New Vistas, New Understandings

Neurotropic Viruses are Emergent and Affect the Life of Human Populations Due to Increased Risk of Mental and Neurological Diseases
New Vistas, New Understandings

It is easy to be aware of the impact that social and economic changes have on the way in which we spend our time, build or lose families, work or get fired, learn, and educate: The impact that these changes have on our relationship with the environment are less obvious: And we are rarely aware of the impact that the changes of the environment have on the flora and the fauna which in turn affect our health. Ting Ting Lee and Ian Paul Everall’s learned paper gives us a glimpse of these interactions. Deforestation and urban development damages the habitat of fruit bats: They migrate, seeking food and a place to live, and often come closer to human settlements; the viruses which affect them get transmitted to other animals and then to humans. Viruses are over-represented among the emergent pathogens, and most of them are zoonotic. Many of them are neurotropic, and their presence will lead to severe mental and neurological diseases: The dark side of having a new golf course may well be the appearance of illnesses that are lethal and unknown until now. Progress of society and the improvement of quality of life of human populations are dependent on our acceptance of the fact that our actions should not be planned nor carried out, and that they cannot be understood unless we see them as part of a complex system whose changes must survive.

On a much more elementary level – that of medicine and psychiatry – changes of the phenomena in our restricted area are more easily visible. Our knowledge about mental illness has increased. We are more aware of the impact of culture on the presentation and course of mental illness. We have evidence that mental illnesses influence not only the functions of the brain, but also its structures. We know more and have learned that some of the ideas, which we had earlier, will have to be abandoned. One of the ways in which changes of our understanding of mental illness is reflected is the decision to change the classification of mental disorders. Michael First...
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which rely on the statistics collected using the classification that the ministries of health in the nearly two hundred member states of the World Health Organization have adopted as their common language about prevention and treatment of diseases worldwide.

The classifications of mental and neurological disorders – like the classifications of any other group of disorders – are no more than hypotheses about the relationships between the objects that are being classified. They have to be regularly reviewed and brought up to date to ensure that they are based on the best of available evidence. If depression affects the brain in a manner similar to that of poisons, we might have to re-conceptualize depression and see it as a behavioural manifestation of an intoxication by substances as yet unknown. The paper by Phillip Gorwood makes us see the relationship between depression and brain damage in this manner: If further similar studies of mental disorders were to show similar results, the classification of these disorders, as well the search for best ways of dealing with them, might have to be fundamentally changed.

It is a great pleasure to express gratitude to people who make you see things in a new way, who open new vistas, and lead you to a better understanding of the world in which we live. Thus the authors of the three major articles in this issue of The Institute Magazine certainly deserve our cordial thanks.
Emerging Neurotropic Viruses – Why and How

Emerging viruses possess a significant threat to human health, and sudden outbreaks can be fatal across national borders. Human behavior must be restricted with strengthened health measures in order to minimize the risk factors associated with the emergence of new viruses.

Introduction

Viruses do not have consciousness that allows them to plan to mutate into super-viruses that are going to devastate humanity. However, they probably have a ‘self-identity’ through consortial genetic action that has resulted in them being very abundant and diverse genetic entities (Villarreal, 2012). This ability of viruses to work co-operatively usually favours a successful and stable relationship with their hosts (Villarreal, 2012; Olival & Daszak, 2005) but allows flexibility to change as the actions of the host changes. It is this change in the relationship shaped by our human activity and behaviours that often results in new disease outbreaks and epidemics from emerging viruses. In this article we will briefly illustrate how the factors in human behaviour can influence viral dynamics and then illustrate the probable factors that influenced the emergence of various neurotropic viruses, including the pandemic human immunodeficiency virus (HIV).

While there are variations in the definition of an emerging virus infection, Tyler (Tyler, 2009; Tyler, 2009) defines it as having at least one of the following qualities (Villarreal, 2012): A disease, which has infected a new host, (Olival and Daszak, 2005) has occurred in new geographical locations, or (Tyler, 2009) has different characteristics in their pathogenesis or are caused by agents not previously recognized as pathogenic (Olival and Daszak, 2005; Tyler, 2009). ‘New’ viral infections can also include a re-emerging virus that had previously fallen to such a low frequency that it was no longer considered a public health threat but has now re-emerged (Heymann, 2009). Examples include measles, mumps, and rubella, which have declined dramatically due to vaccinations but are now on the rise with parents declining the vaccinations due to safety concerns of the vaccines.

The transmission of emerging viruses to humans can also involve vectors, such as mosquitoes or ticks, as well as animal hosts such as pigs, horses, birds, and more recently bats (Olival and Daszak, 2005; Halpin et al., 2007; Mackenzie, et al., 2003); zoonotic viruses are now recognized as an emerging issue. In the twenty first century, (Taylor et al., 2001) it was determined that there are 1415 different human pathogens in 472 genera and of these 15% are viruses or prions. There are two important characteristics with regard to the 132 considered emerging pathogens. The first characteristic is that viruses are over-represented, accounting for 44% of emerging pathogens, and the second is that zoonotic pathogens represent 75% of emerging pathogens. This means that zoonotic viruses represent the largest group of emerging viral infections. More recently Olival and Daszak (Olival and Daszak, 2005) reanalyzed (Taylor et al., 2001) data and concluded that of the 77 viruses, that can be considered emerging, 49% were associated with either an encephalitis or serious neurological disorder, hence emerging viral infections that disproportionately affect the central nervous system. Examples of these emerging viruses and their interacting factors can be found in Olival and Daszak (Olival and Daszak, 2005). The factors that can influence the development of an emergent viral infection are multiple, complex, and especially involve various human activities that have changed in nature over time. Morens (Morens et al., 2008) states that the factors can be genetic, biological, social, political, economic, and could include, but are not limited to those listed below (Morens et al., 2008):

• International trade and commerce
• Human demographics and behavior
• Human susceptibility to infection
• Poverty and social inequality
• War and famine
• Breakdown of public health measures
• Changing ecosystems
• Climate and weather
• Intent to harm
• Lack of political will
• Microbial adaptation and change
• Economic development and land use

We will now illustrate how some of the factors listed above helped shape various disease outbreaks attributable to newly emerged zoonotic viruses, including HIV.
Examples of Bat Borne Zoonotic Neurotropic Viruses

The emergence of new bat borne viruses in the recent decades is an evident example of zoonotic neurotropic viruses. These include Hendra virus, Bat Lyssa virus, and Menangle virus in Australia, Nipah virus in Malaysia and Bangladesh as well as severe acute respiratory syndrome (SARS) (Field et al., 2001).

The disruption of ecosystems, economic development as well as changing human demographic and activities are the major contributing factors for the emergence of these new viruses. Natural catastrophes including storms and bushfires along with human activities such as commercial logging, agricultural establishment, and urban development led to deforestation and therefore damage to fruit bat habitats. This resulted in the migration of fruit bats, abandoning their natural roosting and feeding sites to seek alternate food resources and habitat (Field et al., 2001). Hunting for the purposes of leisure, food, or agricultural protection further contributed to movement of bat populations. In the recent years, permanent fruit bats populations have been found to emerge near or in the urban areas within close proximity to humans (Field et al., 2001; Plowright et al., 2011).

Nipah Virus

Nipah virus first emerged in 1998 in Malaysia among pigs, presenting with marked respiratory and neurological symptoms followed by death (Uppal, 2000; Mohd Nor et al., 2000) Human cases were subsequently reported, primarily presenting with neurological symptoms (Field et al., 2001; Uppal et al., 2000). Amongst 265 human cases, 105 deaths were recorded (39% fatality rate), and the majority were farmers and abattoir workers who had direct contact with the infected pigs.

The spillover of Nipah virus to humans was facilitated by the traditional farming practice in Malaysia. Orchards are usually established near pig farms so that pig manure could be utilised as fertiliser. The exposure of pigs to the virus was greatly increased as the infected fruit bats were being attracted to fruit trees in the surrounding area. Virus laden urine and masticated fruit pellets dropped by the fruit bats are believed to be the main introduction route of the virus into pigs in the farms, and this is thought to have occurred multiple times before the event of microbial adaptation of the virus to the new pig host, most likely as a result of viral mutation (Smith and Wang, 2013). Viral spread amongst the pigs probably occurred as a result of physical contact, and transmission through bodily fluids such as nasal excretions, urine, feces, and birth fluids (Uppal, 2000). This is further exacerbated by the practice of high density pig farming causing a rapid spread of virus within the farm.

The outbreak allegedly originated from pig farms in the state of Perak and then spread to the southern part of the peninsula. Multiple incidents of suspicious pig deaths were reported to the veterinary officers of Veterinary Research Institute in Perak, however, common pig diseases were assumed causal due to the similarity in symptoms (Chua, 2012). This possibly reflected on the inefficiency of animal public health measures whereby the authority failed to identify the early stage of the disease, permitting new virus to become further established in its new host. Trading of pigs is very common in peninsula Malaysia with regular pig movements across states. During the early stage of the pig epidemic in Perak, there was a ‘fire sale’ of animals prior to the disease outbreak leading to the dispersal of pigs across the country, including infected, but asymptomatic animals (Mohd Nor, 2000). Additionally, the rapid widespread of Nipah virus was also attributable to the practice of boar semen trading and sharing between farms, needles or equipment sharing for health intervention, and the lack of disinfection procedures for animal transportation vehicles (Mohd Nor, 2000).

Human cases were primarily pig farm and slaughterhouse workers that had direct contact with the infected pigs. The lack of regulations and practice for the use of personal protective equipment such as gloves, mask, and gowns further exposed workers to infected secretory and excretory fluids and therefore increased the potential to contract the disease (Uppal, 2000; Mohd Nor, 2000). Exportation of live pigs as food supply due to the lack of farming land in Singapore introduced the virus to abattoir workers in that country. An extensive screening confirmed that the outbreak was only limited to a single abattoir that imported pigs from an allegedly infected farm in Malaysia (Paton et al., 1999). The abattoir was subsequently shut down and importation of pigs from Malaysia was banned in Singapore. Since the early 1990s, there was a large influx of Indonesians migrant workers in Malaysia due to better job opportunities and economy. Two pig farm workers, who returned home to Indonesia, were subsequently found infected and died. Fortunately, there was no further transmission reported in this country afterwards (Field et al., 2002).

Another series of outbreaks of Nipah virus, involving direct transmission of the virus from fruit bats to humans without a secondary host, such as pigs, have been reported almost annually from 2001 – 2013 in Bangladesh and India with a fatality rate as high as 70% (Rahman and Chakraborty, 2012; Rahman and Brown, 2013). The outbreaks in Bangladesh appeared to be distinctive from the Malaysian cases, presenting with higher percentage of respiratory symptoms compared to encephalitis (Rahman and Chakraborty, 2012). The major transmission factors were the drinking of raw date juice and direct contact with an infected patient or corpse. Date palm sap is a popular sweet drink consumed in Bangladesh and is usually collected from a cut in tree trunk through a bamboo channel into a clay pot. The collection vessels are usually uncovered, attracting fruit bats to drink the sap and occasionally leaving traces of their saliva, urine, or faeces in the pot. Although date palm sap is usually processed before consumption, many locals still consume raw date juice. With a sufficient dose of Nipah virus, humans who consumed the contaminated date palm sap...
Unlike the Nipah outbreak in Malaysia, a high incidence of human to human transmission was reported in Bangladesh. Caretakers, medical personnel, and family members were thought to have contracted the virus through physical contact with patients (Sazzad et al., 2013) likely due to exposure to bodily fluids. There were two possible cases of corpse to human transmission, where one hugged a deceased family member, while an undertaker was infected from preparing the same corpse for traditional burial (Sazzad et al., 2013).

Hendra Virus

Hendra virus is another deadly virus that emerged in 1994 in a horse training facility in Brisbane, Australia. It infected 20 horses and two humans, all of whom died except for one of the humans. This led to an immediate shutdown of the local horse racing industry. An investigation identified a previously unknown virus as the causal agent, which was later named after the suburb of outbreak Hendra. A further outbreak was reported near Mackay in Queensland, about 800km away from the initial outbreak, and multiple other incidents reported over the years (Field et al., 2001).

Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV)

Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) was first reported in 2002 in Guangdong, China. The infected patients often presented with severe pneumonia-like symptoms, however, the neurotropic potential of SARS has recently been discovered in mouse brains and human brain cell cultures (Tseng et al., 2007). The virus infection continued to spread and developed into a global pandemic in 2003, affecting more than 30 countries across all five continents. There were 8096 reported cases and 774 reported deaths.
(9.56% fatality), and the outbreak was estimated to have cost $US54 billion worldwide (Knobler et al., 2004; WHO, 2003).

The causal agent, which is now recognised as SARS Coronavirus (SARS-CoV), was postulated to have originated from horseshoe bats, its natural reservoir (Chan and Chan, 2013). The virus outspread is believed to have originated from live animal trading markets, and there are two possible route of SARS-cov being introduced into the markets. First, wild animals are believed to have come into contact with bats when exploring caves and consequently exposed to the virus, the animals were then hunted and traded at the markets (Wang and Eaton, 2007). On the other hand, the virus may have been introduced directly when bats were traded, subsequently exposed to other animals at the markets. This is believed to have occurred over multiple events until the virus adapted to the new hosts, leading to a cross-species spill over. In China, it is known that animal traders usually trade multiple species, increasing interspecies contact especially when cages were stacked on top of each other or when different animals were kept in the same cage (Wang and Eaton, 2007; Field, 2009). Moreover, there is little biosecurity enforced at markets where animal cages are usually heavily contaminated with bodily fluids and traders do not carry out hygiene protective procedures (Field, 2009). The rich custom of wildlife consumption and trading in China probably endorsed this excessive amount of interspecies viral spread. While bats are considered medicinal in Chinese culture, other wildlife is believed to be beneficial for human health (Field, 2009).

The initial human cases were all reported to have had direct contact with animals, and human to human transmission subsequently occurred via ‘super-spreading’ events where a large number of secondary infections occur from few infected individuals (Wang and Eaton, 2007). Chinese officials did not make an announcement until three months after the initial outbreak, leading to a delay in potential control protocol (Hughes, 2004). The disease spread globally soon after the outbreak due to the high connectivity of international travelling (Hughes, 2004). After seeing an infected patient, a Guangdong doctor travelled to Hong Kong and stayed in a hotel where 12 other guests were later found infected. The virus then spread globally when the international guests returned to their country, leading to infection in many other countries and eventually led to a pandemic (Hughes, 2004).

The Pandemic of Human Immunodeficiency Virus (HIV)

The HIV and the AIDS epidemic appeared in the western world in the early 1980s and represented an apparently new and lethal viral infection. While the AIDS was first characte-
rized by the often-lethal opportunistic infections and tumors that accompanied immunosuppression, we now know that it is neurotropic. HIV infects the brain very early after infection and can result clinically in cognitive impairment and dementia. This currently affects up to 50% of individuals living with HIV who have been successfully treated with antiretroviral drugs (Hult et al., 2008).

In tracing the origin of this pandemic, HIV is an example of how there can be a variety of determinants that can promote viral establishment and spread. As explained in the following, the evolution of the HIV pandemic is at the least a combination of microbial adaptation and change, economic development and land use, international trade and commerce, change in human demographics and behavior, and finally lack of political will. Below are presented a number of examples of unsuspected events that facilitated the emergence of HIV and the spread of the pandemic. Due to the brief nature of this article, the examples are not exhaustive, more comprehensive reviews can be found elsewhere (Shilts, 2007; Halperin, 2012). Contrary to the initial view that HIV is a new virus, it is now clear that HIV is a descendant of a much older virus in primates called simian immunodeficiency virus (SIV), and that HIV emerged sporadically in the late nineteenth and early twentieth century in the former Congo (Halperin, 2012).

The microbial adaptation and change provided the opportunity for the virus to jump the species barrier from monkey to human. There are probably two elements to this adaptation: The first is that SIV, from which HIV is derived, is a RNA based virus and these types of viruses have much higher mutation rates because of the high error-reading in the RNA polymerase (Domingo et al., 1996). The high mutation rate leads to the evolution of quasi-species and new species, such as the SIV found in chimpanzees that were almost identical to HIV (Gao et al., 1999). Each of the major clades of HIV: M, N, and O are each thought to represent separate transmission events into humans of newly mutated SIV/HIV (Gao et al., 1999). The opportunity for this virus to move from primate to human and then initiate its highly significant spread globally was dependent on changes in human behaviours resulting from the European colonization of Africa, especially Congo, as this geographical region represented new economic opportunities and international trade (Halperin, 2012).

The Initial Move from Primate to Humans

There were multiple factors at play here that cover the areas of economic development and land use, international trade and commerce, and change in human demographics and behavior. There are a number of theories as to how transfer to humans occurred, one theory is the neutral transfer theory, hunter theory or bush meat theory, is that the blood of chimps that were hunted, killed and eaten, got into cuts in the hunters skin, which effected viral transmission (Sharp et al., 2001). There were probably multiple transfer events, not all of which were successful. Transmission of viruses from primates to humans in Africa is still relevant today as in 2004. Wolfe et al. found that in a sample of over one thousand individuals in Cameroon, one percent was infected with simian foamy virus, an infection that was only previously thought to infect primates (Wolfe et al., 2004).

Other factors for SIV transmission to humans resulting in HIV involve the consequences the European colonization of Africa, which affected population structure and behavior (Chitnis et la., 2000). Examples include displacement of the male population to form labour forces for the colonial companies, often logging or harvesting rubber during the First World War. As a result, some local residents left their villages to avoid conscription, and those who were conscripted had little time to farm the land with a resulting increased reliance on bush meat, which would have increased the exposure opportunity to SIV in order to supply the workers with food (Chitnis et la., 2000). In one estimate a single logging camp of about 500 people in the republic of Congo resulted in an annual harvest of 8251 individual animals, equivalent to 124 tons of wild meat. The colonial infrastructure projects, such as railroad links and the establishment of steamboat services for transport of goods also resulted in increased personal mobility. This allowed the interaction of individuals who would previously never have met, thereby increasing the opportunity of transmission from infected to uninfected individuals. The labour forces and increased mobility were accompanied by a breakdown of traditional social structures and practices with labour camps having many men and few women. Chitnis (Chitnis et la., 2000) describe that women were sometimes present in the labour camps for "recreational" purposes, thereby further facilitating sexual transmission.

Another colonial practice that acted as a vector for transmission were large vaccination programs against small pox and other endemic infections, such as sleeping sickness without the proper resources to carry out the campaigns (Drucker et al., 2001; Marx et al., 2001). Two practices in particular would have facilitated multiple opportunities for transmission: They were arm-to-arm vaccination and the repeated use of needles and syringes on many individuals being vaccinated. In arm-to-arm one person is infected with pox exudate, and then when they develop a vesicular lesion exudate drawn from that lesion it is used to vaccinate the next person. Added to this was the practice of reuse of instruments; apparent-ly in one campaign to vaccinate 90,000 people against sleeping sickness, there were six syringes available and an even fewer number of needles. A further complicating factor was the arrival of Christian missionaries. The missionaries dissuaded the longstanding practice of circumcision as they saw it as heathen; it was practiced as part of a rite passage during initiation in to manhood (Halperin, 1996). Hence circumcision became uncommon. Circumcision is now recognized as a signifi-cant protective factor against the spread of HIV, almost halving the transmission of HIV in African men (Gray et al., 2007).
Colonialisation also resulted in the establishment and growth of new towns and cities, such as Kinshasa, which are postulated to have resulted in the repeated sexual spread of HIV in urbanized populations that carried other sexually transmitted diseases resulting in genital ulcers that aided the heterosexual transmission of HIV (de Sousa et al., 2010). Chitnis (Chitnis et al., 2000) described the emergence of HIV in colonial Africa coincided with various events facilitating individuals to exposure to SIV, and then the episodic spread of HIV between infected carriers as described above. The authors break the factors that facilitated the emergence of HIV down to three main groups:

1. Increased exposure risk to bush meat and/or changes in hunting or butchery practices,  
2. Increased the probability of virus transmission by sex and blood-blood routes, and  
3. Increase in the probability of virus adaptation to humans as a host, this adaption and becoming more suitable to a human rather than a primate host accelerates with increasing number of exposure events.

**Increased Viral Transmission and Establishing the Pandemic**

With the establishment of viral pool within human hosts the next step that facilitated the spread of the infection was migration and increased access to air travel. The first step was the transmission of the established HIV infection to Haiti. According to Timberg and Halperin (Halperin, 2012) in order to escape the evolving dictatorship of Francois Papa Doc in the early 1960s, many professional Haitians departed for new opportunities in Congo, which had become destabilized following the end of colonial rule. The Secretary General of the United Nations, Dag Hammarskjöld, attempted to stabilize the political situation in Congo with an infusion of skilled professionals. Apparently, the Haitian expatriates thrived especially in places like Kinshasa and they were able to afford visits home, and it is speculated that on these trips they probably took HIV with them as this probably accounts for the very high number of Haitians in the first wave of the AIDS epidemic. Those, who became infected with HIV in that first wave of the AIDS epidemic, consisted of the 4 ‘H’s: Haitians, homosexuals, hemophiliacs and heroin users. Haiti became a central node in this developing pandemic, the HIV, which was transported from Kinshasa, spread widely in Haiti, and in the 1970s, blood products were imported from Haiti to the USA (Lepin, 2011). At the same time, Haiti was a popular holiday destination for gay American men. Both of these events provided effective transmission routes to bring HIV and AIDS to continental USA to infect homosexuals and hemophiliacs. Intravenous drugs users soon became infected with HIV due to needle sharing. Three groups out of the initial four ‘H’s were socially marginalized and stigmatized during the early 1980s, and the ensuing perceived lack of political will by the US administration to tackle the growing AIDS epidemic was seen as partly responsible for allowing the epidemic to get such a grip in the US (Shilts, 2007).

The further spread of HIV to Europe was assisted by other new social trends, such as the emergence of low cost airlines. One such example was Freddie Laker, the UK entrepreneur who founded Skytrain in 1971, which provided cheap no frills flights between London and New York. Such emerging access to international travel allowed significant numbers of UK and other European gay men to visit New York and other American cities where the epidemic was silently spreading, and in their own turn contributed to bringing HIV from the States to Europe. Finally in the book “And The Band Played On: Politics, People, and the AIDS Epidemic” by Randy Shilts (Shilts, 2007), there was discussion about the role that Gaëtan Dugas, a Canadian air steward, played in the spread of the AIDS epidemic. He died in 1984 and become known as ‘patient zero’, because he could be linked with at least 40 of the first 240 AIDS cases in USA. He was thought to have carried the virus out of Africa and introduced it to the gay community on North America (Auerbach et al., 1984). However, as can be seen from the discussion above, such an assertion that Dugas was the main vector for the US epidemic may well be naive. With the recognition of the global pandemic, we have been reliant on political administrations to provide information to prevent HIV transmission, such as safer sex and safer injecting practices, screening and treatment facilities as well as providing effective anti-retroviral treatment to resource limited countries. Despite the interventions to date, an estimated 33 million people live with HIV and the cost of the pandemic is estimated to rise to $35 billion a year by 2031 (Hecht et al., 2009)

**Conclusion**

The examples described a few among the large and growing numbers of the newly emerged viruses that possess significant threat to human health. There are many other deadly zoonotic neurotropic viruses that have emerged with the evolution of humanity, known to cause encephalitis and cognitive impairment (Olival and Daszak , 2005). In the recent years, infection of neurotropic viruses such as measles, herpes, and Borna disease virus has been associated with cognitive impairment and is speculated to be a risk factor of the development of psychiatry disorders later in life, leading to a theory of viral based aetiology (Thakur et al., 2009; Watson et al., 2013). In conclusion, the sudden outbreaks of emerging viral infections, including neurotropic viruses can sometimes take decades to erupt and often occur in response to changes in the natural world or the unwitting consequences of human activity. While it is almost impossible to reverse the already emerged viruses, preventive approaches could be put in place to minimize the emergence of new viruses in the future. Many of the human behaviors mentioned in the examples could be restricted with a strengthened public health measures in order to minimize the risk factors associated with the emergence of new viruses. Only by being aware of the consequences of our actions, we can be able to diminish the frequency with which such catastrophic viral events occur.
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Overview

The 5th Edition of the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders (DSM-5) has been revised and subjected to several changes.

Elimination of Multiaxial System

A significant change is the elimination of the multiaxial system in DSM-5. The multiaxial system was first introduced into the DSM-III in 1980 in order to improve clinical assessment practices by encouraging clinicians to focus their assessment on issues above and beyond simply the psychiatric diagnosis. For example, placing medical conditions, and psychosocial, and environmental stressors on separate axes served to increase clinical focus on these important aspects of the presentation. The multiaxial system was eliminated in DSM-5 for several reasons. First of all, it was felt that having a multiaxial system of assessment put psychiatry at odds with medical diagnostic coding, creating a potential chasm between psychiatry and the rest of medicine. Moreover, it was felt that placing personality disorders on a separate Axis facilitated the reimbursement discrimination of personality disorders by allowing insurance companies to claim that personality disorders were fundamentally different than the other mental disorders in the DSM. Finally, there were questions about whether clinicians felt that the multiaxial system was clinically useful, as evidenced by the fact that most clinicians only used the multiaxial system if they were required to.

Consequently, in DSM-5 all conditions (i.e., mental disorders, personality disorders, and medical conditions) are listed together without differentiation into separate axes. Generally, the condition that was the reason for the clinical encounter is listed first, followed by the other conditions in order of decreasing clinical importance. In lieu of listing psychosocial and environmental problems on Axis IV, DSM-5 offers diagnostic codes corresponding to various kinds of psychosocial and environmental problems in the section for “Other Conditions That May be a Focus of Clinical Attention,” such as V60.0 for homelessness and V60.2 for extreme poverty.

In lieu of the GAF, DSM-5 includes the 36-item self-report version of the World Health Organization Disability Assessment Schedule (WHO-DAS) as one of the dimensional measures in Section III for “Emerging Measures and Models.” Diagnostic entities included in this section “require further study are not sufficiently well established to be a part of the official classification of mental disorders for routine clinical use” (DSM-5, page xliii). The WHO-DAS assesses disability in adults 18 years or older by asking the patient to rate how much difficulty he or she has had in specific areas of functioning over the past 30 days. Six domains of functioning are assessed, including...
“Understanding and Communicating,” “Getting Around,” “Self-care,” “Getting along with people,” “Life Activities,” and “Participation in Society.” Unfortunately, since the WHO-DAS was developed for general medical use (as opposed to psychiatric use), it contains items of questionable relevance to most psychiatric patients, such as “In the past 30 days, how much of a problem did you have washing your whole body?” and “In the past 30 days, how much of a problem did you have standing for long periods, such as 30 minutes?” Moreover, according to the instructions for use included in DSM-5, the clinician is asked to review the individual’s response on each item on the measure and to “correct” the score based on clinical interview and other information available. Thus, compared to the GAF, which can be scored in a matter of minutes, the WHO-DAS will likely take much longer, making its routine use as an ongoing measure of disability problematic.

Moving Beyond the Descriptive Approach

When the DSM-5 revision process first started over 15 years ago, the hope was that this revision would be revolutionary in terms of being able to define at least some of the disorders in terms of their neurobiological or genetic underpinnings, reflecting the long held view that psychiatric disorders are brain diseases (Kupfer et al., 2002). However, despite years of searching for objective laboratory findings that might be useful in making a psychiatric diagnosis, not a single psychiatric disorder in DSM-5 is defined using objective findings such as neuroimaging, genetic testing, or other laboratory tests. This might seem surprising given all of the advances in psychiatric research over the past 30 years in which it is common for journal articles to present pictures of brain scans showing differences in brain structure or function between individuals with a disorder, such as schizophrenia, and individuals without that disorder. The problem is that while such abnormalities can be established for groups of patients with schizophrenia compared to groups of individuals without schizophrenia, information which is useful in potentially advancing our understanding of the pathophysiology of at least some subgroups of patients with schizophrenia. These tools are not yet sufficiently diagnostically specific to help in making a diagnosis of a particular disorder in an individual patient, which is the basic task of clinicians when using the DSM diagnostic system.

Even though it was not possible to go beyond the descriptive approach to psychiatric diagnosis in terms of the content of the DSM-5 criteria sets, our albeit limited understanding of the neurobiology, genetics, temperament factors, and other risk factors underlying the DSM disorders has permitted a reconsideration of how the disorders are grouped together, the so-called “metaclassification” (Hyman, 2011). In DSM-IV, diagnostic classes were largely based on how the disorders presented symptomatically with disorders sharing common presenting symptoms included in the same diagnostic grouping. For example, the Anxiety Disorders grouping in DSM-IV included Panic disorder, the phobias, Generalized Anxiety Disorder, Obsessive-Compulsive Disorder (OCD), and Posttraumatic Stress Disorder (PTSD), reflecting the fact that patients with these disorders almost invariably present with some degree of anxiety. Although we still do not understand enough about mental disorders to base their definitions on etiology and pathophysiology, we do know enough about the underlying neurocircuitry, familial inheritance, risk factors, comorbidity patterns, and treatment response of OCD and PTSD to move them into their own separate groupings, Obsessive-Compulsive, and Related Disorders, and Trauma and Stressor-Related Disorders (Stein et al., 2011).

Consequently, the entire structure of the classification has been reorganized (see table 1), beginning with the Neurodevelopmental Disorders, which include disorders that have their onset during the neurodevelopmental period from birth to approximately age 18 (such as Intellectual Disability, Learning Disorders, Communication Disorders, Autism Spectrum Disorder, ADHD), Schizophrenia Spectrum, and Other Psychotic Disorders (which now includes Schizotypal Personality Disorder, given that it is on the genetic spectrum with Schizophrenia), Bipolar Disorders, Depressive Disorders, Anxiety Disorders, Obsessive-Compulsive and Related Disorders (which also includes Hoarding Disorder, Body Dysmorphic Disorder, Trichotillomania, and Excoriation Disorder), Trauma and Stressor-Related Disorders (which includes PTSD, Acute Stress Disorder, Adjustment Disorder, Reactive Attachment Disorder, and Disinhibited Social Engagement Disorder, the latter two included in this grouping because, by definition, they occur after exposure to a stressful life experience, in this case severely pathogenic care as an infant), Dissociative Disorders, Somatic Symptom Disorders, Feeding and Eating Disorders, Somatic Symptom and Related Disorders (which also includes Somatic Symptom Disorder, Kleptomania, Conduct Disorder, and Antisocial Personality Disorder), Substance Use and Addictive Disorders (which include Gambling Disorder in addition to the more traditional disorders associated with psychoactive substance use), Neurocognitive Disorders, Personality Disorders, and finally, the Paraphilic Disorders.

Moving Towards a More Dimensional Approach

In recognition of the limitations of the DSM-IV categorical system (Widiger and Samuel, 2005), a major emphasis of the DSM-5 revision process has been on the introduction of a dimensional component to DSM-5. “The single most important precondition for moving forward to improve the clinical and scientific utility of DSM-V will be the incorporation of simple dimensional measures for assessing syndromes within broad diagnostic categories and superordinate dimensions that cross current diagnostic boundaries” (Regier et al., 2009). During the revision process, the DSM-5 workgroups were asked to either develop severity measures (clinician-administered or
self-report) or else suggest existing severity measures for each DSM-5 disorder (First, 2013). In addition, a disability measure, the World Health Organization Disability Assessment Schedule and a modification and enhancement of the psychiatric symptom measures from the National Institute of Health’s Patient Reported Outcome Measurement Information System initiative (Irwin et al., 2010; Pilkonis et al., 2011) were proposed for inclusion in DSM-5 and tested in the DSM-5 field trials. However, because of concerns about their clinical utility, reliability and validity, the published DSM-5 ended up relegating virtually all of these dimensional measures to its Section III, the section for proposed elements of the DSM for which “the scientific evidence is not yet available to support widespread clinical use” (American Psychiatric Association, 2013).

Other changes also reflect DSM-5 taking a more dimensional view of psychopathology. In particular, the DSM-5 category of autism spectrum disorder replaces what in DSM-IV were five separate pervasive developmental disorders: Autistic disorder, Asperger’s disorder, Rett’s disorder, childhood disintegrative disorder, and pervasive developmental disorder. This reflects the DSM-5 conceptualization of autism as occurring on a spectrum, ranging from milder cases (which were called Asperger’s disorder in DSM-IV) to the more severe cases (i.e., DSM-IV’s autistic disorder). Similarly, the DSM-5 reconceptualizes substance use disorders as occurring on a severity spectrum, replacing the DSM-IV categories of Substance Abuse and Substance Dependence with a single category called Substance Use Disorder that has three specified levels of severity: “Mild”, for cases with 2 to 3 out of the 11 dimensional symptoms, “moderate” for 4-5 of the 11 symptoms, and “severe”, for 6 or more of the 11 symptoms.

There was also a proposal to replace DSM-IV personality classification consisting of 10 categories with a complex hybrid classification that included six personality disorder categories (schizotypal, borderline, antisocial, narcissistic, avoidant, and obsessive-compulsive) with a
### DSM-5 Metastructure with Corresponding DSM-IV Groupings/Disorders

<table>
<thead>
<tr>
<th>DSM-5</th>
<th>DSM-IV-TR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurodevelopmental disorders</strong></td>
<td>Disorders Usually First Diagnosed in Infancy, Childhood, or Adolescence</td>
</tr>
<tr>
<td>(Includes Intellectual Disability, Global Developmental Delay, Autistic Spectrum Disorders, Learning disorders, Communication Disorders (including Social Pragmatic Communication Disorder), ADHD, Motor Disorders (Tics, Stereotyped Movement, Coordination)</td>
<td>Mental Retardation, Learning Disorders, Communication, PDD, Tic Disorders, part of Disruptive Behavior</td>
</tr>
<tr>
<td><strong>Schizophrenia Spectrum and Other Psychotic Disorders</strong></td>
<td>Schizophrenia and Other Psychotic Disorders</td>
</tr>
<tr>
<td>Includes Schizophrenia, Schizotypal PD, Schizoaffective, Brief Psychotic, Delusional Disorder, Substance-Induced Psychotic Disorder, Psychotic Disorder Due to AMC, Catatonia Associated with Another Mental Disorder, Catatonia due to AMC</td>
<td>Schizotypal PD (in Personality Disorders)</td>
</tr>
<tr>
<td><strong>Bipolar and Related Disorders</strong></td>
<td>Mood Disorders</td>
</tr>
<tr>
<td>Includes Bipolar I, Bipolar II, Cyclothymic, Substance-Induced Bipolar, Bipolar Due to AMC</td>
<td></td>
</tr>
<tr>
<td><strong>Depressive Disorders</strong></td>
<td>Anxiety Disorders</td>
</tr>
<tr>
<td>Includes MDD, Chronic Persistent Depressive Disorder, DMD (Disruptive Mood Dysregulation Disorder), PMDD (Prenatal Dysphoric Disorder), Substance-Induced, Due to AMC</td>
<td>Separation Anxiety and Selective Mutism within Disorders Usually First Diagnosed in Infancy, Childhood or Adolescence</td>
</tr>
<tr>
<td><strong>Anxiety Disorders</strong></td>
<td>Body Dysmorphic Disorder within Somatoform Disorders</td>
</tr>
<tr>
<td>Includes Separation Anxiety, Selective Mutism, Social Anxiety, Specific Phobia, Panic, Agoraphobia, GAD, Substance-Induced Anxiety, Anxiety due to AMC</td>
<td>Trichotillomania within Impulse Control Disorders</td>
</tr>
<tr>
<td><strong>Obsessive-Compulsive and Related disorders</strong></td>
<td>Reactive Attachment Disorder within Disorders Usually First Diagnosed in Infancy, Childhood, or Adolescence, Adjustment Disorders</td>
</tr>
<tr>
<td>Includes OCD, BDD, Hoarding, Trichotillomania, Excoriation Disorder, Substance-induced, Due to AMC</td>
<td></td>
</tr>
<tr>
<td><strong>Trauma- and Stressor-Related Disorders</strong></td>
<td>Reactive Attachment Disorder within Disorders Usually First Diagnosed in Infancy, Childhood, or Adolescence, Adjustment Disorders</td>
</tr>
<tr>
<td>Includes PTSD, Acute Stress, Reactive Attachment, Disinhibited Social Engagement Disorder, Adjustment Disorders</td>
<td></td>
</tr>
<tr>
<td><strong>Dissociative Disorders</strong></td>
<td>Dissociative Disorders</td>
</tr>
<tr>
<td>Includes Depersonalization/derealization, Dissociative amnesia, DID</td>
<td></td>
</tr>
<tr>
<td><strong>Somatic Symptom Disorders</strong></td>
<td>Somatoform Disorders</td>
</tr>
<tr>
<td>Includes Somatic Symptom Disorder Illness Anxiety, Conversion Disorder, Factitious Disorder, PFAMC</td>
<td>Feeding Disorders of Infancy and Early Childhood, Eating Disorders</td>
</tr>
<tr>
<td><strong>Feeding and Eating Disorders</strong></td>
<td>Feeding Disorders of Infancy and Early Childhood</td>
</tr>
<tr>
<td>Includes Anorexia, Bulimia, Binge Eating Disorder, Avoidant/Restrictive Food Intake, Pica, Ruminatation Disorder</td>
<td>Eating Disorders</td>
</tr>
<tr>
<td><strong>Elimination Disorders</strong></td>
<td>Elimination Disorders within Disorders Usually First Diagnosed in Infancy, Childhood, or Adolescence</td>
</tr>
<tr>
<td>Includes Enuresis, Encopresis</td>
<td></td>
</tr>
<tr>
<td><strong>Sleep/Wake Disorders</strong></td>
<td>Sleep Disorders</td>
</tr>
<tr>
<td>Includes several new disorders from International Classification of Sleep Disorders including REM Sleep behavior, Restless Leg Syndrome</td>
<td>Sexual Dysfunctions within Sexual Disorders</td>
</tr>
<tr>
<td><strong>Sexual Dysfunctions</strong></td>
<td>Gender Identity Disorder within Sexual Disorders</td>
</tr>
<tr>
<td>Includes Male Hypoactive Sexual Desire Disorder, Erectile Disorder, Early Ejaculation, Delayed Ejaculation, Female Sexual Interest/Arousal Disorder, Female Orgasmic Disorder, Genito-Pelvic Pain/Penetration Disorder</td>
<td>Disruptive Behavior Disorders ODD, Conduct, Impulse Control Disorders Pyromania, Kleptomania, IED Antisocial PD within Personality Disorder</td>
</tr>
<tr>
<td><strong>Gender Dysphoria</strong></td>
<td>Substance-Related Disorder Pathological Gambling within Impulse Control Disorders</td>
</tr>
<tr>
<td><strong>Disruptive, Impulse Control, and Conduct Disorders</strong></td>
<td>Delirium, Dementia, Amnestic and Other Cognitive Disorders</td>
</tr>
<tr>
<td>Includes ODD, Conduct Disorder, Antisocial PD, Pyromania, Kleptomania, Intermittent Explosive Disorder</td>
<td>Personality Disorders</td>
</tr>
<tr>
<td><strong>Substance Use and Addictive Disorders</strong></td>
<td>Paraphilias within Sexual Disorders</td>
</tr>
<tr>
<td>Includes Substance Use, Substance-Induced, Intoxication, Withdrawal, Gambling Disorder</td>
<td></td>
</tr>
<tr>
<td><strong>Neurocognitive Disorders</strong></td>
<td>Paraphilias within Sexual Disorders</td>
</tr>
<tr>
<td>Includes Delirium, Major Neurocognitive Disorder, Mild Neurocognitive Disorder</td>
<td></td>
</tr>
<tr>
<td><strong>Personality Disorders</strong></td>
<td>Paraphilias within Sexual Disorders</td>
</tr>
<tr>
<td><strong>Paraphilic Disorders</strong></td>
<td>Paraphilias within Sexual Disorders</td>
</tr>
<tr>
<td>Table 1:</td>
<td>Table 1:</td>
</tr>
</tbody>
</table>

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five domain 25 facet trait model, which defined personality disorder in terms of having at least moderate impairment in personality functioning in at least two domains of functioning (identity, self-direction, empathy, and intimacy) plus at least one pathological personality trait (Skodol et al., 2013). The categorical and dimensional models were tied together by virtue of the diagnostic criteria for the categorical personality disorders being redefined in terms of required impairments in personality functioning and facets from the trait model. Ultimately, because of concerns about its clinical utility, validity, and usability, the proposed hybrid model was rejected and placed in the above-mentioned Section III, leaving DSM-5 with a return to the much-maligned DSM-IV personality criteria sets.

**DSM as a Living Document**

One of the oft-repeated statements about the DSM-5 during the revision process is that it is to be a “living document” (Kupfer et al., 2008). While such statements were initially primarily rhetorical in nature, infrastructure is being put into place to allow for interim revisions of the DSM-5 in response to new scientific findings. For example, let’s say a diagnostically specific, non-invasive, and relatively inexpensive laboratory test became available to diagnose Alzheimer’s disease. Rather than having to wait 10 to 15 years for it to be added as part of the next major revision (i.e., DSM-6), the change could be added to the diagnostic criteria and text for Major and mild neurocognitive disorder due to Alzheimer’s disease without changing the rest of the manual in the form on an interim revision (e.g., DSM-5.1).

Scientific findings that come from studies using the National Institute of Mental Health’s alternative Research Domain Criteria (RDoC) framework (Cuthbert and Insel, 2010) might also lead to changes in the DSM-5.1.

**Table 1: DSM-5 Metastructure with Corresponding DSM-IV Groupings/Disorders**
Major Depressive Disorder as a Neurotoxic Disease

Depressive disorders can be toxic for the brain. The purpose of this article is to clarify three points, which have to be managed in order to improve the outcome of depressive illness and avoid functional impairment and cognitive abnormalities.

Introduction: The concept of neurotoxicity applied to major depressive disorder

Apart from co-morbidity amongst neurological and psychiatric disorder, these two types of disease are accompanied by a range of symptoms involving alterations in mood, motor behavior, appetite, sleep, diurnal rhythms, and cognitive function. The precise nature of changes is difficult to define, and the relationship of changes in cognition to alterations in mood, reward, motor performance and effort can be difficult to tease out, while numerous factors modify cognitive performance and its measurement in a patient and disorder-dependent fashion. Education level, presence of a professional activity, cultural background, age, and gender are all being involved in cognitive skills, and therefore have to be taken into account in studies devoted to relationship between cognitions and psychiatric disorder. The neuropsychological test (cognitive battery) employed, its context (concomitant imaging, laboratory conditions or naturalistic), and the means of quantification (self-rating, semi-quantitative scales or informant assessment) are all key considerations as is the fact that the subject is (or is not) under treatment. While cognitive abnormalities are frequently considered as tagging the patient’s vulnerability, they may also represent a stigma of the disorder, therefore being also involved before and after (rather than only during) the current depressive episode. We have proposed the concept that major depressive episodes are being neurotoxic (Gorwood et al. 2008), explaining why for example cumulative duration of depressive episodes and their repetition have a detrimental effect on recurrence rates, the chances of antidepressant response, time to obtain remission and presence of social recovery. Such “acquired vulnerability” could be more precisely explained by a direct negative impact of depressive episodes on the brain. Memory impairment, atrophy of the hippocampus (McKinnon et al, 2009) and higher risk for dementia (Kessing, 2012) were indeed more frequently observed in patients with past depressive episodes.

We tried to further understand how depressive episodes could be neurotoxic in five studies, which try to answer different points. Firstly, the neurotoxicity of depressive episodes has been mainly demonstrated thank to direct correlation between the size of the hippocampus and the lifetime being depressed according to imagery technics. But if this effect is meaningful, it should also be observed at a clinical level. The first study was therefore devoted to a cognitive test performed by clinicians and related to the integrity of the hippocampus (delayed narrative memory). The impact of number past depressive episodes took into account all potential confusing factor - an ability we had due to the size of the studied sample (N>8.000). Secondly, we focused on older patients trying to understand if longer cumulative depressive episodes could be an explanation of their usually poorer response rate, and if with older age these patients are more vulnerable to the burden of an acute depressive episode. Thirdly, we analyzed other aspects of cognitive functions apart from memory skills, assessing attention and retardation aspects. Fourthly, we moved

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from unipolar (recurrent depressive episodes) to bipolar (manic and depressive episodes) patients, checking if the cognitive deficits, that are considered as more typical of bipolar patients, could be more clearly explained by the number of past depressive rather than past manic episodes, and if cognitive-behavioral therapy could help ‘reducing the scar’ of past episodes.

Each New Depressive Episode, Patients Lose 2% of a Hippocampus related Memory Capacity

The majority of the studies linking hippocampus and major depressive illness have employed quantitative structural or functional MRI or PET - methods which are not easy to access in ordinary clinical practice. However, hippocampal size has usually correlated inversely with illness duration. This was found in a very chronic depressed sample and in patients with variable illness durations seen in secondary care. Hippocampal size may also be related to other measures of illness intensity such as number of past hospitalizations and recurrence of the disorder. Moreover, hippocampal abnormalities have been observed to occur in the early years after illness onset. Meta-analyses have confirmed hippocampal volume reduction and the total number of depressive episodes may be particularly correlated with right hippocampal volume. The samples in imaging studies have often been rather small, and potentially unrepresentative of the majority of outpatients with depression. We have been interested by measures of cognitive function that will assay the function of the hippocampus, but are much easier to conduct on a really large scale in every day medical care. 8,229 outpatients, who fulfilled DSM-IV criteria for major depression disorder according to the clinician, were tested for delayed recall, a memory function particularly related to hippocampal integrity in man during two visits separated by 6 weeks. As expected, at presentation with depression, current illness severity was the major determinant of performance, while the intensity of previous depressive history (number and length of past
episodes) was not. However, following clinical response, at the second visit, the length of previous depressive history became more significant than current symptoms. Age, educational level, and profession had a significant independent impact.

We concluded that frequent, long or chronic states of depression have impairing effects on brain function. Therapeutically, there may be advantages in treating early for a long enough period, and for not tolerating chronicity or even partial remission. Failure to treat adequately may impair the global outcome of major depressive disorder, because brain recovery may be incomplete. The existence of even small cognitive effects has important implications for how we think about depression in the general population. There is a current tendency to demean the significance of depressive symptoms as evidence of distress rather than illness. We would not seek to dispute the distress, but our data support the idea that recurrent or prolonged depression has effects on the brain that make it a significant and disabling illness.

Older Patients Have the Same Vulnerability to Toxic Effect of Past Depressive Episodes

From the same sample we compared 1115 depressed outpatients at least 65 years old to their younger counterparts. Understanding why depressed old age patients have apparently higher memory impairment after treatment response than their younger counterpart requires disentangling different potentially contaminating factors. We define our three hypotheses as following: Poorer memory performance observed in old aged patients is explained by either lower baseline competence (which would argue that the impact of a depressive episode is the same on the hippocampus-related cognitive functions regardless of age), or by poorer treatment response (which would reinforce the importance of an adequate treatment) or by a longer lifetime being depressed (a result that would require more preventive strategy).

We were able to demonstrate once again that after treatment response, older patients have decreased narrative memory capacities compared to younger ones. But this observation was essentially explained by poorer baseline memory performance and partly because of more remaining depressive symptoms. Controlling for baseline value of delayed narrative memory abolished the role of age in memory performance after treatment response. We could rule out the role of a longer duration of past depressive episodes, if response was achieved, and an excess of remaining depressive symptoms, and concluded that the "neurotoxicity" of depressive episodes on cognitive functions that are theoretically more soliciting the hippocampus activity could have a similar impact on old age patients and younger ones, providing they respond after 6 weeks of antidepressant treatment.

Apart from Memory Impairment, Neurocognitive Retardation is also a Stigma

Neurocognitive deficits might constitute a core feature of major depressive disorder as also observed during clinical remission, predicting higher follow-up symptoms over and above initial symptoms. The cognitive functions involved concern reduced memory capacities as reminded in the previous paragraph, but also decreased flexibility and psychomotor speed, attention and set-shifting.
deficits, reduced vigilance, and psychomotor slowness.

We assessed the respective role of Retardation Depressive Scale fulfilled by the clinician and the time required to perform the neurocognitive d2 attention test and the Trail Making Test in a new sample of depressed outpatients before and after treatment remission. We found that the time needed to perform the TMT-A test reduced to a non-significant trend the direct relationship between the number of past depressive episodes and the chances of remission after treatment. Furthermore, the speed at which the TMT-A test was done was correlated to the number of past depressive episodes at baseline, but also after treatment, and even when restricting the analyses to patients in remission. Retardation might therefore capture the negative impact of past depressive episodes in accordance with Widlocher description (1983) who proposed that retardation (including both observed motor behaviour and inferred mental functions) is a ‘primary disturbance’ in affective disorders. Apart from the present study, this view is supported by different positive studies showing stable cognitive abnormalities after remission (Kessing, 1998) and even correlation between lifetime being depressed and a composite score of cognitive impairment (Hasselbach et al., 2013). If this result can be prospectively confirmed, intervention might be proposed for at-risk individuals, mainly at the early stages of depressive disorder. First-episode disorders might indeed be more sensitive to care, especially as psychotherapy early in life and at early stages of illness might reduce the rate of recurrence in depressive episodes, and as the development of psychotropic drugs is now focusing on neurocognitions (Milla et al., 2012).

Cognitive Behavioral Therapy Might Reduce the Scar

Depressive, manic, anxiety symptoms, and explicit memory for emotional words were initially assessed in 69 remitted bipolar I patients. Six months later with an attrition rate of 18.3%, patients were (Docteur et al., 2013) re-assessed after CBT or a control condition (waiting list). The expected impact of CBT was assessed through the improvement in the Dysfunctional Attitudes Scale. Controlling for age, the number of past depressive episodes (but not of past manic episodes) is significantly correlated with greater recall for negative information (r=.368) rather than less recalled neutral and positive words (r=-.220). After CBT, an increase was observed for the number of recalled neutral and positive words, whereas a decrease was observed for negative words. The number of past depressive episodes is no longer correlated with the number of recalled negative words after CBT. CBT treatment improved memory biases, alongside a reduction of depressive symptoms and a modification in the emotional representation of words. Therefore, qualitative and quantitative aspects of memories were improved, modifying the bipolar patients’ cognitive schemas, which could contribute to decrease cognitive vulnerabilities.

Conclusion

If cumulative length being depressed is toxic for the brain, why whatever we do to reduce or avoid symptoms would have positive impact on the long term. But patients frequently visit their GP or psychiatrist too late, remaining symptoms are frequently either unnoticed or tolerated, and proposing a treatment on the very long term is rare. These three points are now clearly considered as worsening the global prognosis, and convergent data seem to get to the conclusion that if we struggle against these three points, we should improve the outcome of depressive illness and avoid functional impairment and cognitive abnormalities. Associating psychotherapy also seems to help reducing the negative effect of being depressed, probably through different mechanisms.

References


