a mathematical curiosity, but contained of the far-reaching consequences of the important information on the properties Taniyama-Shimura theorem, which became of space. Although many considered the essential for the development of modern Taniyama-Shimura Conjecture unprovable mathematics. by current tools, Andrew Wiles, a British mathematician with a passion for Fermat's Last Theorem in 1637? It would imply problem dating back to readings as a 10-year- that he somehow pre-empted 350 years' old boy, took up the challenge. After six worth of work by hundreds of the best years of work in the complete seclusion of mathematicians in multiple fields, including his attic, Wiles presented a 200 page-long group theory, Galois theory, theory proof of the Taniyama-Shimura Conjecture of modular forms, theory of elliptic at a 1993 conference in Cambridge. This equations, Riemannian topology, crystalline proof provided the last missing link to homology, L-functions, Galois cohomology, prove Fermat's Last Theorem. At the time, and Gorenstein rings. Or could Fermat, as only a handful of mathematicians were inveterate enthusiasts insist to this day, able to grasp Wiles' proof, which borrowed have found some elegant trick requiring techniques from various areas of cutting- only today's middle school mathematics? edge mathematics. Still, peer review Such an assumption would assume a true revealed a mistake in the proof that used an α quantum leap in porcine aviation. Euler system developed in 1993 by Victor Kolyagin and Matthias Flach. Unwilling to let his life's work be claimed by others, Wiles refused to let the faulty proof go public so others could amend its shortfall. He worked one more year on a solution with his former student, Richard Taylor, and found it using horizontal Iwasawa theory that he had abandoned prematurely years earlier. Wiles' final October 24, 1994 version of the proof ran 108 pages and established the

Mathematician Joseph Silverman summarized Wiles' proof as follows: Let $p \ge 3$, p prime. Suppose there exists a solution (a,b,c) of $a^{p+}b^{p-}c^{p}$, with a,b,c in Z and qcd(a,b,c)=1. Let E_{ab} : $y^2 = x(x+a^p)(x-b^p)$ be the Frey curve. By Wiles' Theorem, E_{ab} is modular (its *p*-defects *a* follow a Modularity Pattern). But by Ribet's Theorem, E_{\perp} is so strange that it cannot be modular. Therefore, $a^{p+b^{p}=c^{p}}$ cannot possibly have nonzero integral solutions.

modularity theorem for semistable curves.

Efforts at making the result accessible to the mathematics community resulted in a ten-day conference in 1995 and 600

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Could Fermat possibly have proved his



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Be Careful What You Eat Laura Yf

Illustration by Vangle Shue

With companies like Whole Foods and Trader Joe's children had an allergic reaction to Eggo Waffles and was shocked to find that peanut allergies doubled from 1997 cially in the United States, are becoming more interested in where their food comes from. These markets sell organic foods targeted to health-aware consumers, but what about other foods? Processed foods, like cereal and ramen, are polar opposites of organically grown foods. Organic foods are grown in adherence to guidelines determined by the Organic Trade Association to develop long-term environmental approaches to food production. Though studies conflict on whether organic foods so that they can tolerate high amounts of weed killer. are nutritiously superior to conventionally grown foods, consumers are often caught between deciding whether the high cost of organic foods offset the long-term environmental benefits. On the other hand, processed foods are usually manufactured, canned, or preserved. They are treated to remove pathogens and to prevent food countries like Australia, Japan, Canada and all of Europe spoilage. Thus, processed foods contain high amounts of sodium, which, upon consumption, may lead to negative O'Brien further elaborated on how the milk industry health effects like high blood pressure. The long-term effects on people who consume processed foods are surprisingly deleterious.

try and conducted by a University College London team examined 3,486 civil servants in the United Kingdom produce our milk. Once again, other countries refused to and discovered a correlation between the consumption of processed foods and depression. Subjects whose diet because they weren't proven safe. comprised mostly of processed foods developed depression at a higher rate. Another study in the Journal of Clinical Investigation conducted a controlled experiment on rodents. Scientists fed rodents a high-fat diet and upon examination, found that the diet had led to brain scarring and damage to the hypothalamus. The hypothalamus is the part of the brain that controls body temperature, Even Birke Baehr, an 11-year-old who has decided to beage to the hypothalamus distorts the brain's perception of what the body really needs, and instead, leads to seems to me that we can either pay the farmer or pay the reaching for another hamburger instead of vegetables to hospital," he said, in a TEDxNextGenerationAsheville talk. satisfy hunger cravings. The same study discovered that the brain's Proopiomelanocortin (POMC) cells were reduced by 25 percent. POMC cells regulate the body's fat control system, suppress appetite, and prevent excess weight gain. Inflammation, also known as neuron injury, consuming fatty foods and refined oils.

industry analyst and Fulbright grant recipient, further examined the nation's food supply after one of her four

to 2002. In a TEDxAustin talk, she divulged her findings about the food supply after authoring The Unhealthy Truth: How Our Food Is Making Us Sick and What We Can Do About It. In her book, O'Brien discusses genetically modified organisms used in food production and eventually consumed by the average grocery shopper. New types of proteins are engineered into seeds and these seeds are planted and grown for food. Soy plants were engineered Corn plants were engineered so that they release their own insecticides. According to O'Brien, none of these proteins were tested on humans to see if they were safe. "We took a different approach. We said it hasn't been proven dangerous, so we'll allow it," she said, while other rejected these crops because they were not proven safe. boosted profits by engineering proteins and synthetic arowth hormones to be injected into cows to increase milk production. However, these same chemicals caused A study published by the British Journal of Psychia- ovarian cysts, mastitis and skin disorders, to name a few, leading to an increase of antibiotics use in animals that introduce these chemicals into their dairy and milk supply

Data on cancer rates in the United States are supporting O'Brien's claims that these proteins are harming our health. People in the United States have the highest rate of cancer in the world. Within the U.S., one in three women is diagnosed with breast cancer, but only one out of ten breast cancer incidents are due to genetic causes. hunger, thirst, fatigue, sleep, and circadian cycles. Dam- come an organic farmer, recognizes that the money saved from not buying organic foods is used on healthcare. "It

What exactly are processed foods made up of? Steve Ettlinger set out to seek an answer to this guestion, in his book, Twinkie, Deconstructed. Ettlinger settled on the Twinkie because it is the "archetype of processed foods," he said in an interview with the New York Times. was also found in rats and mice only three days after He learned that processed foods in the United States are part of an industrial complex he dubbed the Twinkie In-Robyn O'Brien, former Wall Street financial and food dustrial Complex. Processed food ingredients are made from common industrial chemicals, like ethylene, which comes from natural gas, phosphoric acid, and sulfuric



acid. According to Ettlinger, phosphoric acid, though a sumed blue Gatorade, Top Ramen and gummy bears. The common food-processing ingredient, is mined in Idaho and other group took the SmartPill and consumed hibiscus stored in a spherical tank in the Midwest due to its po-"Gatorade," a natural version of Gatorade made by mixtential danger. While phosphoric acid is considered a weak ing hibiscus tea with a small amount of sugar and salt, acid, sulfuric acid is a strong acid that readily dissociates homemade chicken stock with handmade noodles made in an aqueous solution. Ettlinger claims to have a Twinkie from water, salt, flour and eggs from the local farmer's from 2005, and according to him, old Twinkies become market, and gummy bears made from pomegranate and solid but do not spoil. For research purposes, Ettlinger cherry juice. Bardin's video mainly tracks the passage also made his own Twinkie from scratch with yellow cake of the noodles, and it is important to note that the and cream filling from whipped cream with sugar and vagastrointestinal tract of subjects in the first group is nilla. "I wrapped one in plastic wrap and put it aside, and already stained blue from the blue Gatorade. Bardin exit was solid green in a week," he said. The shelf life of plains that the recipes for artificial flavors and color-Ettlinger's homemade Twinkie was nothing compared to ings used in products like blue Gatorade are considered that of an actual Twinkie. intellectual property, so manufacturers are not required Stefani Bardin, a TEDxManhattan 2011 Fellow, took a to report their ingredients. After two-and-a-half hours inside the gastrointestinal tract, Top Ramen noodles' shape was still intact whereas the handmade noodles became an unrecognizable mass. "That's because Top Ramen is made to survive Armageddon. Our homemade ramen noodles are made to be eaten," said Bardin.

different approach in researching processed foods. Along with Dr. Braden Kuo at Harvard University, she developed a SmartPill capsule with sensors that measure the pressure, pH and temperature of the gastrointestinal tract. They also developed the Mouth 2 Anus, or M2A, a device that is equipped with a camera and wireless trans-College students have many choices in what they can mitter that sends images to a receiver pack worn by the choose to eat, whether it is a burger and fries from Five subject. With the SmartPill and M2A, Bardin and Dr. Kuo Guys or a salad from Westside Market. The next time you studied the body's consumption of processed foods and head over to the vending machine for a guick fix, think about organic foods. One group took the SmartPill and conwhat you're putting into your body and if it's worth it.

Fuel Efficiency and What It Means

Andrew Sumner Illustration by Evelyn Warner



 \Box rom the household to the global media, "fuel efficiency" of C₂H₁₆ to C₁₁H₂₄ and other additives that has been modi-I has become an important phrase in casual conversation as fied over time to maximize heat of combustion and minimize well as political platforms. Today, oil supplies are not only health hazards. As an estimate, gasoline contains about 36.6 scarce but also tied to deep international conflicts, and the kWh/US gal) (higher heating value) or 13 kWh/kg, and across effects of fossil fuels continue to deeply tax the environment. the industry, this value is expected to differ by approximately However, the necessity of transportation in everyday life per-4%. However, gasoline on its own can only be modified so far. petuates our dependence on oil, and so the engineers of our Efficiency, commonly represented by gas "mileage," is also a generation have taken on the task of designing cars than can function of gas use as well. On a highway where a constant run better on less and cleaner fuel. Although anyone casuhigh speed is maintained, engines burn gasoline much more ally tossing around the phrases "fuel efficiency" or "fuel econefficiently, whereas in the slow, stop-and -go traffic of cities omy" may have a general concept of fuel efficiency's goals gasoline is used very inefficiently. Thus, hybrid cars have been and effects, the actual meaning of "fuel efficiency" is not well designed to capitalize on this highway vs. urban road disparunderstood . What exactly does fuel efficiency mean, and in ity by switching between electric and gas power when one is what ways can it be improved? Without going into heavily rigmore effective than the other. Biofuels such as ethanol fuel orous detail, fuel efficiency can be better understood in terms have also been put to use. These fuels, although less energy of how favorable qualities in fuel and car design actually make efficient than gasoline, are a renewable resource and burn far more cleanly than gasoline. In these ways, the effectiveness a vehicle more efficient. To define fuel efficiency, we will begin with the basic com- and cleanliness of gasoline are constantly pushed closer to bustion of hydrocarbons. The general formula for a combustheir upper bounds.

tion reaction is the conversion of a hydrocarbon "fuel" and the complete combustion of methane gas is shown below.

$CH_4(q)+2O_2(q) \rightarrow CO_2(q) + 2H_2O(l)$

products are of lower energy than the reactants and a net fuel, engines convert this released heat into mechanical energy and use it to power cars and various modes of transportamore useful for different engines and tasks.

of fuel consumed - i.e. kilojoules per mole. The simplest heat sumes that the water generated is a liquid; this is called the est designs could be added to more economical cars. "higher heating value." In reality, the high temperatures in most heating value" is more accurately used, which subtracts away the heat of vaporization. Furthermore, this model is complicated by the competing reaction of "incomplete combustion." Inresult is the production of carbon monoxide rather than carbon of combustion - each kilogram of CO formed means a loss of 5654 kCal of heat - but the subsequent products, carbon monoxides and nitrogen oxides, are often hazardous for society and even CO₂) emissions, and suitability for car engines.

line, a complex mixture of hydrocarbons ranging from chains or with electric/biofuel cars. 🕸

Although efficiency of fuel has the most command over gas oxygen into carbon dioxide, water, and heat. The formula for mileage, efficiency of exterior design also has power over the ability of a car to run on less gasoline. As fuel is modified to give the best possible energy yield, automobile design allows cars to travel even further with less energy. Newton's second law dictates that acceleration is inversely related to mass; thus This reaction is characteristically exothermic, meaning the lightweight cars require less energy and less fuel to accelerate. Furthermore, non-conservative frictional and drag forces, amount of heat is released. By controlling the combustion of which can be detriments to a car's acceleration and cause gas mileage to suffer, may be minimized with better tires and more streamlined features, respectively. However, despite the tion. Most fuels draw from this basic combustion mechanism remaining room for improvements with today's cars, these enand yet each has different burning qualities, making some fuels ergy saving features also have limits. Although some cars have gotten smaller in order to improve gas mileage, the popularity The effectiveness of a fuel can be quantified by its "heat of SUV's and other over-sized vehicles has led many to quesof combustion" or the amount of energy released per amount tion the safety of driving a relatively smaller car that would be vulnerable in a collision. Furthermore, expenses play a role in of combustion considers only the above formula and thus as- whether or not the highest end lightweight materials and sleek-

In the end, a balance must be struck between cost, safety, engines convert all of the water to vapor, thus the "lower and design. Meanwhile, the improvements that can be made to fuel efficiency are reaching their limits. Despite the progress that cars have made so far in fuel efficiency, the scarcity and harmfulness of gasoline are increasing much faster. Rather complete combustion occurs with oxygen deficiency, and the than focus as much on miles per gallon, perhaps overall gas usage should be decreased instead? A study made by the Jourdioxide. Not only does incomplete combustion lower the heat nal of the American Planning Association found that America specifically lags behind other countries in gas consumption versus population density in urban areas, showing that better urban planning may be a way to get more cars off the road. the environment (Smith). With these requirements and issues Higher population densities, strong urban centers, and physical in mind, engineers have sought to perfect fuels by finding the planning agencies in general have been shown to have a higher best balance between a high heat of combustion, low CO (and effect on reducing gas emissions by getting more cars off the road. The best solution lies not in the efficiency of our fuel, The result of engineers efforts thus far is today's gaso- but the elimination of it, whether via fewer cars on the roads

Gliding Towards a "Glia-centric" Approach to Neuropsychiatric Disease: The Grand Feast of the Microglia

SASHA WEISS ILLUSTRATION BY ASHLEY LEE



Understanding microglia development and function will allow us to better grasp the pathogenesis and treatment of many neurodegenerative and neuropsychiatric diseases, especially autism and schizophrenia.

Tial cells are not just typical brain cells; unlike neurons, they brain regions, including the thalamus, cerebellum, olfactory bulb, Jare dynamic immune cells comprising 80-90 percent of the and hippocampus. The early development of the visual system is a perfect expopulation of cells in the brain. Although glia cannot produce electrical impulses of their own like neurons, they can change ample of activity-dependent synaptic pruning. In the visual system, retinal ganglion cells, a type of neuron located near the the behavior of firing neurons, play a huge role in injury and disease, and mediate early brain development. Originating in the inner surface of the retina of the eye, project to the dorsal lateral geniculate nucleus of the thalamus, which in turn projects blood as offshoots of the immune system, microglia, a type of glial cell, carry out many functions during development and to the primary visual cortex (also known as V1 or the striate in maturity, including mediating neurogenesis, controlling neucortex). Hubel and Wiesel's famous 1959 experiment studied rotransmitter turnover, supporting neuronal metabolism, and the neural connections in the primary visual cortex of an experiregulating angiogenesis and cerebral blood flow. In the event mental cat that was deprived of normal visual experience during of injury or immune system activation from infection, microglia the critical period for development of vision. After closing one become more reactive by tagging foreign material for removal eye of a kitten early in life, they performed electrophysiological with certain immune molecules. Microglia engulf these cellurecordings on the mature cat's brain. These recordings, measurlar debris, "swallowing up" (phagocytosing) dying neurons. Howing the electrical activity of single neurons in the primary visual ever, under normal circumstances, microglia constantly survey cortex of the anesthetized cat, showed that few neurons could their surroundings. Time-lapse video shows that they frequently be driven from the deprived eye. In fact, most of the cortical contact synapses, the connections between brain cells. Consecells were driven by the eye that had remained open. Therefore, quently, emerging evidence highlights a pivotal role of microglia the time when a kitten's eyes open (about a week after birth) is in healthy brain development. It follows that, impaired function, critical, as visual experience determines the wiring of the visual cortex. Moreover, recent studies have found that microglial inor even changes in the number and/or morphology, of microglia in brain regions involved in cognitive and emotional areas of beteractions with synapses are modified by visual experience. In havior may result in neuropsychiatric disorders. particular, a 2010 study showed that microglia appear to engulf There is overlap between the symptoms of illness or infecdendritic spines (postsynaptic elements) in the visual cortex of tion and those of certain neuropsychiatric disorders. For instance, healthy, three-week old mice when researchers switched mice to the symptoms of depression are similar to behaviors of sicka 24-hour-dark environment for a week. From adapting to their ness, including decreased food intake, reduced activity, and sleep new, dark environment, the mice may have required fewer synproblems. This overlap has led some researchers to hypothesize apses in the visual cortex. This new environment thus resulted in that many psychiatric diseases may involve a regulatory problem activity-dependent synaptic pruning—the microglia engulfed the of either the peripheral or central immune system, even in the extra synapses.

In order to evaluate the effects of microglia function on neural circuit development and investigate microglial phagocytosis of extra synapses, researchers have utilized the developing visual system in the mouse. This system comprises the connections between the retina and the lateral geniculate nucleus of the thalamus, the primary relay center for visual information received from the retina. During early postnatal development Microglia play a role in specific features of neural developbefore vision, spontaneous activity of retinal ganglion cells excite the retina. This retinal activation causes the retinal projections to the dorsal lateral geniculate nucleus to segregate and form nonoverlapping, eye-specific domains in the dorsal lateral geniculate nucleus. During this period of synaptic pruning, retinal ganglion cell inputs compete for territory in the dorsal lateral geniculate nucleus of the thalamus. This process eliminates less active, weaker retinal ganglion cell pre-synaptic inputs and strengthens the more active synapses in the correct eye-specific region of the dorsal lateral geniculate nucleus.

absence of a true pathogenic invasion. The links between neuropsychiatric disease and neuroimmune dysfunction have been found in post-traumatic stress disorder, generalized anxiety disorder, Autism Spectrum Disorders, Rett Syndrome, depression, and schizophrenia. Therefore, it is important to explore the pathogenesis of neuropsychiatric disorders by focusing on the neuroimmune system and development. ment, including cell proliferation, the formation of synapses, and synaptic pruning, either from producing certain immune molecules or from identifying other immune molecules produced by neurons. Microglia are particularly important during the first two weeks of postnatal development in the process of synaptic pruning, the elimination of weaker synapses in the brain. At this time of synaptic plasticity, new synapses are being formed and remodeled, with neurons first establishing many more synaptic connections than are maintained in the adult brain. This is an activity-dependent process. "Use it or lose it" is the motto; the In an exciting, new 2012 study, researchers discovered through weaker synapses are permanently eliminated, while the stronger, high-resolution imaging and immuno-electron microscopy that more active synapses are strengthened. Although the mechamicroglia engulf presynaptic retinal ganglion cell inputs in the nism of this synaptic pruning is unclear, many lines of evidence dorsal lateral geniculate nucleus during the peak pruning pesupport that microglia are essential mediators of this process. Inriod for the development of the visual system. Using tracers, deed, during synaptic pruning, activated microglia, acting through researchers labeled the neural projections from the retina to the different neuroimmune molecules, have been found in many dorsal lateral geniculate nucleus of genetically engineered mice

whose microglia fluoresce green. They tracked neural projections and C3, abundant at synapses, interact to mediate engulfment from their source (the cell body) to their end point (the synapse) by injecting dye into the eye of the mouse and visualized the retinal ganglion cell inputs in the dorsal lateral geniculate nucleus. Researchers reported pruning of inputs from both eyes, as labeled contralateral and ipsilateral retinal ganglion cell synaptic inputs were engulfed and found inside microglia. To further confirm that microglia were the actors, they labeled retinal ganglion cell inputs from both eyes with a pH- sensitive dye/tracer that fluoresces only when it enters the lysosome, an acidic cellular organelle involved in breaking down cellular debris. The researchers discovered that most of the engulfed retinal ganglion inputs were co-localized within microglial lysosomes, validating that microglia engulfed these retinal ganglion cell inputs.

Additionally, the researchers demonstrated that microgliamediated engulfment of retinal ganglion cell inputs is developmentally regulated. When the mice were five days old, a time of high synaptic pruning, they found more regions of labeled retinal ganglion cell synapses inside the microglia, showing that the microglia had "eaten" the presynaptic elements. When the pruning process slowed down when the mice were nine days old, there were fewer full microglia in the brain area, suggesting that microglial engulfment of synapses had been nearly completed. Moreover, when the researchers labeled each eye with a different dye (tracer) and triggered increased retinal ganglion cell activity in an eye by injecting the chemical forskolin into the eye, they discovered that microglia prefer engulfing the synapses coming from the less active eye. Further supporting that neural activity regulates microglia-mediated-"eating" of retinal ganglion cell inputs, they found that eye inputs treated with a neurotoxin that blocks retinal ganglion cell activity led to more microglial engulfment of inputs as compared to controls. These studies support that, while retinal cells form many connections with the lateral geniculate nucleus early in development, later on, they compete for territory, and the weaker synapses are eliminated.

Furthermore, recent research suggests that the classical complement cascade, a biological pathway in which complement proteins tag debris or pathogenic invaders and attract phagocytic cells to "eat" them, is involved in eliminating certain synapses. In the innate immune system, the complement proteins tag pathogenic microbes or debris for elimination by phagocytic cells. These complement proteins act in the same way in the brain to clear cellular material that has been marked for elimination. Additionally, these complement proteins are present in developing synapses in the brain during periods of active synapse elimination and are required for brain wiring. The exact mechanism by which the complement eliminates specific synapses remains to be determined. However, many recent studies support that C3, a complement protein that is present at developing synapses in the brain, "tags" the surface of cells and debris, marking them for elimination by phagocytic microglia that express C3 phagocytic complement receptors (CR3's). In the 2012 study discussed previously, researchers explored the possible molecular mechanism of how microglia CR3, expressed on the surface of the microglia,

of synaptic elements that are being pruned. Using immunohistochemistry to stain microglia with a particular antibody, a protein that binds to CR3, researchers found that CR3 was increased in microalia in mice that were five days old, compared to mice at older ages (20 days old). Also, CR3 knockout (KO) mice (mice without functional CR3's) had less engulfed retinal ganglion cell inputs than normal mice (CR3 wild type mice). Further supporting these findings, they reported increased retinal ganglion cell synaptic density in adult CR3 KO's. These studies suggest that mice lacking either complement 3, an immune molecule, or its receptor CR3 have microglia that are less able to engulf synapses, resulting in deficits in brain wiring and synaptic connectivity. These studies emphasize that we must continue to explore the mechanisms of how synapses tagged with complement proteins may be eliminated by microglial cells expressing complement receptors.

Ultimately, with recent studies demonstrating the importance of microglia in the healthy brain, understanding microglia development and function will allow us to better grasp the pathogenesis and treatment of many neurodegenerative and neuropsychiatric diseases, especially autism and schizophrenia. Many studies have shown changes in glial cell number and characteristics in the adult brains of patients with psychiatric disorders and in mouse models. In fact, a recent study found an increased amount of extracellular matrix proteins in astrocytes, another type of glial cell, in part of the medial temporal lobe of schizophrenic patients, suggesting a problem in astrocyte function. The medial temporal lobe is important for declarative memory, including visual recognition memory. Multiple studies support the idea that cortical "dysconnectivity," as a result of abnormal postnatal development, may be responsible for psychosis, a defining symptom of schizophrenia. A 2008 report showed that microglia were activated in gray matter of brains of people with recent-onset schizophrenia, providing evidence that schizophrenia is associated with neuronal damage. In addition to the elevated number of microglia cells in cortical areas, there is enhanced neurodegeneration in people with schizophrenia, suggesting that microglia turnover rate in those with schizophrenia is higher than in nonpyschiatric controls. This finding agrees with the developmental hypothesis of schizophrenia that perinatal injury leads to increased numbers of microglia later in the adult gray matter, which serve a neuroprotective function. People with schizophrenia also have significantly increased numbers of microglia in the frontal and temporal cortex, as well as signs of activated microglia in the prefrontal and visual cortex. However, researchers still need to discover whether changes in microglial activation and number are present only during active periods of the disorder or whether they are markers that are present throughout the course of disease.

Moreover, a study presented at the International Meeting for Autism Research demonstrated that there are more activated microglia in many brain regions in people with autism than there are in controls, by using a new radiolabeling technique, in which

a radiotracer binds only to activated microglia. These radioactive, activated microglia are then detected using positron emission tomography imaging (PET), a functional imaging technique that produces three-dimensional images of tracer concentration within the body. Thus, it is possible that there is increased pruning of inactive synaptic connections in autism. However, we still need to find out whether these microglial changes are an effect or microglia are activated and inappropriately pruning synapses.

Microglia are fascinating cells in the brain, producing many cause of autism-whether more synaptic connections are inacimmune factors during neuroinflammatory or infectious events, tive in brains of those with autism than in control brains, or if the "eating" dead or dying cells, and affecting the development of the nervous system. The recent studies that have demonstrated Glia may also be an essential factor in exploring the causes a role for glia in the early-life programming of behavior, learning, memory, and anxiety are particularly important for identifyof many neuropsychiatric disorders that have a strong sex-bias in their symptoms or prevalence, including autism. In addition ing potential mechanisms underlying neuropsychiatric disorders. to the many sex differences within the developing brain, there Although the research on the relationship between microglia, are sex differences in the number and morphology of glia. In complement cascade deficits, and diseases associated with fact, within the neonatal cortex and hippocampus, researchers synapse loss, dysfunction, and development is intriguing, many have found sex differences in the proliferation of new cells, the questions are left unanswered. Do microglia initiate the eliminacolonization of glia, and the expression level of certain immune tion of synapses, or do they just arrive to clean up afterwards? We must identify the glial signals that control activation of the molecules produced by microglia. It is likely that researching sex complement cascade in the brain and determine why some syndifferences in glial number or function during early brain development and into adulthood will be important in understanding the apses are targeted by the complement cascade but not others expression of sex differences within the brain, which are estabto develop future therapies for neuropsychiatric disorders, such lished during critical periods of development and maintained into as therapeutic inhibitors of the classical complement cascade. adulthood. Males are more likely to be diagnosed with disorders In order to glide into a "glia-centric" view of neuropsychiatric diswith certain developmental origins, such as autism or schizophreease, we must answer these questions and better understand nia, while females are more likely to be diagnosed with disorders the mechanisms underlying microglia-synapse interactions in the that appear after the onset of adolescence, such as depression developing brain.. 🕸

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and anxiety disorders. By understanding this association between neuroimmune function and sex differences in neuropsychiatric disorders, we will better grasp how sex differences in the localization and function of glia within the normal developing brain may lead to certain critical developmental periods between males and females.







Epigenetics: What Cells Remember

Ricardo Raudales Illustration by Allison Cohen

le often think of our genetic code as our biologi-W cal trademark. Each of us takes on an entirely Nearly everyone's genetic code is unique-the only guence. However, even twins show signs of divergence soon after birth. As twins age, a distinguishing physical manifestation can usually tell them apart. Interestingly, researchers noticed that these phenotypic differparent to researchers that the cells of twins not only behind the epigenome were not immediately clear. respond to changes in their environment, but somehow

the source of what was referred to as cellular memory. Before epigenetics, most of the genetic information new combination of alleles from our parents, a ge- of DNA was thought to be contained within its onenome that is shared by all but a few cells of the body. dimensional base sequence. Epigenetics, however, represented an entirely new take on gene theory. In addiexceptions being twins, who have the same gene se- tion to the "what" information found of the genome, researchers discovered that DNA's three- dimensional structure could influence when, where, and how genes feature, personality quirk, or perhaps an early disease are expressed. This second category of information was contained not in the sequence itself but rather in the chromatin, the higher-order structure of DNA. Sciences often change dramatically with age, despite the entists referred to this classification as the epigenome, fact that twins' genetic makeup do not. It became ap- a sort of second genome. However, the mechanisms Eventually, scientists discovered two ways cells can

"remember" the experience. With the emergence of a rewrite the epigenome. These changes work by modinew field called epigenetics, scientists could pinpoint fying either the DNA directly or its associated proteins,

Epigenetics may indeed be the basis for establishing cell identity during organism development. Through differentiation, cells with the same genome can acquire specialized functions. What once began as a single cell known as histones. In the first mechanism, enzymes gives rise to everything from epithelial cells to the add methyl groups to certain cytosine-guanine dinuvast array of neurons that make up the brain. Before cleotides in the DNA, a process known as DNA methepigenetics, biology could not explain how cells reylation. A second mechanism called histone acetylamember their identity or why differentiated cells do tion adds acetyl groups to lysine residues in histone not revert back to more primitive forms. We now know proteins. Depending on the extent of DNA methylathat this sort of information is kept in the epigenome, tion and acetylation at a given DNA site, chromatin which enhances the expression of certain genes while structure may either condense or loosen. DNA that is inhibiting the expression of others. Related to epihighly condensed will "silence" or block the binding of genetics is transcriptomics, or expression profiling, transcriptions factors, reducing the expression of the which has emerged as a new way of measuring gene acaffected genes, whereas loosely packaged chromatin is tivity. Researchers are already using these techniques more likely to be transcribed. Together, these epigento better understand cancer and other diseases of the etic modifications offer a crucial link between genetic cell. Epigenetic drugs may even offer the opportunity structure and function. to bypass the genome, essentially picking up where When scientists started studying the epigenome in gene therapies have failed in the past.

more detail, the level of specificity they found aston-The most controversial aspect of epigenetics reished them. Unlike the genome, which is typically the mains the question of heritability. Studies have shown same across all cells in an organism, epigenomes were that the expression of some inherited traits may defound to be unique to individual cells. Since cells are pend on the parent-of-origin, a phenomenon known continually impinged by a slew of chemicals, it was as genomic imprinting. In other words, imprinted genes feasible hat epigenomes were also unique across time. are only expressed if transmitted from mother to off-Such reprogramming was hypothesized to be constant spring but not father to offspring, and vice versa. In and shaped by even small changes in the extracellular addition, there is a growing body of evidence that milieu of the cell. A simple elevation in a drug or stress suggests the methylation state of DNA itself may hormone would have the potential to leave a lasting be reproduced and actively maintained during embrymark on the epigenome. In mammals, early adverse life onic cell division. This may enable differences in gene experiences have been shown to do just that, alteractivity acquired during the lifetime of the organism ing the expression of specific genes, in some cases, up to be transmitted to offspring. It is an idea perhaps through adulthood. Stress, in particular, has been immore Lamarkian than Mendelian, and surely one that plicated in the regulation of glucocorticoid receptors, will continue to guestion our underlying assumptions which may control everything from digestion to mood about heredity. and cognition. Thus epigenetic regulation seemed to In its current state, the field of epigenetics reprovide a level of fine tune control over cell activity. mains young and full of potential. For the first time,

What remained unclear was how changes occurring scientists have been able to demonstrate that cells outside a cell could lead to epigenetic regulation inencode past experience through epigenetic modificaside the nucleus. Here, cellular signaling was key. For tion. Still, much remains to be understood. The intrione, it appeared that some receptors, upon binding to cate molecular pathways linking a cell's surrounding the right signal molecule, initiate a cascade of intrato its epigenetic machinery are just beyond our reach. cellular messengers that eventually reach the chro-With next-generation sequencing already becoming matin. Other receptors are themselves internalized available, we may soon find out how different unique into the nucleus. In either case, the final step involves our cells really are. 🕸

a group of enzymes that specifically target DNA or histone proteins for epigenetic modification. Interestingly, some of these enzymes seem to have a role in actively maintaining the epigenome. The targeting of these different enzymes by experimentation has given scientists a way of testing the effects of epigenetic modifications on entire organisms.

Can Science Tell Right from Wrong?

Carl Jago ILLUSTRATION BY ASHLEY LEE

We are at a moment in history when technology permits even the individual, if motivated enough, to bring death and suffering to millions of people. And so while humanity has long been deeply divided over issues of religion and moral code, it is now more important than ever before that we converge on some globally unified sense of right and wrong. Some have suggested that science makes this possible due to its ability to transcend nationality and ascertain facts. But can science actually tell right from wrong?

This question was addressed in 2010 by a group of scientists and philosophers who came together in a forum at Arizona State University aptly called, "The Great Debate." Physicist Lawrence Krauss, psychologist Steven Pinker, and neuroscientists Sam Harris and Patricia Churchland argued that science can indeed tell right from wrong. On the other side of the debate were Peter Singer and Simon Blackburn, who argued that science cannot distinguish between right and wrong. The scientists claimed that we need only pay attention to the connection between morality and well-being in order to understand how morality falls within the purview of science. That is, we do not feel moral obligations towards rocks because rocks have no capacity to experience well-being. Harris explained that since well-being is a physical phenomenon experienced at the level of the brain, understanding it and explaining it means to take into account "things like genetics, neurobiology, psychology, sociology and economics." In other words, details of well-being, it can also account for morality.

To the contrary, philosopher Simon Blackburn argued that science is in the business of facts rather than values, and that it tells us about the way things are rather than the way things ought to be. He turned to an argument made by the 18 th century Scottish philosopher David Hume; one cannot derive a value from a fact. Scientists Churchland and Krauss dismissed this argument claiming that we can and do obtain values from facts all the time. As an example, Krauss asserted that upon determining the fact that educating women in developing nations generally leads to more stable economies and

ing women in developing nations. In response, philosopher Singer acknowledged that while facts can lead to values, in order for a fact (e.g. educating women in the developing nations leads to more stable economies) to be translated into a value (e.g. women in developing na-Harris believes that since science can account for all the tions ought to be educated) one must already have a premise in place (e.g. more stable economies are something worth valuing). Said another way, Singer's argument was that facts can lead to values, but only when we have a fundamental premise or deeper value with which we can judge and decide between the likely consequences of each alternative. Science, according to the philosophers, cannot provide us with any core values.

> While the philosophers were correct in arguing that a new value can only be arrived at by extrapolating upward from a deeper value, I believe they were wrong in implying that the real burden that faces us is a need to decide upon a deepest, or core, value. And while the sci

entists offered well-being as the deepest value, I think animals. One kind of clue that suggests a behavior has they failed to acknowledge that well-being is not simply an inborn biological basis is when it functions despite culture, experience, or belief, and this is the case with the a good choice, but rather that we don't have a choice at all. The fact of human nature is that it is inherited and system underlying the Westermarck effect. The Westercommon to all of us. This is what it means for humans marck effect is a mechanism that discourages incest by to have a nature. There are very good reasons to believe causing children who are raised together to be sexually that our deepest values are coded for by the biology of averse to one another. In an anthropological study from our nervous systems and therefore bundled in as a part 2003, Debra Lieberman found that what matters to a of our very nature. This is why we needn't look outward girl's feelings about incest is not the way she is raised, in an effort to adapt core values with which to judge nor whether she believes a boy to be her brother or right and wrong, but instead inward, because we already not, but rather how many years she co-resides with him. have them, and in fact we cannot escape them. Therefore this biological system for recognizing kin and behaving appropriately with them not only shapes our For decades now, studies in the fields of primatolbeliefs and attitudes but is also resilient to them. Frans ogy and anthropology have shown that mechanisms

for such morally relevant behaviors as those associat-De Waal, a famous primatologist highlighted a different ed with reciprocity, incest aversion, fairness and equity, moral domain when last year he presented the video of the mother-infant bond, and the preferential treatment a famous experiment he conducted in which capuchin of relatives and group members are not only universal monkeys are given either cucumber or grapes in return across human cultures, but also evident in nonhuman for tokens. The monkeys are pleased to eat the cucum-



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ber until they see another monkey being offered the much-preferred grapes. At this point, the upset monkey hurls the cucumber back at the experimenter and shakes the cage door aggressively in an angry outburst ity is not predicated on human-level intelligence, moral resembling the behavior of a jealous child, demonstrating some understanding of fairness and equity. It should be no surprise that the nonhuman animals whose morally relevant behaviors most closely resemble our own are the other primates, the animals whose molecules of inheritance, DNA, mostly closely match our ownan approximate 93% match exists between humans and chimpanzees. And so whether or not a penchant for concerns, these concerns are inherited nonetheless.

The many common behaviors and deep concerns displayed across cultures and even across species should highlight the fact that we are not born with minds like blank slates, and for this reason we are not faced with the impossible task of determining a system of morality without a point of reference. No amount of logic stops a mother from caring about her child, and this is because such caring comes out of a deep emotional motivation that has little to do with reasoning. The powerful motivation behind the mother-infant bond is experienced by most mammalian species whether or not they have

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the ability to ponder the greater purpose of their lives. We didn't think our way into our morality and we're not going to think our way out of it. But even though moralambiguity is inevitable in the complex world we have created, and it demands that we use this intelligence along with the best tools and methods we possess in order to navigate this space.

Moral ambiguity rarely occurs at the deepest levels where concerns are automatic; more typically, confusion and disagreement arise at the less pivotal level of everyday-choices to which we try to branch out from well-being is the very best way to describe our inherited our core values. Wanting your child to be healthy and happy is one thing, knowing the finer details of how to raise her is yet another. It is in the difficulty of forming links between the obvious and not so obvious where science will prove most useful for questions of morality. While the deepest motivations of morality are dictated by inherited mechanisms and are not open to negotiation, how we translate them into the choices and policies that govern our daily lives is open to change, and does indeed need to be negotiated. It is science that can do most to bridge the gap and ultimately inform this area of discourse.

Won't individual differences keep us from ever reaching any significant level of agreement? Personal differences do exist, but I believe they are most present at the most superficial levels. We tend to focus to such a degree on the ways in which people differ that we tend to underestimate how similar they really are. During a talk he gave at Columbia's business school, Harvard Psychologist Dan Gilbert pointed out that when one person likes chocolate flavor and another likes vanilla, we tend to overlook the fact that both of them like sweettasting calorie-dense desserts. The likeness typically runs deeper than the difference. This applies not only to differences between people, but between nations and cultures. Fortunately, true science transcends opinion, tradition, bureaucracy, and dogma, whether religious, cultural, or political.

Ultimately, neither science nor philosophy can reinvent morality, but science can and should continue to reveal our existing, shared values in greater depth and detail, and with its ability to predict consequences, identify right and wrong actions based on whether or not they are congruent with our deepest values. We can tell right from wrong without science, but with science we'll do a much better job, and stand a better chance of converging upon a globally unified moral code fit for the 21st century. 🕸

Looking Inward: The Anomaly of Consciousness

 γ f all the puzzling and mysterious areas of inquiry $\,$ and free will, are in fact no more than the behavior \mathcal{J} facing science in the 21st century, the biological of a vast assembly of nerve cells and their associated nature of consciousness is perhaps the most unfathommolecules." Not one to pull any punches, Crick conable. Other classic scientific conundrums like protein spicuously leaves out any consideration of the soul folding and dark matter may be guite vexing, but the or any sort of immaterial attribute traditionally assoscientists who study them have always believed that ciated with transcendental human specialness. Many well-thought-out experiments and technological adscientists had been denying the existence of the soul vances may eventually lead them to a breakthrough. for years, though, so what makes the titular hypoth-The problem of consciousness is not quite so tractaesis really astonishing is its implication, simultaneously ble. Until this century scientists largely ignored any obvious and shocking, that no element of any action, questions having to do with consciousness, preferring thought, or impulse is produced ex nihilo but is rather to leave such debates to philosophers. Indeed René an automatic, prewired response to a certain stimulus. Descartes and Immanuel Kant are both well known for Whether that stimulus is external or internal, the wiring their writings on how we experience the world. The of one's neural circuitry determines the appropriate bepsychoanalysts of the late 19th and early 20th cenhavioral response, meaning any subjective experience of freely "choosing" to act in a certain manner is pure illuturies were the first to make the internal actions of the mind a topic of scientific discourse. Led by Sigmund sion. Consideration of whether the notion of free will is Freud, they strove to develop the techniques of introcompatible with this idea will quickly lead to a quagmire spection and dream analysis as tools for understandof philosophical contemplation, however, so it may be ing the mind, but their efforts were guickly brushed more productive to focus instead on what is even more aside when B. F. Skinner and the behaviorist school astonishing about the Astonishing Hypothesis: the fact that any sort of subjective experience can exist at all in supplanted psychoanalysis as the forefront of brain science. The behaviorists had no use for unempirical a system of purely electrochemical reactions. descriptions of internal states, choosing to rely instead If all of our thoughts and perceptions can be reduced on controlled stimuli and observable behaviors in their to electrical and chemical activity of our neurons, how experiments. As a result, consciousness and internal then can we explain the "blueness" of blue? What excognitive processes did not reemerge as topics of reactly is it to feel happiness, hate, pleasure, or sadness? search until much later in the 20th century. One of These subjective experiences are called gualia, and they the reasons the topic of consciousness was avoided present a primary mystery of consciousness: everyone for so long was that it is so hard to study without is assumed to experience them, but how can our internal impression of reality be explained in the physical an understanding of the biological mechanisms behind neural circuitry in the brain. However, now that electriconnections between nerve cells? To begin addressing cal and chemical signal transduction between neurons these questions, some scientists look to the evolutionis generally well understood, consciousness is once ary beginnings of consciousness for insight. NYU neuroagain a formal topic of investigation. What it actually scientist Rodolfo Llinás argues in his book I of the Voris, though, seems to be no easier to define than it was tex: From Neurons to Self that conscious experience is a hundred years ago. produced as a by-product of the linking of sensory in-Francis Crick, most famous for working with James puts to the predictive powers of the brain. According to Watson to discover the molecular structure of DNA, him, the nervous system evolved as an "internalization opens his 1994 book The Astonishing Hypothesis with of movement," a way for organisms to sense informaan abrupt, impactful summation of where neuroscition about their surrounding environments and produce ence has gotten us so far: "The Astonishing Hypothesis motor responses that maximize their survival and reis that 'You,' your joys and your sorrows, your memoproductive capacities. In order to do this, the nervous ries and your ambitions, your sense of personal identity system must evolve to make predictions about what

Illustration by Esha Maharishi



make a decision on which movement to make. For in- This unified mental image of the boy riding a bicycle is stance, a fish must be able to perceive an approaching net and rapidly determine which direction to swim, taking into account the trajectory of the net, the proxim- contends that electrical firing between the thalamus ity of safe areas, and the velocity at which the fish is capable of swimming. Humans are similarly capable of predicting the outcome of making movements, but our conscious experience seems to extend beyond computer-like matching of inputs to outputs. To us, multiple aspects of a stimulus, say a rampaging elephant, are perceived in parallel: its shape, motion, sound, smell, etc. Amazingly, all of these aspects, even though they are in time. In simpler terms, one can imagine this recurrent processed separately in the brain, are perceived as one object, which the brain can then categorize as threat- frame will carry information about sight, sound, taste, ening before producing the appropriate muscle movements to escape. It is necessary for these sensory modalities providing information about the elephant to be frame in sequence will carry slightly different informabound together in order for the brain to recognize what it is, but how this is accomplished is unknown. This is the "film" that determines our internal representation called the binding problem.

The binding problem addresses how we perceive multiple sensory modalities as a unified experience. In the book In Search of Memory, Columbia's own Eric Kandel poses the binding problem in terms of a boy riding a bike: "How [do] we see a boy riding a bicycle internal representation of the external world." Hownot by seeing movement without an image or an image ever, University College, London professor Semir Zeki is that is stationary, but by seeing in full color a coher- guoted in Kandel's book pointing out a flaw in the logic

will happen as a result of certain movements, and then ent, three-dimensional, moving version of the boy?" called a percept, and Llinás believes he may have found the biological basis of its formation in the brain. He and cortex regions of the brain at a steady rate of 40 times per second is responsible for the synchronization of sensory input into unitary percepts. Sensory information can only be transmitted to the cortex at reqular 40 Hz intervals, giving the brain the ability to have all of the sensory modalities undergo higher processing simultaneously, effectively binding them together thalamo-cortical resonance as a length of film. Each touch, and smell all at the same time, but no information will be transmitted between the frames. The next tion 1/40th of a second later, ultimately composing of the outside world.

> Llinás views this binding of sensory information into percepts, combined with our brains' ability to make predictions based on this information, as the "self," or the "loom that weaves the relation of the organism to its

of sensory integration: "If all the visual areas report to sity, saves us the trouble, denying that there is a dua single master cortical area, who or what does that alism between a "Hard Problem" and "Easy Problems" single area report to?" Who is watching this "film" made of consciousness, but rather that the Hard Problem by the 40 Hz thalamo-cortical resonance? Of course, will fall as the Easy Problems are solved. Dennett one is tempted to answer, "I am." But who or what is believes that the Hard Problem is illusory, and that this I? Does such a thing even exist? Using such logic, eventually all of consciousness will be explained by one will find himself floundering in infinite regression, natural phenomena in the brain. Once all the building but the complexity of the issue is apparent. blocks of conscious experience are established, the The binding problem isn't the only issue vexing those Hard Problem will be determined to be nonexistent, in a similar fashion to how alchemy was deemed unscientific once the chemical elements were understood as intransmutable.

who study consciousness, as our internal experience goes beyond just the integration of sensory inputs. Perhaps the biggest question is why we perceive percepts the way we do, in a way that is not at all analogous to It will be a long time before any of these questions the actual form in which sensory information is transare answered, or even determined to be answerable. mitted. If one were to attempt to explain the color The struggle to understand consciousness may prove blue to a person who had never seen color before, it to be an exercise in futility, a paradox in which a syswould be impossible. One could explain how the partem can never fully comprehend something exactly as complex as itself. Crick is optimistic, however, pointticular wavelength of light enters the eye and strikes the retina, activating photoreceptor cells in such a way ing out that "the history of science is littered with statements that something [is] inherently impossible to as to produce an electrical response that is transduced along the optic nerve to the brain, and so on, but it understand," only to be proven wrong time and again. would never be possible to aptly describe the "blue-What appears to be insurmountable today could be ness" of blue, what is called to mind when we think of the breakthrough of tomorrow, but it's hard to deny the color blue. The same goes for feelings of happiness the possibility that fully understanding our own conand pleasure, hate and envy. Each feeling is associated sciousness might require an extent of mental contorwith certain behaviors, but the subjective experience is tion bevond our capacity. 🕸 locked inside our heads.

Australian philosopher David Chalmers refers to the existence of such gualia as the Hard Problem of consciousness. In his essay "Facing Up to the Problem of Consciousness," he asks, "Why should physical processing give rise to a rich inner life at all? It seems objectively unreasonable that it should, and yet it does." After all, computers are capable of processing inputs and producing corresponding outputs, yet we do not consider them to be conscious, because we assume they have no qualitative awareness of that process. So why aren't humans "philosophical zombies," as Chalmers calls them, people who respond to stimuli and produce human-like behavior but have no subjective experience? Chalmers believes that the Hard Problem is the ultimate question of neuroscience and is distinct from numerous Easy Problems, such as: why mental states are reportable; how we can discriminate, categorize, and react to stimuli; and how we have deliberate control of behavior. These problems are "easy" in that they seem to be solvable within the current empirical understanding of neuroscience and may yield to scientific investigation given enough time. The Hard Problem, on the other hand, may not be solvable by the same methods, if at all.

Daniel Dennett, a cognitive scientist at Tufts Univer-





Body Politics

Exhibits like the popular BODIES...The Exhibition that display preserved human bodies may be educational, but to what extent are they ethical?

 \mathbf{Y} f all the scientific marvels that can be put on display, Uthere are perhaps none more fascinating than the intricate systems of organs and tissues that constitute the human body. Since 2005, the showcase entitled "BODIES... The Exhibition" has offered the public the chance to view the inner workings of the human body in the sort of incredible anatomical detail previously privy only to the eyes of medical professionals.

Today, at a cost of \$24 per adult, patrons of the exhibit's South Street Seaport location can view over 200 real human

specimens, ranging from whole bodies to individual body systems and organs. The bodies have been meticulously dissected and preserved through a process called plastination, in which tissues are permanently preserved by replacing their cells' water and fat contents with liquid silicone rubber that later hardens. BODIES offers some truly amazing sights, including a figure stripped down to nothing but its nervous system by years of painstaking dissection, and another consisting of the vessels of the circulatory system displayed in their original

conformation. While the educational value of this and similar Furthermore, Roy Glover, Chief Medical Director and exhibits like Body Worlds and Our Body: The Universe Within is spokesman for BODIES, candidly admits that previously no undeniable, the public presentation of human cadavers raises a attempts were made to obtain informed consent. Of the host of ethical concerns. bodies, Glover says: "They're unclaimed. We don't hide from it, Although the exhibit's website claims that the bodies are we address it right up front." Without informed consent prior to being "respectfully displayed," some argue that arranging death, there is no way of knowing whether what is being done human corpses into a variety of life-like poses, such as that of with these bodies goes against the living wishes of the people throwing a football or playing poker, is disrespectful towards who once animated them. That the people whose bodies are the dead. Reverend Tadeusz Pacholczyk, a Catholic priest and exhibited might not have been willing to have their remains professional bioethicist, doubts "whether all of the subjects preserved indefinitely in plastic, let alone in a public arena, is really approved of their new 'show business careers." Even disturbing to say the least.

those in the business of profiting off of spectacle have been One of the foremost tenants of medical ethics is respect critical of the *BODIES* exhibit for violating human dignity. Philip for patient autonomy and the resulting need to obtain Lipson, director of the Seattle Museum of the Mysteries, informed consent prior to medical treatment. According to the opposed the exhibition in his home town, claiming that the National Commission for the Protection of Human Subjects of BODIES exhibit is "...not treating them with dignity and is just Biomedical and Behavioral Research's 1978 Belmont Report, making a peep show out of dead bodies." Moreover, many "Respect for persons requires that subjects, to the degree that members of the general public are offended from a religious they are capable, be given the opportunity to choose what or moral standpoint by certain elements of the showcase. Of shall or shall not happen to them. This opportunity is provided particular concern is the display of human fetuses at various when adequate standards for informed consent are satisfied." stages of development, which is housed in a separate area that While this ethical principle of informed consent is typically has a sign posted to its entrance warning patrons "This part of strictly enforced in dealings with the living, little regard is paid the exhibit might be disturbing to some viewers." Others, like to it when considering the posthumous treatment of a body. New York attorney general Andrew Cuomo, have criticized the Different states do have some regulations concerning the exhibition for taking advantage of the general public's morbid rights of the deceased, but they are widely varying, with some curiosity in order to make a profit. "The grim reality," according to states but not others expressly prohibiting practices such as Cuomo, "is that Premier Exhibitions has profited from displaying cryogenic freezing, stacking corpses, mutilation of the corpse, the remains of individuals who may have been tortured and and necrophilia. Although there are certain legally binding ways executed in China." for a person to control what will be done with his or her body The greatest issue at hand does seem to be the origin of after death, like including a cremation request in his or her will, the cadavers that were obtained for the exhibit. In February of for the most part legal autonomy ends with death.

2008, ABC's 20/20 reported that the bodies being displayed were those of Chinese prisoners who had been executed and their remains later sold on the black market. Premier Exhibitions, the company that operates *BODIES*, maintained that all the bodies it uses are obtained legally from a Chinese medical school; yet they made no mention of any attempts to secure consent to display the bodies, either from donors before their deaths or from their next of kin. Prompted by the 20/20 report, a formal investigation of the *BODIES* exhibit was launched in 2008 by attorney general Cuomo. The resulting settlement requires Premier to "obtain documentation demonstrating the cause of death and origins of the cadavers and body parts it

displays as well as proof that the decedent consented to the Though some exhibits like the Human Body Exhibition that use of his or her remains in such a manner." first opened earlier this year in Dublin, display only bodies that Although the settlement clearly advocates the practice of have been freely donated with informed consent, unfortunately obtaining informed consent, it does not effectively enforce that for the most part the policy of obtaining informed consent has practice. The settlement does not even require Premiere to stop been neither observed nor enforced. Cultures across the planet exhibiting the remains of those who may have been tortured that may differ in every other aspect typically share one belief in common: that the dead should be allowed to "rest in peace." or executed. Premiere simply has to issue a series of warnings to its customers, like the following non-committal statement Both time-honored cultural traditions and modern bioethical currently displayed at the exhibit's entrance: "With respect to principles stipulate that unless a person requested otherwise the human parts, organs, fetuses and embryos you are viewing, while living, he or she should be undisturbed in death. Perhaps Premier relies solely in the representations of its Chinese partners this reflects a certain sentimentality on the part of our society, and cannot independently verify that they do not belong to but in terms of ethical standards, it is one creed that science persons executed while incarcerated in Chinese prisons." would do best to abide by. 🕸

Nevertheless, there is no reason that the same rationale that prompts physicians to obtain informed consent before treating the living should not be extended to apply to the care of human remains as well. It is respect for basic human dignityas well as acknowledgement of the fact that a person should maintain ownership over his or her own body-that motivates the medical community to defend patient autonomy. Those very same principles should make those involved in the business of displaying cadavers realize that it is completely unethical to subject a person's body to treatment that he or she did not consent to, especially if that treatment differs wildly from culturally accepted norms.

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