THE AGING BRAIN
Editorial

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More Than Just a Number

With another year behind us, and for our sixth issue as Editors-in-Chief, we cover a theme that makes many of us a little anxious yet no one can avoid. Whether you ask a biologist, a social scientist, or a financial analyst, aging is a talking point that is always exciting and controversial.

Is it just me or does grandpa and his friends smell funny? Will I be able to learn how to drive a hovercraft when I’m seventy? Do our brains literally slow down in our golden years? This issue, our brilliant team of authors takes a look at living longer, looking younger, and maintaining a fulfilling life in old age.

As the MedNeuro program celebrates its fifteenth year in 2016 (see News in Brief), its family of students and alumni continues to grow both in number and accomplishments. It’s no secret that victories come few and far between for graduate students, that’s why this issue we parade the accomplishments of our fellow MedNeuro members (see page 21).

With age comes wisdom, at least that’s what we’re often told. But according to our anonymous critic, science hasn’t learned its lesson and a change is long overdue (see page 21). It’s about time we applied the rules of Good Scientific Practice, and that means getting rid of some of our archaic traditions – not an easy feat.

After bidding farewell to our graphic designer Viktoria (see page 19), we welcome our talented new creative catalyst, Judith Traudes, who joined us in January. She is making sure our newsletter keeps getting better with every issue. We’re also delighted to have Helge Hasselmann joining our editorial team.

We hope you enjoy this issue – live long and prosper!

Ahmed Khalil and Apoorva Rajiv Madipakkam
Editors-in-Chief

Contest

We are always interested in including your contributions. You can submit anything you see fit on the topic of neuroscience. Send us your most exciting microscopic pictures, a creative photo, thoughts on neuroscience or self-written poems – whatever comes to mind! The best contribution will be published and rewarded with the book "Advice For A Young Investigator". So, what are you waiting for? Start the engine of your mind and get going! Trust us, it’s worth participating! Send your contribution to cns-newsletter@charite.de to win. Deadline for submission for the next issue: April 20, 2016.

This issue’s winner is Elena Kochova who wrote two excellent pieces about learning and sleep patterns in old age (see pages 9 and 16) ... Congratulations Elena and thank you very much for your contributions!
Age and Aging Societies

It is common knowledge that Western societies are facing demographic change. But why is it a problem everyone is concerned about?

Germany's Demographics

Demography is the social science dealing with statistical measures of populations, including humans. It analyzes several features of populations (including age, health, reproduction as well as migration, education and religion) in order to extrapolate future development. In Germany, the Federal Statistical Office which monitors demographics, estimated the number of inhabitants in 2014 to be more than 80 million people (the 16th most populous country in the world). The estimated average life expectancy is 81 years and the fertility rate is 1.4 children per woman [1] (in contrast to Somalia where life expectancy is less than 50 years and the fertility rate is 6.4 [2]).

Paying it Backward?

These numbers summarize what the demographic change looks like: higher life expectancy with fewer births. People live longer due to better hygiene and medical care. In addition, the more young people are educated and socio-economically situated, the fewer children they have. This is called the demographic-economic paradox [3]. Especially in Germany, the demographic change is critical as the social and health insurance systems are based on an idea called the intergenerational contract (Generationenvertrag). This system, implemented after the Second World War, required jobholders to pay taxes into a pay-as-you-go system to provide financial security for a limited number of elderly retirees [4].

Back then, considering the shape of Germany's population pyramid, the system made sense. People born in these years (1945–1965) are today commonly referred to as baby boomers [5], which justifies this concept. However, birth rates dropped steadily by 1967, plateauing since 1990 to their current levels. But, low birth rates do not keep people from aging, they only lead to fewer people taking care of an increasing number of older people. Thus, aging of the population is a socio-economic problem, which has to be addressed by significant changes in the financing of social pension programs.

Healthcare and Aging Populations

Retirees are getting older: With improved medical care, the life expectancy at birth has increased by 28 years in the last century, with women living several years longer than men [6]. Unfortunately, old age is accompanied by several age-related comorbidities.

This adds to the socio-economic costs of an aging society, as healthcare burdens increase, with rising costs and a lack of staff. To make things worse, the diseases of the elderly will be accompanied not only by an increase in the number of cases, but also an increase in complexity. Although personalized therapy is a promising solution for many diseases, it requires more extensive diagnostics leading to imbalances in the ratio of workforce to qualified personnel in the medical sector [7].

In addition, changes in household structure also play a major role in the outbreak and spreading of infections. In the olden days, families were large and infections spread easily. Now, families are much smaller. Today, however, those opposed to vaccination (“anti-vaxxers”) make society susceptible to outbreaks of numerous diseases [8].

Familial Trends

Demographic change does not solely affect societies; it also affects the family by changing its composition. In the 19th century, only a minor proportion of young adults got to know their grandparents. Today, about 80% of people have at least one living grandparent. This causes an increasing demand to nurse the elderly generation, which threatens individuals’ financial, psychological and physical abilities [6]. With improvements in gender equality and the education of women, the mean age at first childbirth has increased from 21 years in the 1970s to 25 years today. Together, these factors cause a “crunch” situation for people in their 50s and 60s where raising their children and caring for their own parents compete [6]. As families become smaller, parents distribute their money and time more equally among their offspring and grandchildren [6].

Demographic change may appear to be a problem of Western countries, but it is definitely a global one. Ten years ago, the WHO reported a global mean age of 27.6 years, with 10% of the population being older than 60 years. By 2050, the United Nations expects the mean age to be 38 years with 22% of people being older than 60. Further, the proportion of children is predicted to decrease from 30% to less than 20% [9]. The socio-economic impact of these changes cannot be ignored.

[1] bit.ly/1ScMbK1
Is Retirement Bad for Your Brain?
To Relax, Or Not to Relax, That is the Question

With less stress and fewer obligations, retiring at age 60 and relaxing for the rest of your life might solve many of your problems. Keep in mind, though, that retirement not only affects your bank account but also your mental acuity. We might all look forward to filling our days with beers and catching up with old friends, playing golf, watching movies and thinking about nothing. Appealing as that sounds, mounting evidence has revealed that retirement can have a significant impact on your cognition. As the saying goes, youth (and mental well-being) is wasted on the young!

As a case in point, a study empirically investigated the effect of retirement on cognition in the US, England, and eleven European countries [1]. It showed that retirees have reduced performance in memory tasks involving immediate and delayed recall of words. On the other hand, people still going strong at their jobs did far better on these tasks.

Brains: Use It or Lose It

Two hypotheses about mental decline after retirement have been proposed. The first states that employed people engage in a challenging atmosphere in their everyday working lives as they have to troubleshoot problems, attend meetings and so forth, on a daily basis. Retirees, on the other hand, often find themselves faced with a less stimulating environment, for instance at home, without a coherently structured day. This theory, called the “unengaged lifestyle hypothesis”, assumes that retirees don’t use their mental abilities as much as those who work [1]. The brain is like a muscle - if you don’t use it, you lose it!

The second hypothesis, called the “central hypothesis”, suggests that aging is associated with slowed mental processing. Two mechanisms are thought to be responsible for your brain hitting the brakes. The first is the “limited time mechanism”, which refers to decreased capacity to store memories. With age, the brain increasingly fails to retrieve information that is needed for accomplishing coordinated mental activities during conscious processing – in a manner of speaking, information is simply “lost”. The “simultaneity mechanism”, on the other hand, refers to the brain’s ability to handle and coordinate many tasks at the same time. Collectively known as executive functions, these mental tasks include reasoning, response inhibition and working memory [1].

Retire or Be Retired!

When you feel financially secure, take it upon yourself to make the decision to quit. Studies suggest that people who retire voluntarily tend to be in better mental and physical health than those who are forced into retirement [2]. Clearly, the take-home message is that retirement becomes less stressful when it’s voluntary. Involuntary retirement has much more serious repercussions for retirees – they tend to consume more alcohol, increase their smoking habits and decrease their physical activity [2]. As the saying goes, “the best time to start thinking about your retirement is before your boss does”.

You might think that retirees are more vulnerable to depression. This was stated in many studies referring to the relation between depression and early retirement. However, the Health and Retirement Study found that depressed employees were more likely to retire and, when they did, their depression was markedly reduced [3]. So this is one thing less to worry about. And if you are at the age where you could retire and feel overwhelmed by your job’s hazelles, looking out for a golden handshake or an early retirement plan could be your way out.

Avoiding Retirement Frustration

On the other hand, there is also some evidence pointing to beneficial effects of “staying in the game” longer: For instance, studies show that retiring at the age of 55 or earlier can endanger your mental health, as retiring later was associated with a delayed onset of Alzheimer’s disease in males [4].

As always in life, with early retirement the cup can be half empty or half full. Therefore, our wise CNS MedNeuro expert consortium has come up with an elaborate checklist that helps you avoid common downsides of retiring and maximize the most of your post-professional life:

1. Do not stop working completely: find a part time job.
2. Maintain social contact: visit family and friends, do volunteer work or be an active part of the community.
3. Stay physically active: do volunteer work or be an active part of the community.
4. Plan the future: do something you love and try new things!

[1] Rohwedder & Willis, J Econ Perspect, 2010
Careers After Retirement

As the population grows older, retirement becomes a topic that sparks heated debate - but what comes next for retirees? Many people who used to do jobs (often for decades) that come with many responsibilities and require a high level of education find themselves struggling with the sudden spare time that comes with retirement. Fortunately, retirees are not doomed to boredom. There are many opportunities whereby pensioners can invest their time for non-profit projects or continue working, but on their very own schedule [1].

"Adopt" a Child
Many retirees decide to take over an "Ehrenamt" (honorary position) which means volunteering in an organization serving the public. An appealing project here in Berlin is "Vorlese-Paten", which seeks volunteers to read texts and books to young children, especially those with a migration background [2]. Children benefit enormously from this patronage, as they actively work with the new language, an opportunity they do not have with their parents, who are not native German speakers. Similar projects focusing on teens and adults have emerged with the increasing number of refugees arriving in Germany these days. Most of them do not know any German, some only a bit of English. Here, many voluntarily invest their time to take care of the refugees' basic needs, but also to simply accompany them, teach them some German and help them find a way through the administrative jungle [3].

Back to School
Retirees who would rather not take over such responsibilities, but want to stay mentally active and keep in touch with new people, could consider applying for university (again)! You can enroll as a regular student, facing schedules and examinations also allow guest auditors [4,5]. This means that you can regularly attend lectures and seminars without the trouble of preparing for exams. "Volkshochschule" (also known as VHS) are local facilities that usually offer many different topics, ranging from Adobe Photoshop classes to Zumba training for adults [6].

Citizen Science
Another option to keep your brain active and stay in touch with others are initiatives such as citizen science. These groups take over small research projects which do not require a lot of material, but rather time and knowledge. Often, it is about topics and questions which usually would not receive funding to hire personnel. Two projects currently running in Berlin deal with urban wildlife as they evaluate fox and hedgehog populations in downtown Berlin [7] and another one investigating light pollution [8].

Be(e) Busy
If you like working outdoors, becoming a bee keeper could be an option for you. Several initiatives (e.g. "Berlin summit") teach people the importance of wild and honey bees as well as other insects and are currently seeking volunteers to contact one of the many urban gardening (also city gardening) projects [11]. These groups take care of local parks and open spaces in their neighborhoods or run community-driven gardens on roofs or abandoned places [12]. Urban gardening not only keeps people busy, but is also a useful instrument to teach children and adults alike the value of food, where it comes from and how much it takes to grow crops.

Craft Your Way to New Work
Of course, people work after retirement not only to keep themselves occupied, but also to earn some additional money. Some retirees simply continue working, as many companies are willing to keep years of experience close by and hire former employees in consulting positions [13,14]. Another option might be to start your own business, offering your expertise to others. This also includes maintaining facilities: why not hire an experienced handyman instead of having to spend hours figuring out how to remove a lost earring from the washing machine?

"Craftapreneur" might be an interesting game for everyone with skilled hands. As many of us like to learn crafts such as painting, knitting or pottery, in retirement, why would you not simply try to sell what you enjoy making? Platforms like Etsy and Dawanda allow you to easily sell your homemade goods [15,16]. However, when starting a business of any kind you have to be aware of the legal requirements, which regulate income with regard to taxes and pension [17,18].

Apparently, there are tons of options for a second career after you have finished your first one! But more importantly, many of these options do not have to wait until you retire.

[1] bit.ly/1OuRGe3
[15] http://etsy.me/1KQZQTi
[17] bit.ly/1Jgi4Qz
[18] bit.ly/1JWI3wl


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Old But Gold?
Mental Illness in Old Age

Aging is accompanied by many diverse frailties. As one of the often-overlooked problems, today’s pensioners often face significant mental illness, including dementias, depression, anxiety or delirium (and often in combination with one-another). Indeed, the Berlin Aging Study, a large study that enrolled 516 Berlin residents aged between 70 and 100 years, found that 3 out of 4 complained of at least mild psychopathological symptoms [1]. Roughly one quarter fulfilled the criteria for a full-blown diagnosis, with 18.1% showing insomnia, 17.8% depression and 13.8% dementia. Interestingly, dementia was the only diagnosis that increased with ascending age.

Comorbidity Complications
Besides mental illness, the Berlin Aging Study also reported that nearly every person beyond 70 years suffered from at least one “severe” medical illness (96%), with approximately one in three showing five or more [1]. These figures fit well with the commonly held belief that aging is a steady progression towards chronic illness – which seems true for most somatic, however not necessarily for mental, complaints. Against the backdrop of this misconception, “late-life” psychiatric problems are often under-recognized and not treated appropriately.

Geriatric Mental Health
To make matters worse (although this probably depends on the viewpoint of patient vs. clinician) geriatric depression is habitually quite mild and sub-syndromal. It is often akin to dysthymia (neurotic depression with less severe but longer lasting symptoms) with high risk of becoming a chronic condition. Adding another layer of complexity, the overlap of genuinely depressive and medical symptoms grows with age, which precludes an accurate diagnosis. For instance, insomnia and loss of appetite can be due to “idiopathic” depression, but may also follow as a symptom of “ordinary” aging. Indeed, while physical health is an important factor in depression in old age [2], the relationship is far from causal [3].

Age of Anxiety
Besides depression, anxiety disorders affect a significant percentage of old people, and are often also comorbid with depression [4]. Interestingly, the preponderance of female patients with anxiety decreases with age as compared to juvenile years; old age is actually associated with reduced prevalence of anxiety disorders except generalized anxiety [5]. The Longitudinal Aging Study Amsterdam found that roughly every tenth person was suffering from clinical anxiety, with generalized anxiety disorder being most prevalent (7.3%) [6]. On the other hand, the prevalence of other forms of anxiety, such as phobias, was surprisingly low.

The Twist in Treatment
Mental health problems in the elderly are often poorly diagnosed and inadequately treated – if at all. For instance, one study with nearly 1000 elderly participants reported that only 16% of depression and 8% of anxiety cases were receiving pharmacological treatment [7]. Worryingly, the authors claim that none of the patients had been offered psychotherapy. This comes as no surprise, since elderly people are chronically overprescribed benzodiazepines for all sorts of conditions [8], often with little concern for their adverse long-term effects. Also, they do not treat the “underlying mechanisms” (like most psychotropic drugs), but rather work superficially by exerting hypnotic/relaxing influences. Recently, benzodiazepines have been associated with increased odds of dementia, which should make clinicians wary of its indiscriminate use in this particular cohort [9].

Clearly, geriatric patients represent a special population whose medical needs and problems cannot be equated with juvenile, “medically healthy” psychiatric outpatients. However, as demographic shifts change the makeup of tomorrow’s society, clinicians will increasingly be seeing geriatric patients in their surgeries.

The claim is simple: Use personalized computer software to exercise certain cognitive capacities, and fix age-related changes in the brain. How do these computer programs actually work? Most mainstream cognitive training packages that target age-related decline based on exercises and games are drawn directly from neuropsychological tests. For example, participants might be asked to single out distractors from targets, or make fine visual acuity judgements [1].

Making the Grade
To be considered truly effective, cognitive training paradigms have to meet several benchmarks. First, they should be long-lasting: what use is an upgrade in cognitive power if it disappears the moment you step away from your computer? Several large, randomized controlled trials have shown relatively good maintenance effects after several months [1, 2, 3]. Second, researchers strive to make cognitive training generalizable. Ideally, the exercises that are performed on-screen should lead to better outcomes in everyday cognitive situations. Here, results are much more varied: some programs have great transfer effects, but others fail to apply to broad cognitive processes [1,4]. Finally, developers seek to have a direct biological readout of cognitive successes. For example, there are a number of successful studies looking at cortical volume after participation in a training program [1,5].

Buyer Beware
Despite all the excitement, there are still drawbacks to cognitive training as it exists at present. First, as with any potentially lucrative medical interventions, there are a lot of low-quality products out there that have never been tested in a scientific manner [1, 6]. Even the industry giants have succumbed to too much excitement. Just this past month, the brain training company Lumosity was fined by the Federal Trade Commission for making dubious claims about reversing aging [7].

Will cognitive training in aging ultimately live up its promises? Stay tuned!

[2] Ball et al., JAMA, 2002
[7] 1.usa.gov/IMRIE1
Why Your Body Doesn't Care About Aging Gracefully

Sure, aging is associated with decreases in memory, stamina and intellectual abilities. But besides what happens in the brain (or at least, what we know about it), how does aging affect the rest of the body?

As the basic unit of bodily function, cells unsurprisingly constitute the backbone of aging. On a cellular level, aged cells often are less functional than their younger counterparts and, at some point, sadly die to make room for the younger generation. Their time of death is determined primarily either by inborn genetic switches that triggers apoptosis (i.e. a kind of programmed cellular harikiri) or when their capacity to divide has been exhausted. In most organs (but not necessarily the brain), withering cells are not replaced, which leads to functional decline with age.

Losing Our Senses
The first functions to decline in healthy aging are visual and auditory, which usually deteriorate quite early. For instance, as we age, the eye lens become stiffer, impairing near vision ("presbyopia"), and yellows, which affects color perception. In addition, high-pitched sounds are less audible to the aging ear, a phenomenon called presbycusis, and earwax production is increased [1].

Fat Does Not Equal Fat
Muscle mass and strength also degenerate with age, although not to an extent that might be expected. Indeed, beyond roughly 60 years of age, annual strength loss was determined to be less than 3% by some [2], while others estimated a total reduction of 20-40% from age 20 to 80 [3]. Body fat takes an inverse route with age and, after 30, most of us will steadily stock up on it. For both sexes, later life often sees progressive weight loss, although, ironically, this is because fat (which weighs less) increasingly replaces lean muscle mass (which weighs more).

In quite the inverse, the protective fat layer underneath the skin thins with age, which is part of the reason why the first thing that comes to mind when people think about the elderly is wrinkly. What is more, loss of subcutaneous fatty tissue also decreases heat conservation, which, in addition with fewer sweat glands and blood vessels, compromises thermoregulation.

Irksome Innards
Despite many complaints, the digestive system remains surprisingly serviceable while we age. On the other hand, the kidney and liver lose function over time because of a progressive loss of cells, which slows metabolism. The bladder, on the other hand, can be a real pain for some people. Decreased volume, unpredictable muscle contraction and weakening of the urethral sphincter (the muscles that control when urine leaves the bladder) all contribute to senile insomnia and incontinence. Men are additionally badgered by an enlarged prostate gland that has its own effects on their ability to take a leak.

Metabolism and Immunity
The function of the endocrine system decreases with age, leading to lower levels of growth hormones, aldosterone and insulin. The drop in insulin production and sensitivity contributes to the surge in diabetes risk in older people. What's more, the aging body is less able to replace lost blood cells, because bone marrow function is decreased. This goes hand in hand with a reduction in immune efficiency in the elderly, which explains more severe courses of common colds as well as allergies. Finally, reproductive organs undertake significant changes with time in both sexes, although they are more pronounced in women.

To conclude, aging can be ugly. Really, really ugly. But, to paraphrase Maurice Chevalier, it is not so bad when you consider the alternative.

[1] http://1.usa.gov/1QyODsm

Helge Hasselmann
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How I Taught My Grandfather to Use the Computer

Learning in Old Age

My grandfather used to tell me stories of his childhood which always impressed me as much by content as by the precision of recalled details. I remember when I was 10 and at school we had to learn poems by heart, which I found extremely difficult, but which my grandfather – at the age of 80 – could still recite flawlessly! I just thought he had an amazing memory and I regretted not having inherited it. One day, he asked me to teach him to use the computer for his daily writing. I couldn’t imagine it would be difficult: after all, wasn’t using the computer the easiest thing in the world? But then I realized that for what kids learned in one session, he needed days – he had to write down each step and repeat it many, many times. I was awed – how could he remember such detail from his childhood and not remember how to double-click? Long before I got involved in neurosciences I started thinking: What is it that makes the brains of children and the elderly so different? If children’s brains are like sponges, what happens to them as we get older?

Too Old to Learn?
That fact that cognitive performance declines with age is widely accepted as an axiomatic truth – we all attribute misplacing keys or forgetting names to aging, but can we be ‘too old’ to learn new things? Let’s take language acquisition as a prototype of learning. The critical period hypothesis states that in humans, new languages are best learned up to 6-7 years of age. Likewise for songbirds, the first two months are crucial. However, we now know that brain plasticity continues into adulthood and although there is definitely a difference in the process of learning compared to childhood (such as the time of acquisition and the fluency of word production), language can certainly be learned at an older age.

Strategies that enhance learning abilities in late adulthood have been identified and are based on incremental learning. For example, in adult barn owls, the plasticity of the auditory space map, a localization pathway that has severely limited adjustment capacity in adulthood, increases when an incremental learning approach is used [1]. This reveals the importance of learning methods shown in other brain systems as well, such as skill learning.

Aging Affects Memory Selectively
Working memory is most affected by aging and might mediate decline in other cognitive domains. Non-declarative (implicit) memory, a type of long term memory is relatively spared compared to episodic memory which seems to be more vulnerable to aging. While older adults learn and perform procedural sequences at a slower rate, after initial acquisition, they can relearn a procedural memory task at rates similar to younger adults, even after a pause of two years [2]. The fact that experience can actually be considered an advantage in the learning process may explain why older generations encounter difficulties with technology to which they have never been exposed to during their younger years.

With appropriate methods as well as compensation for other limitations (such as visual or hearing problems) learning is certainly possible far into old age, especially with adequate motivation. Tolstoy learned to ride a bicycle at 67, Queen Victoria learned Hindustani at 70, and my grandfather learned to use the computer at 87. These are all examples of learning much later than any defined “critical period.”

Individual Variability
Genetic factors, health issues (especially cerebrovascular and cardiovascular risk factors) and lifestyle cause variability in cognitive aging. Cognitive reserve is another factor - the brain's functional ability remains best when used regularly and a higher education level correlates with slower cognitive aging. Declarative (explicit) memory scores of older adults with lower levels of literacy decline at a greater rate [2].

Redefining plasticity windows and triggering new ones or reactivating the learning capacity of a child in adulthood could increase our capacity to learn as we age (and improve my ability to learn German, fingers crossed). It could also promote the recovery of patients with many neurological disorders. Learning adds significance to life and keeps us happy and fulfilled. Luckily, it doesn't end with high school or university.


Elena Kochova
MSc Student, MedNeuro

Source: Photo (cc-by-nc) Richard Pyrker, Flickr
Forever Young: Lessons in Longer Living from Around the World

Aging – Our Enemy?
We have all experienced a feeling of panic and unease at some point when thinking about our age. It usually first hits us as we approach 30, but also probably returns when we retire. Reasons for this may lie in the expectations we have for ourselves at the age of let’s say 18, when looking into our future. We expect to look at an extensive summary of our huge achievements, a clear purpose we served and a (mostly) fully functional body and mind. But finding us far from this ideal position can have disillusioning effects. So how can we learn to live the right way from people who have already gone far?

Longevity expert Dan Buettner and his team fathered the term “Blue Zones” to describe little corners on Earth where people live on average a longer and healthier life than in ‘Western’ countries. Their lifestyles add 7-11 years to the average Western life expectancy. Their huge cluster of over 90-year-olds is as impressive as the striking number of 80+ to 90-year-olds of the Blue Zone populations that experience Alzheimer’s and dementia – just a fraction of Western incidence rates [1]. Based on this information, one might think that these Blue Zones populations might have cracked the secrets of longevity.

Mapping the Blue Zones
Three examples of Blue Zones are the Japanese island of Okinawa, parts of the Italian island of Sardinia and Loma Linda in California, USA, each of which independently developed their own ways of life.

Okinawans follow strongly Confucius’ theories, which are ‘moais’: keep lifelong friends (which also serve as close social support groups), ‘hara hachi bu’ (eat until you are 80% full) and ‘iki-gai’ (find a purpose for which you wake up every morning).

Part of the reason for Sardinia’s longevity may be genetic, but scientists believe that only 20-30% of the adult lifespan is accounted for by genetic factors [2]. The Mediterranean diet might explain their longevity. They eat lots of goat cheese and other omega-3 rich foods, drink red wine in moderation and walk a lot, but also take their time for leisure and share the work burden with their spouses.

The religious group of Adventists in Loma Linda integrated their healthy habits to their belief system, by eating and having strategies that prevent overeating. Despite the increasing awareness of healthy nutrition, the vast majority of the Western population is careless about what and how they eat.

(4) The foundation of all of this is how Blue Zone populations connect. They put their families first, take care of their children and aging parents and belong to a faith-based community. But the most important point is they belong to the right tribe, either by being born in it or by pro-actively surrounding themselves by the right people. Both healthy and unhealthy lifestyles of our loved ones, such as our friends, will probably have a measurable impact on our behavior over time.

When it comes to longevity there is no short-term treatment or miracle pill. But when you think about it, choosing the right friends is probably the most significant long-term action we could take to “add more years to our lives and more life to our years” [5].

Make Your Years Count
Dan Buettner and his team summarized the common components of Blue Zones into 4 main points [4]:

(1) All cultures move naturally and constantly using every single occasion. In our society the idea of exercise mostly means to work out for only 30-60 minutes every two or three days, whereas we forget our urge for exercise when we have to decide whether to take the stairs or escalator.

(2) The Blue Zones know how to live with the right outlook to life. Each of these cultures takes time to relax by praying or caring for ancestors. When we are in a hurry and stressed out, our bodies trigger inflammatory responses that are associated with all kinds of disorders, from Alzheimer’s to cardiovascular disease. Slowing down for a few moments may turn these responses anti-inflammatory.

(3) There is no longevity diet, instead these people drink a little bit of red wine, they tend to eat plant-based diets and have strategies that prevent overeating. Despite the increasing awareness of healthy nutrition, the vast majority of the Western population is careless about what and how they eat.

(4) The foundation of all of this is how Blue Zone populations connect. They put their families first, take care of their children and aging parents and belong to a faith-based community. But the most important point is they belong to the right tribe, either by being born in it or by pro-actively surrounding themselves by the right people. Both healthy and unhealthy lifestyles of our loved ones, such as our friends, will probably have a measurable impact on our behavior over time.

When it comes to longevity there is no short-term treatment or miracle pill. But when you think about it, choosing the right friends is probably the most significant long-term action we could take to “add more years to our lives and more life to our years” [5].

[1] www.bluezones.com
Intergenerational Integration

Interaction and communication between different generations are not necessarily easy. Young people are full of energy, dreams and projects. Elderly people are full of experience and wisdom to share. Both generations are very distinct; they are separated by several years and usually have different perspectives and expectations about life. At the same time, though, they can have a lot in common, such as similar interests, hobbies or simply a lot of stories to share.

In order to provide a solution to the needs of both, the elderly and the young, and to improve the quality of life of these two generations, several initiatives have emerged, allowing an integration between these two groups. “Homeshare” and “Speaking Exchange” are two of these great programs. They are based on the principle of exchange that both parts have needs to fulfill but also a lot to give in return.

Homeshare

The purpose of this program is to offer accommodation in exchange for help with domestic duties and companionship. It emerged as a solution for the high demand of students looking for cheap accommodation. It provides a solution to the needs of the two parts: the householder and the homesharer. The homesharer is usually a young student in need of affordable housing, and the householder, an older person living alone, in need of support to be able to live at home rather than going to a nursing home [1]. The accommodation price is agreed by the two parts, as well as the level of support that can include household tasks, gardening, shopping, cooking, pet care and companionship.

This program was created in 1972 in USA by the late Maggie Kuhn, who dedicated part of her life to advocate for elderly rights [2]. Since then, the initiative has been spread around the world, particularly in Europe and Australia. In the UK, the first official program was launched in 1993, and in Spain it started in 1991 with the name “alojamiento por compañía” or “housing for companionship”, following the same principle [3]. The program is now officially running in 14 countries around the world, including Germany, France, Italy, New Zealand and Canada.

Homeshare has been very successful. As mentioned on their homepage, students have the opportunity to interact directly with native English speakers from a retirement house via video chat. CNA students are connected over the Internet with seniors living at the Windsor Park Retirement community in Chicago. They spend some time talking freely to each other and later the conversation is uploaded to a private Youtube channel to be evaluated by one of the English teachers [4].

Speaking Exchange

Another initiative was implemented in 2014 by CNA, a Brazilian language school, based on the same win-win principle [4]. In this case, young language students have the opportunity to interact with native English speakers who are living in a retirement house. The idea came up because there are many students in Brazil trying to learn English and speak fluently but most of them do not have the chance to travel abroad and interact with native English speakers. On the other hand, for the elderly people it is very motivating; they have the chance to do an activity that is different from their daily routine, share experiences and also learn about other cultures.

The project, which is still in its trial period, was proposed with the slogan “more than better students, better people” [5]. Its purpose is to provide useful tools to students who want to practice and improve their English skills while they offer companionship and even friendship to elderly people who only want someone to talk to. “A conversation exercise is also an act of solidarity and personal growth. It is an exchange in which everyone wins” [5].

Laura Moreno Velasquez
PhD Student, AG Schmitz

MORE THAN BETTER STUDENTS, BETTER PEOPLE

A WIN-WIN SITUATION


* CNA Speaking Exchange website - visit for touching examples of intergenerational integration
The Gray Wave (Of Excitement)

Go just about anywhere in the world, and ask what happens to the brain when we age. “It slows down”. “You start having problems remembering things”. “You get confused more often”. Everyone has an idea of what cognitive decline during aging looks like. But ask a scientist, and you might just end up with more questions than answers. Understanding what happens in the brain during aging is a massive (and some would say, massively underrated) field of study. There are hundreds of papers concerned with genetic and metabolic changes in the brain, not to mention studies of large-scale structural processes such as demyelination. However, this article will focus on just one question: what’s so exciting about aging?

All Together, Now!

The way we talk about aging, especially in the brain, has to do a lot with speed. As we age, our bodies seem to move more slowly, and it takes longer for well-known facts to spring to mind. Does this mean that brain activity is also slowing, eventually coming to a grinding halt? Quite the contrary! Many fMRI studies have shown that loads of areas, particularly in the frontal cortex, actually increase activity with aging [1]. Then why is performance still lower on cognitive tasks compared to younger controls? One major hypothesis is that this extra activity is a form of compensation, whereby more processing power is siphoned off to new brain regions to make up for ones that are lagging. But it is still unclear whether this is ultimately adaptive [1].

A related theory has to do with generalization of cognitive tasks: operations that formerly required a single structure or area are spread to new ones. In other words, patterns of activity in the aging brain may be far less specialized than in younger brains [1]. These findings in humans have been corroborated by more invasive work in aged animals. For example, several groups have looked at tonotopic mapping in the primary auditory cortex. In younger animals, neurons that respond to tones of increasing frequency are mapped in an orderly fashion (not too unlike a piano keyboard) on the cortex. However, in older animals, the once organized map is smeared out, meaning that responding to specific frequencies is suddenly a free-for-all [2]. Similar findings have also been documented in the human, rodent, and monkey visual cortices [1,2,3]. Therefore, many researchers conceptualize cognitive decline during aging as a form of inefficiency: the young brain’s neurons are selective. In the aging brain, everyone gets to join the party!

The Old and the Restless (Neurons)

One theory behind this diffuse, disorganized activity is a fundamental deficit in inhibitory neurotransmission. Once again, both animal and human data appear to support this idea. For example, it is well known that older adults generally perform poorly on cognitive tasks that require high suppression of responses and low distractibility – both functions in which inhibitory neurotransmission plays a critical role [1,2,4,5]. More indirectly, it is known that the incidence of epilepsy greatly increases with aging [6]. Hyperexcitability and selective neuron loss have been reported in several cortical areas of aged rodents and primates, and correlate well with cognitive decline [4,5]. Authors somewhat disagree on the exact neuronal populations affected first (or most severely), but the overall pattern is hard to deny.

BRAIN ACTIVITY INCREASES WITH AGING

What is it about these interneurons that make them especially susceptible to age-related changes? To put it simply, many of these cell types, particularly fast-spiking varieties have a very high metabolism. This means that they are exquisitely sensitive to changes in the extracellular milieu, including generation of reactive oxygen species or other markers of cellular stress [7]. Therefore, it is hypothesized that they are the first to suffer from small age- or disease-related changes, for example, blood flow. To add insult to injury, as it were, these interneurons are also critical for many forms of large-scale network activity such as theta and gamma oscillations [7]. Therefore, age-related decline of inhibitory interneuron populations could potentially have consequences for interregional, cognition-related activity.

Take a Chill Pill, Already

If, indeed, a decline in inhibition is responsible for many of the cognitive hallmarks of aging, what is the remedy? As you might have guessed, many groups have experimented with cranking up inhibitory tone. Several studies have used the common anti-epileptic levetiracetam to test whether enhancing GABAAergic transmission correlates with better cognitive outcomes. Indeed, in both rodents and humans, this approach correlated with reduced hippocampal overexcitation, and improvement on several working memory tasks [4].

So should all elderly individuals kick back with a steady dose of tranquilizers? There may actually be easier ways to achieve the same effect. Recently, interest has been growing in the applicability of cognitive training in reducing age-related deficits and potentially salutary deficits in inhibition. Without getting into the nuts and bolts (that’s on page 7), some approaches appear to be quite efficient [1,2]. For example, in rodents, a regimented auditory training paradigm was found to both normalize age-related abnormalities in receptive fields, and increase expression of markers for inhibitory interneurons [2]. Changes after cognitive training for humans have yet to be mapped out in such detail, but it is an exciting new field that may hold great promise for altering neurochemical and structural changes that happen during aging.

1. Grady, Nat Rev Neurosci, 2012
2. Mishra et al., Neuron, 2014
3. Liang et al., Brain Res, 2012
5. Pires et al., Neuropsychol Rev, 2014

Constance Holman
PhD Student, AG Schmitz

The Philosopher's Stone
Anti-Aging Compounds and the Science Behind Them

Since long before the first Harry Potter book came out, the idea of a philosopher's stone, or the 'elixir of life', has existed. The search for something – anything – with rejuvenating properties has always been a popular scientific topic. There are countless products on the market promising anti-aging effects and a more youthful appearance. But what are the mechanisms behind their active ingredients? And do they really lead to substantial improvement?

Peptides
As we age, our body produces less collagen and elastin, so our skin becomes thinner and less plump. Many anti-aging creams contain different types of peptides – most frequently pentapeptides and copper peptides. It is believed they are able to stimulate skin cells and increase the production of collagen and elastin. But there is no convincing evidence supporting their effectiveness. Also, peptides are rather large molecules and may not be able to penetrate deeply enough into the skin to exert a beneficial effect [1].

Hydroxy acids
Hydroxy acids – including glycolic, citric, lactic and salicylic acids – work as exfoliants. They remove the upper layer of dead skin and stimulate the growth of new skin cells underneath. In this way, they allow for a faster appearance of a fresh layer of skin. The results, however, are not always very evident and their use may cause skin irritation and sensitivity [2].

Retinol
Retinol is one of the forms of vitamin A, which is essential for skin health. Dermatologists seem to find this compound one of the most effective ones for reducing signs of aging. Retinoids increase cell turnover, improve collagen synthesis and help the skin retain more water. Retinoic acid (also called tretinoin) seems to be a more potent form of retinol, but also has stronger side effects and is only available via prescription. Pregnant women should not make use of retinol products, as they may affect embryonic development [3].

Antioxidants
A major part of the cell damage and inflammation observed in aging processes is attributed to the oxidation caused by free radicals and reactive oxygen species. Antioxidants work on the opposite direction and are therefore believed to prevent these harmful effects. Substances with antioxidant properties are found in many foods, as well as supplements and moisturizers. These include beta-carotene, lycopene, selenium, and vitamins A, C and E [2].

In addition to skin creams, more promising pills are increasingly gaining market.

Resveratrol
Sirtuin is a family of enzymes capable of regulating epigenetic gene silencing associated with aging. Researchers have found that boosting the activity of sirtuins can extend lifespan of yeasts, worms, mice, and other animals. Two compounds that are able to increase the activity of sirtuins are resveratrol and the metabolic co-enzyme nicotinamide adenine dinucleotide, or NAD+ [4].

Resveratrol can be found in red wine and is also available as oral supplement. It has numerous biological functions and is being studied for possible application in prevention and treatment of cancer, cardiovascular disease, and neurodegenerative diseases. Although its administration has been shown to slow down age-related decline in several species [4], similar effects have not yet been confirmed in humans.

NAD+
Over time, bodily levels of NAD+ decrease. Replenishing this critical compound had significant rejuvenating effects in mice muscles. In 2013, Harvard researcher David Sinclair (who also pioneered findings on resveratrol) and his group showed that after giving two-year-old mice a boost of NAD+ for a week, their tissues looked more like those of six-month-old mice [5].

Very recently, the startup Elysium Health, cofounded by Sinclair’s former mentor Leonard Guarente, started selling online their first version of NAD replacement: a pill called Basis. Since it would take decades to prove that a drug that extends the lifespan of animals can do the same in people, Elysium Health decided to market his pill as a ‘nutraceutical’, which does not require clinical trials or approval from the FDA (Food and Drug Administration). They plan to follow up with clients over time using surveys and post-marketing studies. Until something more concrete is proved, the scientists claim they do not propose to increase lifespan, but "healthspan" [6].

The Fountain of Youth
For those who prefer not to seek help in the pharmacy, the good news is that calorie restriction diets and regular physical activity are known to cause similar effects to NAD+ [5]. In addition, skin treatment compounds are present in many foods, including fruits, vegetables, and milk. But since the ultimate goal would be to slow down aging without interfering much in our habits, researchers need to continue their efforts towards finding a "magical" solution.


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PhD Student, AG Harms

Source: Wikimedia Commons (bit.ly/1nC3GrI)
When using the phrase “old person smell”, an image is immediately conjured of stuffy nursing homes, old houses, and perhaps even a touch of old perfume or cologne. In other words, a pungent combination. But do older humans really smell any different than their younger counterparts, or is this just another form of tired ageism?

One of the first teams to systematically study “old person smell” had volunteers wear special underarm pads in t-shirts at night. After subjecting the samples to mass spectrometry, they determined that the chemical compound 2-nonenal (described poetically by the authors as “grassy and greasy”) was most elevated in elderly participants. The chemists running the study reasoned that age-related changes in metabolism, namely breakdown of fatty acids on participants’ skin, was likely to blame for the chemical’s presence [1].

So even if “old person smell” had a chemical substrate, is it clearly distinguishable from body odors of younger people? In a more recent t-shirt sample study, a research group had students try and guess the age of the participants from which samples came. And lo and behold, while samples from young and middle-aged participants were often confused, samples from the elderly stood out a mile away [2].

The Sweet Smell of Senescence

However, the punchline of this study came in a second segment, where the smelling participants were asked to rate the body odors for pleasantness and intensity. Here, the smell of samples from elderly men were rated the least intense and most pleasant (in contrast, middle-aged men had the “worst” smell in the study). So it seems that “old person smell” isn’t as aversive as we are led to believe. And there may be a very good reason from evolutionary biology for this: if a person manages to survive to old (or very old) age, they likely have a good combination of genes and intelligence [2]. Exactly the type of (older) person our ancestors would love to hang around!


How Old Are We Really?

Comedian Chris Rock once said, “If a woman tells you she's twenty and looks sixteen, she’s twelve. If she tells you she's twenty-six and looks twenty-six, she's probably near forty.” Funnilly, there is some truth in his words. Researchers published a study in July 2015 whose results can basically be summed up as – if you think you look older and you feel older than you are, it is because you probably are older [1]. So what does this actually mean?

Researchers followed approximately 1000 individuals from birth up until the age of 38. Eighteen different biological markers such as cholesterol levels, gum health, DNA and body mass index, among others, were monitored over a period of 12 years (from age 26 to 38). The aim was to see the rate of change in these parameters in different people.

The results showed that their sample of adults with a ‘chronological age’ of 38 had ‘biological ages’ varying from 28 to 61! In other words, a 38-year-old sometimes had the cholesterol profile and cardiovascular tissue structure of a 61-year-old. The scientists also calculated the ‘pace of aging’, i.e. how much organs changed in one chronological year. While some people showed zero years of biological change per chronological year, others showed three years of biological change in the same time. So people with an older biological age had a more rapid pace of aging. This higher biological age was also associated with feeling less healthy and looking older at age 38 [2].

Unfortunately we do not know yet whether drug treatment or lifestyle changes can impact biological aging, but we certainly now know why some 80-year-old people can still go skiing!


Apoorva Rajiv Madipakkam
PhD Student, AG Sterzer

IT’S KIND OF GRASSY AND GREASY

Source: Wikimedia Commons

Old Spice?

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That Smells Like Grandpa

The Science Behind Odors of the Elderly

Constance Holman
PhD Student, AG Schmitz

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Progeria: Tumbling Through Time

In F. Scott Fitzgerald’s short story “The Curious Case of Benjamin Button”, the title character is born an old man and gets younger until he dies at 84 years of age in the body of a newborn. It’s extremely bizarre, perhaps even for a work of fiction, but reality can be just as odd.

Imagine an eighty-year lifespan – complete with all its biological ups and downs – condensed into little more than a decade. People with a disorder known as progeria age about ten times faster than normal from the moment they are born. Hard to believe? First described over a hundred years ago [1], the disease is very real but fortunately very rare, with only about one hundred people living with it worldwide.

At birth, there is nothing unusual about babies with progeria. But within a few months their hair starts to fall out and their skin becomes thin and wrinkled. On the inside, their arteries harden decades before the process usually starts and, as a result, they suffer from kidney disease, blindness, and heart problems. Shortly after learning to walk, the structure of their bones disintegrates and they often cannot move properly because of stiff joints.

Physically, they do not grow much, but their psychosocial development and mental capacities are normal. They usually die before adolescence of heart attacks or stroke [2].

The usual culprit in progeria is a mutation in the LMNA gene, which encodes a protein that helps maintain cell stability [3]. As a result, the cell’s nucleus is damaged, which causes these dramatic features of aging to appear (although it is not clear exactly how).

Perhaps studying this fascinating but devastating disorder can help us understand more about how and why we age.

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Ethics and Biogerontology

Is it unethical to do research on aging? In light of an increased interest in biogerontology (i.e. the study of aging), several ethical, religious, and social questions have come up. Here, I will mention one of the main objections towards this kind of research – you know, just to get you thinking.

The Nature of Aging

One major objection towards biogerontology is that it is tries to alter a natural process and thus goes against nature itself. But then what is natural and what is not? One could argue that we are already taking measures to improve and even halt the natural processes of life. Take, for instance, the use of medicine against chronic pathologies. We have decided that it is not okay to live with diabetes, so we have taken measures to do something about it, even though it undoubtedly alters the life course of a diabetic patient [1,2].

Should We "Cure" Aging?

Is Aging a Disease?

So, when are we obliged to do something, and when should we let nature take its course? Biogerontologists often point to the fact that their main research focus is on age-related pathologies. Given the debate on what is natural and not, is diabetes at a young age an unnatural event, whereas Alzheimer’s disease a natural part of life? Is curing cancer in young people something we are morally obliged to do, whereas curing elderly cancer patients starts becoming problematic as it may increase their (already lengthy) lifespan? It is difficult to draw the line [2].

The ethics of biogerontology often comes down to the definition of aging and whether it can be considered a disease. In fact, it has been proposed that aging itself should be redefined clinically as a disease state [2]. But does this include aging as a whole? Surely there is more to it than pathology. And if aging is a disease state, then the next question that arises is whether it is a pathology that requires a cure.

Sleep Patterns Across the Lifespan

We are all familiar with the concept of ‘sleeping like a baby’. But why do babies sleep so much (other than to keep parents sane)? What is the difference between the quality of sleep in a newborn and, say, an 80-year old?

The Dreaming Fetus
Sleep patterns can be seen even in the fetus, whose main job is, in fact, to sleep in the cozy womb while being devotedly nourished by his sleep-deprived mother. The wake-sleep cycle emerges somewhere around 32 weeks of gestation; both ‘active’ and ‘silent’ sleep phases can be distinguished, comparable to REM (rapid eye movement) and NREM (non-rapid eye movement). Short periods resembling the waking state interfere, but are still immature and disorganized; they comprise only 5% of fetal life. The spontaneous twitching ("kicking") of the fetus is more indicative of REM sleep than wakefulness [1] and is essential for the development of somatosensory maps in the brain [2]. Precisely how sleep "happens" is far from understood, but these findings show that sleep generator neurons mature prior to other brain areas and that sleep plays a role in the overall development of the neocortex.

Sleeping Like a Baby
Right after birth, newborns encounter a new problem: food. With a small stomach they have to eat frequently and save energy for their incredibly fast growth. The average newborn sleeps around 18 hours a day, which reduces to 14 hours by the end of the first month. Similarly to the fetus, ‘active sleep’ is interchanged with ‘quiet sleep’ - the deep sleep that enables babies to sleep through a concert. As the baby grows, feeding becomes less frequent and the circadian sleep rhythm starts to develop; usually at about 7 months, infants sleep mostly at night, with a few naps during the day. The latter tend to condense with time and the sleeping pattern becomes stable. Toddlers will usually sleep 10-12 hours every night while afternoon napping gradually becomes less important and disappears by the age of 5 years.

Puberty and Adolescence
Somewhere after the age of 10, a significant change in the sleep pattern occurs. It is no coincidence that this is when puberty kicks in. We often blame social interactions for teenagers’ nocturnal behavior, but the drive to fall asleep late in this population has a physiological background. Pubertal changes alter the homeostatic and circadian regulation of sleep resulting in a shift in the circadian rhythm of 1-3 hours.

The tendency to fall asleep later is also more pronounced in boys than girls. They tend to be more active in the evening and sleepy during the day. Teenagers have an internal clock that interprets environmental time cues differently from adults. The need to wake up early for school and the need for more sleep causes sleep deprivation in most teenagers. Grades go up when teenagers go to school later in the day [3].

Animal studies show similar changes in sleep patterns around the time of sexual maturation in mice, rats and monkeys [4]. Removal of the gonads and the administration of estrogen, testosterone, or progesterone produce immediate effects on the circadian properties and sleep architecture of adult rodents [5].

Adulthood
In the early twenties, sleep delay and sleep need are balanced at about 8 hours. It is thought that the need for sleep diminishes in older adults; in fact, what changes is the sleep architecture - it is more difficult falling and staying asleep. Sleep becomes a less restorative and less satisfying reward. There is yet another shift in the circadian rhythm: the elderly go to bed and wake up earlier compared to younger adults - a sleep phase similar to that of early childhood. The sleep is fragmented with frequent awakenings, often causing daytime sleepiness and the tendency to ‘doze off’. The prevalence of insomnia and sleep apnea increases with age, especially in men. Pregnancy and menopause cause drastic changes in women as well, further indicating that hormones play a role in the circadian rhythm and homeostatic drive. Associated medical problems and medications certainly contribute to sleep disturbances.

It appears that the more time people have, the less they are able to indulge in sleep. But sleep patterns are both a reflection of, and an influence on, the overall health of a person. Certain acute and chronic factors (caffeine or alcohol intake, exercise and nutrition, stress) are major determinants of sleep hygiene. Until science provides more detailed answers about the precise role of sleep, we continue with the vague knowledge that we need sleep for our physical and mental wellbeing.

With that I leave you, hoping that reading this has not augmented your sleep need.

Who Wants to Live Forever?

Biogerontology (the study of the biological aspects of aging) is a particular field of research that is struggling for recognition by the scientific community as a proper intellectual domain. One impeding factor is the difficulty to separate this field of study from the “anti-aging” industry, which have somewhat of a blemished history and tarnished reputation (see “The Philosopher’s Stone” on page 13). Nevertheless, biogerontology has slowly started to become more accepted and, in parallel, the interest in age-related research has started to boom. So if these scientists are not just producing anti-aging products, what are they doing?

The Puzzling Questions

Separating the anti-aging industry from the work of a biogerontologist is difficult, mainly because they are trying to achieve similar ends. However, for a biogerontologist, the focus is to understand what aging is (a solid definition is still lacking) as well as to understand the aging process. Ultimately, their goal is to alter the degenerative process of aging and thus to keep people healthy and fully functional up until the time of death [1].

The intriguing thing about biogerontology is that the most basic questions still remain unanswered. As such, it is a field of study where possible breakthroughs may lurk in the distance. One fascinating question includes why some species in general live longer than others (reference inter-species aging article?). Getting old is a universal across all species, yet horses generally live longer than rats but have shorter lives than humans. Aging affects species in a similar fashion, such as losing hair and muscle tone, getting age-related diseases etc. Yet, these happen at a differential rate across species. We still do not know why this is the case [1].

What are They Working On?

When it comes to investigating the lifespan, biogerontologists have often turned to genetics. Several genetic pro-longevity mutations have been identified by the usage of model organisms such as yeast, fruit flies and mice. Most of the identified genes are involved in aspects specific to evolution, including growth regulation, energy and reproduction.

Apart from genetics, specific prominent models have emerged. One model that especially has attracted attention is the so-called “Naked mole rat” – also known as the “supermodel” of age research. The mouse-sized rat is normally found in the horn of Africa and has a marvelous lifespan of 30 years (!), as compared to the average 3 years of a normal lab rat [2]. Its long life span has been linked to its good health and cancer resistance. So obviously some processes have evolved in these species that allow them to stay fit for such a long time in comparison to a lab rat. Surprisingly enough, these rats exhibit high levels of oxidative stress and short telomeres – findings usually linked to an accelerated aging process. Yet, despite this, they still cope well with cellular stressors and show stable genetic integrity. The mechanism of how they are able to do this still remains a mystery [3].

Any Breakthroughs Yet?

There is still a lot which remains to be discovered. Yet, one major finding in aging research is that dietary restriction (under-feeding with a 30-40% reduction in calories, without malnutrition) extends life in both nematodes, spiders and dogs. The idea that life is prolonged during times of less food is thought to serve as an evolutionary advantage, as this enables animals to postpone reproduction until food is available. The underlying mechanism is unclear, yet the hypothesis is that decreased caloric intake slows down metabolic activity, thus reducing the production of toxic reactive oxygen species and ultimately the aging process [4,5].

Can We Extend Life?

Biogerontologists do find that different genes/pathway/processes are involved in the aging process when investigating different species. Despite this, translational approaches are challenging as aging processes, while bearing similarities across species (e.g. the effect of dietary restriction), also substantially differ from one another (naked mole rat vs a lab rat).

This brings us to the general problem of translating preclinical findings into something useful in the clinics. Considering that we still need to understand the basic mechanism of aging, there is a long way to go before eternal life is possible. We will all eventually “suffer” from getting old. Yet, who knows? Given the increased interest in biogerontology, aging might with time (ironically) become a process which, to some extent, can be postponed or at least improved.


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The “supermodel” of age research - the naked mole rat
Source: http://bit.ly/In4aVZa
Twilight

It is a regular weekday in the spring of 1965. Sara, a mother of two and a registered nurse at the local hospital, gets ready for everyday’s hassle. She prepares breakfast, rushes her kids to school, and heads towards a seemingly endless 8-hour shift. Like every other human being, Sarah’s life is a motion in time, sometimes she stumbles upon the inevitable hardship of being and other times she enjoys her moments, every day and every event is a matter of the passing of time. While Sara struggles with today’s details, deep down within her memory there is a little girl running around the park with her little brother and enjoying a small meal her mother prepared with patience and love. And somewhere else is a dream she carries for her children’s tomorrow - but all she has is a present whose passing relies on the meticulous beating of her heart. As Khalil Jibran said, “The timeless in you is aware of life’s timelessness. And knows that yesterday is but today’s memory and tomorrow is today’s dream.”

We learn from the past, exist as long as we endure the present and we look forward to tomorrow. But a striking truth to our existence is that as we age we ultimately face death. And one aspect we clearly share with the laws of physics is that our aging process correlates with time, the universe’s fourth dimension. In his book “Confessions” (AD 397-400), St. Augustine of Hippo remarks on our ignorance of what time really is. He reflects on the idea that the past, present and future define our world. But then he questions, if the past does not exist, and the present moves on to something non-existent, then what is time? We do not see time but our lives are governed by it. Time is this invisible, obscure, and mysterious ruler of the universe and everything within it.

For Sara, time flows and forces her life towards the shores of the future like a wave - except that it never heads back to the past. However, the concept of time flowing is not consistent with any physical theory because it has no arrow. Not only that but also because of the irreversibility of some of the processes occurring over time, such as aging. When Sara celebrates her fortieth birthday, she knows she cannot reverse the ongoing process of aging and that from there she could only move on to her 50s and 60s and ultimately become part of the past. A consistent physical theory connecting time and aging is the second law of thermodynamics. In this law, all systems in equilibrium are comprised of a variable called entropy (a measure of disorder) and all the transitions that a system goes through will only lead to increasing and irreversible entropy. Think of Sara’s kids playing around after school and ultimately causing a glass of juice to fall on the floor. The shattered glass and the split juice are an example of the irreversible process of entropy or disorder occurring thereof and which increases towards the future. And without any external force the glass cannot reversibly un-shatter because it is following the universal movement of everything from order - before the Big Bang when the universe was a highly ordered cluster of mass and energy - to disorder. And as such, as we age, we accumulate entropy and head towards the future of disorder.

But others argue that another element of time could be related to why we age. “Internal time”, they presume, could be created by biological, psychological, and social processes all of which lead to intrinsic time being the property of the dynamics of our system. In this sense, if intrinsic time is the property of each individual system, it could also act according to the special theory of relativity where each system has its own intrinsic time because it would depend on its velocity.

In short, the dynamics of aging may be related to the physical laws of thermodynamics. Several possible theories may rule our existence, from a proposed internal entropy in which accumulated disorder leads to aging to internal time following in the footsteps of Einstein’s special theory of relativity wherein each individual’s aging process is unique and relative. Despite our efforts, time remains an enigmatic process to which we, and our systems, adhere. It started with the Big Bang, when the universe was set into infinite expansion and motion, begetting Sara whose existence is uniquely timed and set to end like a melancholic twilight elegantly announcing the end of the journey.

Yasmine Fathy
RA/PhD candidate,
Vrije University Medical Center

Check out:
From June 2011 to December 2015, and for a whopping 19 issues, the monumentally talented graphic designer Viktoria Stoiser has been the creative driving force behind the CNS Newsletter. Every three months, she would take some words, often sent to her by the editors in the dead of the night (and almost always behind schedule) and transform them into the vibrant and captivating periodical we've grown accustomed to. As Editors-in-Chief, we're delighted to have worked with her for the past five issues. As a token of our appreciation, we've conjured up some irrefutable proof (shown below) that, to the artistically challenged (like ourselves), what she does is nothing short of magical! All the best, Viktoria!

Ahmed Khalil and Apoorva Rajiv Madipakkam
Gaining Control Over Itches

Do you know the itch created by a barely felt movement of your hairs on the skin’s surface? This type of itch, caused by the lightest mechanical stimulation, is created via a dedicated neural pathway, a new study published in Science last October suggests. Such a mechanical itch sensation is normally suppressed by inputs from mechanoreceptors; however, in many forms of chronic itch, this gating mechanism is lost. In the study, Bourane and colleagues demonstrate that a population of spinal inhibitory interneurons that are defined by the expression of neuropeptide Y act to gate mechanical itch. Mice in which these neurons are selectively ablated or silenced develop a mechanical itch without an increase in sensitivity to chemical itch or pain. When poked with a tiny filament, they even fall into scratching fits. The neurons only seem to react to light touch; chemical itches, like those caused by a mosquito bite or an allergic reaction, are not transmitted by the same neurons. This can help researchers understand chronic itchiness in conditions like eczema or diabetic neuropathy and determine why certain patients do not respond to antihistamines.

(Bourane et al, Science, 2015)

Controlling the Brain Using Ultrasound

How do we reliably activate individual neurons? Optogenetic tools to switch neurons on and off with pulses of light are currently the best solution. However, to target neurons in deeper brain regions, invasive surgical procedures are necessary to place an optic fibre. Researchers from California’s Salk institute and the UCSD came up with the idea to use low-pressure ultrasound as a non-invasive trigger to activate neurons. Unlike light, low frequency ultrasound waves can pass through tissue unhindered. With neuron-specific misexpression of TRP-4, (the pore-forming subunit of a mechanotransduction channel) in the nematode C. elegans, they could sensitize neurons to ultrasound stimuli and manipulate the function of sensory neurons and interneurons to modify locomotor behavior. To transduce the ultrasonic power into the worm body, the worms were synchronized by the timing of food availability. The findings suggest that consuming food at the ‘wrong’ time of day can have far-reaching effects on hippocampal physiology and learning. Research on humans is needed to confirm the findings.

(Loh et al, eLife, 2015)

Late-Night Snacking May Have An Effect On Memory

We all know that eating late at night can have negative effects, such as weight gain. Now, a study published last December suggests it also may impair our ability to learn new things and store memories. “We believe that late-night snacking may affect our learning capabilities by affecting the parts of the brain responsible for learning and memory, specifically, the hippocampus,” Dr. Dawn Loh, lead author of the study, told The Huffington Post. “The timing of food consumption is what we believe to be the primary cause of the impaired memory that we describe.” Mice were put for a two-week period on a schedule with food access only in their sleep time. This mis-timed feeding resulted in dramatic deficits in hippocampal-dependent learning and memory. The researchers further showed that that under mis-timed feeding, the molecular clock in the hippocampus is synchronized by the timing of food availability. The findings suggest that consuming food at the ‘wrong’ time of day can have far-reaching effects on hippocampal physiology and learning. Research on humans is needed to confirm the findings.

(Loh et al, eLife, 2015)

How Your Brain Wakes You Up

In December 2015, neuroscientists discovered that activating a circuit associated with rhythmic neuronal activity that occurs during sleep causes awakenings from light sleep and anaesthesia. On the other hand, inhibiting the circuit deepens sleep. During light sleep, synchronous synaptic activity in the thalamocortical network generates low-frequency oscillations that are modulated by inhibitory inputs from the thalamic reticular nucleus (TRN). The Swiss team found that GABA neurons from the lateral hypothalamus exert a strong inhibitory control over these TRN GABA neurons. Optogenetic activation of this circuit recapitulated state-dependent changes of TRN-activity and induced rapid awakening from sleep or anesthesia. When they stimulated these neurons for an extended period, the mice stayed awake. When they silenced the neurons in the circuit, the mice slept longer, more intensely, and with fewer interruptions. New therapeutic approaches for vegetative or minimally conscious state patients and more targeted treatments for sleep disturbances in general may be on their way.

(Herrera et al., Nature Neuroscience, 2015)
“Good Scientific Practice” – Ideals vs. Reality

The more corrupt science gets, the more universities, funding agencies and journals inform us about how to maintain research integrity and good scientific practice. In their guidelines we learn, for instance, how to prevent misconduct, what qualifies for authorship, and how to establish proper research procedures. So theoretically, everyone should know how proper science ideally works, right? Why are we then still faced with retractions, fraud, and questionable research practices?

As important as such policies may be, it is at least equally important to ask how realistic the implementation of such lofty goals is, given the current scientific system. It is naïve to assume that the whole system could be healed by the formulation of some guiding rules, but without also putting basic scientific principles up for discussion. The scientific publication system, for instance, is always deemed a cornerstone of science and has rarely been questioned. But it is also inevitably linked to the well-known pressure to publish, meaning that a scientist’s reputation is dependent on their number of publications, preferably in “high-impact” journals. However, such high-profile journals usually favor novel and interesting findings and are simply not interested in so-called “null findings” or replications, independent of the scientific accuracy and rigor of the work. It is thus highly insincere when journals, on the one hand, demand proper research procedures, but, on the other hand, base their decision about the acceptance of manuscripts on completely different criteria. The enforcement of good scientific practice has to operate on the foundations of the scientific system, for example by the limitation of the power of publishing companies or alternative models of publishing.

There are dozens of other examples – like hierarchical structures that hamper scientists (especially young ones) from enforcing their rights, for instance in authorship disputes – showing that the sole formulation of codes of conduct is in itself not much more than a lip service. It is much more critical to establish the structures for their realization, even though this often implies striking new paths and throwing old structures overboard. The motto for the future should thus be: facta, non verba!

IT’S TIME TO TAKE ACTION

Anonymous

MedNeuros in the Limelight

MedNeuro PhD student and CNS editorial board member Mariana Cerdeira has an exciting new blog, Chronicking her multifaceted lifestyle. In the EuroZone covers everything from her frequent travels to eating, education, and entertainment in Berlin. Available in both English and Portuguese, the blog is a must-read! Check out http://intheeurozone.com/

Timo Schmidt, MedNeuro PhD student, puts scientific communication into practice with his new startup, Schlauluchs. Under the slogan “Neuroscience meets handicraft”, they manufacture useful products that illustrate how our brains work (a perfect present for family, friends and kids!). Check out www.schlauluchs.de (website) and http://on.fb.me/20EtOE8 (Facebook page).

CNS editorial board member and MedNeuro PhD student Constance Holman and colleagues recently asked a question that makes many preclinical researchers uneasy: What happens to those data points that never make it to the final paper? Their meta-analysis showed that attrition is more than just wasteful, it can be downright dubious when not properly reported. Check out: Holman, C., Piper, S. K., Grittner, U., Diamantaras, A., Kimmelman, J., Siegerink, B., & Dirnagl, U. (2016). Where Have All the Rodents Gone? The Effects of Attrition in Experimental Research on Cancer and Stroke. PLoS Biol, 14(1), e1002331.
A Resurrection

Another day went by as I lay in bed at 8 am. Well aware of the need to get up but every part of me was numb. Years ago, there used to be so many reasons to get out of bed and go on with life. I prepared coffee and stood in front of the window watching the slow dancing movements of trees and the playful birds, the squeaking of crows and the sound of an airplane passing through the floating clouds. Another day where light could escape the bars of darkness to be unleashed into the world.

The fresh breeze mixed with the delicate warmth of spring’s sun reminded me of my childhood. The details were somewhere far in my memory but the feeling strongly permeated my soul; it was a weekend early in spring 1952 when I woke up early enough to find my mother cleaning the house and preparing breakfast. We sat on the table closest to the window. Warm milk, butter, jam, eggs, juice, and a porcelain teapot that she cherished laid on the wooden table. The curtains were tied to the sides and a banana tree sitting in the garden precluded the sun from fully attending our family breakfast. My head reached slightly above the table and I had a cup of milk in front of me while my mother allowed herself to alternate between reminding me to eat everything and kissing me. We discussed my friend’s birthday party and the new dress she was going to buy me.

I dressed up in my favorite white and purple dress and a long braid that mother always put a lot of effort into creating and decorating with a flowery head band. That morning at the mall, and after trying on a few dresses, we ended up coming out with a big bag containing a beautiful dress. As we headed towards the car, mother took me to this pastry shop where a few people were sitting, some skimming through newspapers and others enjoying a quiet morning. I stared at the glass cupboard full of desserts. The creamy crème and decorated with a thick layer of cooled chocolate along with a cup of juice. We sat down facing the window, my little body next to her warm one and my little world filled with the sweet scent of her presence.

Being, as Heidegger explains, is the most universal and emptiest concept in the dictionary of existence. With the slow ticking of an old clock and a rhythm defining the condition of my heart, I stand by the mirror pondering upon the new me that I wouldn’t have recognized years ago. “Hibiscus”, my dad whispered into my ears as I stood staring at a flower one day at the park. My face touching his soft black hair and my eyes shifting between his loving gaze and the elegance of a red hibiscus softly caressed with pearly raindrops under sunlight. As the sky celebrates the farewell of a long day, I step into the past with my bare feet searching for an old dream and a little girl smiling relentlessly at the universe. I am the past, the present, and the future intertwined and a constellation of all that which cannot be said.

“Time crumbles things; everything grows old under the power of Time and is forgotten through the lapse of Time.” Aristotle.

Yasmine Fathy
RA/PhD candidate,
Vrije University Medical Center

Open Position for Master/PhD Students

Type: Master’s Thesis
Title: Expression, function and endogenous modulators of the transient receptor potential (TRP) channels TRPV1, TRPV4, TRPM8 und TRPA1 in human corneal endothelial cells and human corneal keratocytes
Field of Research: Role of TRPs in ocular function and medical relevance.

Starting Date: From March 2016
Research Group: Experimental Ophthalmology, AG Stefan Mergler (Charité Eye Clinic, Campus Virchow-Hospital)
Contact: PD Dr. Stefan Mergler, stefan.mergler@charite.de, phone: 030 450 559648

HFSP Program and Young Investigator Grants

The Human Frontier Science Program’s (HFSP) has opened a new round of applications for the Program and Young Investigator Grants. Research grants are provided to teams of scientists from different countries who wish to combine their expertise using innovative approaches to questions that cannot be answered by individual laboratories. You must register and obtain a 2016 reference number via the website by March 21, 2016. Submission of Letters of Intent deadline: March 31, 2016. Further information: bit.ly/1bYzVor

MINT Excellence Stipends

The financial service firm MLP offers 30 stipends to STEM students that also include exclusive seminars and soft skill training. Deadline: April 15, 2016. Further information: https://www.mlp-financify.de/mint-excellence/

Stipends for Master and PhD Students

Master’s and PhD students at the Humboldt University in the transition phase between the end of their Master’s degree and the start of their PhD or who are about to complete their doctorate and wish to conduct a postdoctoral project are eligible to apply for the Humboldt Research Track Scholarship and Humboldt Postdoctoral Scholarship respectively.

• Humboldt Research Track Scholarship: 800 EUR/month for up to six months. Further information: http://bit.ly/1KdRLv
• Humboldt Postdoctoral Scholarship: 1500 EUR/month for up to six months. Further information http://bit.ly/1Ly7nrQ

Deadline: May 15, 2016 for funding starting August 1, 2016.
Join Us: 15th Anniversary of Medical Neurosciences
Believe it or not but the Medical Neurosciences program is now in its 15th year!!! The office is planning to celebrate this milestone on the 8th of October 2016 with its Master and PhD students, alumni and current. For more details or to be a member of the organizing committee, email us at office-medneuro@charite.de.

Soon to Join (I): New Prospective Master Students 2016
Like the last couple of years, our call for applications has been well received. From roughly 200 complete applications from around the world, 62 candidates were invited to sit the first admission test, carried out worldwide. Some fun facts: the gender was almost equally split globally among the world’s regions. Interestingly, in Europe and Latin America, about twice as many applicants were female. In general, 20% had a medical degree, and 15% already had a Master’s degree, equivalent or higher.

Soon to Join (II): Meet Prospective Students During the Admission Symposium
On 17th March 2016, our admissions symposium for the final selection of future MedNeuro students will take place. We are looking for current MSc and PhD students willing to give brief lab visits and/or campus walks. On this day, the casual meet-and-greet with pizza and beer – almost a tradition by now – will be followed by a visit to a local pub to get to know each other and to obtain first-hand information about our program from the current students. Email us at office-medneuro@charite.de to help us out.

AlreadyJoined: Prof. Ferah Yildirim
Prof. Dr. Ferah Yildirim, who successfully graduated from both our MedNeuro Master and PhD program, has replaced Prof. Sarah Shoichet in the examination and admission committee. A professor for neuropsychiatry at the Cluster of Excellence NeuroCure, Prof. Yildrim has already proven her expertise by reviewing this year’s Master’s applications.

Have Joined: Four New MedNeuro PhD Students
We would like to warmly welcome our new PhD students to the program: Dominique Dufour Bergeron (Sigrist), Markus Petermann (Bader), Stefan Voigt (Basta) and Stephanie Wegner (Gertz). Dominique is one of our NeuroCure scholarship recipients, Markus is a BIH fellow.

You May Want to Join: Soft Skills and Training
Are you looking for a specific training or a soft skills course? You may want to check out what the Humboldt Graduate School (HGS) has to offer. Workshops: https://humboldt-graduate-school.de/en/services-en/schluesselkomp2-en/kursprogrammen-en. Or simply contact them by email at hgs-workshop@hu-berlin.de.

Upcoming Events

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Imprint
Charité NeuroScience (CNS) Newsletter
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Humboldt Senior Advisor
Deans or managing directors of institutes at the Humboldt-Universität or groups of at least three junior researchers together with the designated Senior Advisor can submit a proposal to obtain funding for the position of Humboldt Senior Advisor. Senior Advisors provide guidance on research projects, serve as mentors for young researchers, or act as contact persons for non-university projects promoting young researchers. The duration of each Senior Advisor contract is flexible between several months and up to a maximum of one year.
Deadline: May 15, 2016 for funding starting August 1, 2016.
Further information: http://bit.ly/1e6zhgj
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