The first time I went to Madagascar was by accident, really. It was the summer of 1995, and I had just finished my sophomore year of college. Since the study abroad program in Prague for the fall semester was canceled, I had a choice: either go to Prague the following spring semester or pick another program that had space available. I chose a cultural immersion and environmental program based in Antananarivo, Madagascar. I was completely unprepared and unaware of the experiences and varied environments that awaited me.

I use the old saying by Alexander Graham Bell — “When one door closes, another one opens” — a lot when describing my life so far. Adaptability, collaboration, openness to different ways of seeing and doing, and yes, networking, all play significant roles. After my formative semester in Madagascar, I knew I wanted to major in environmental sciences, a discipline that can and does involve many fields of study. I learned how to conduct soil chemical analyses, nutrient cycling analyses, design field studies, and do PCR and DNA sequencing. I learned how to read and write about science, listen and observe, and parse a wide amount of information and sort out the essential pieces. This didn’t happen solely in college; it happened over the course of many years, first with graduate school, then with research jobs, and it is still happening today.

When describing what I do, I usually answer, ‘A little bit of everything,’ A generalist rather than a specialist, perhaps, but with no less focus, attention to detail, or critical thought than you would find in a specialist. Experts are certainly needed, and I’ve tried to surround myself with experts and work for them, as a fact-checker, researcher, and contributor.

Today, I help with research and writing for Alison Richard, an emerita faculty member and researcher extraordinaire at Yale University. This has brought me back to ‘looking at’ Madagascar. This time around, it involves managing a long-term dataset on a population of sifaka lemurs in the southwest of the island, and disseminating ecological and social information and awareness of that field site in particular and Madagascar in general. I don’t know where my next stop will be, but I can be confident that I’ll have the necessary tools to help me enrich my experiences.
The Language of Life

“There must be a way, I thought, that the language of life as experienced — of passion, of hunger, of love — bore some relationship, however convoluted, to the language of neurons, digestive tracts, and heartbeats.”
- Paul Kalinathi, When Breath Becomes Air

By Tan Qian Hui, Peer Tutor

A language is, first and foremost, a world of its own. Each language constructs its own set of paradigms and grows its own rooted meanings. Words are crucibles, conveyor belts of meaning that connect two individuals — a shared understanding, the abstract congealed into the tangible, both neatly packaged into a common sound.

To me, Ancient Greek and Molecular Biology represent two such distinct languages, each crafting schools of thought associated with unique constructed worlds. As a student of both disciplines, I bridge these connections, lodged somewhere between the past and the future.

Socrates once claimed that the unexamined life is not worth living. If Greek explores the definition of a spiritual life, then Biology investigates physical life itself. Language gave Socrates the scalpel with which to dissect spiritual life, from the definition of virtue to the presence of innate knowledge. It gave the Heliaia tools to persuade others towards their cause, and allowed Aristophanes to examine Athenian society through satirical humour. For ancient Athenians, language was not only essential for life — it defined life itself.
In contrast, the language of Biology is the language of genes and genomes. We examine the intricacies of life by building on the central dogma, deepening our understanding of pathologies and behaviours. We run genetic screens to identify candidate genes, perform transcriptomics to elucidate potential drug interaction pathways, and use statistics to identify predispositions for diseases. For modern Biology, the language of life is an empirical one, geared towards understanding life and its historical evolution. Fascinatingly, scientific etymologies tie these two seemingly disparate disciplines together in unique trails, tracing the history of scientific progress and thought. For example, paediatrics from paidas (child) and geriatrics from geron (old man) are still terms we use today. They anchor the past with our present and will continue to connect our present with the future. In language, Biology and Greek intertwine, melding the past, present and future stories of humanity into a coherent whole.

Telling Your Research Story

By Zhu Fangchen, Peer Tutor

Many people have the impression that the hard sciences are all about doing lab work and conducting research in the field, but the truth is that the sciences and writing are intricately connected. Whether it is academic writing such as a lab report or a grant proposal, or science journalism, being able to communicate your ideas through words is essential skill for a good scientist.

As undergrads pursuing the sciences, one of the most important pieces of writing you will have to do is crafting a research statement for your application to research programs or graduate school. Program coordinators will often offer a simple prompt asking for your motivations and interests in research, and it is tempting for applicants to just narrate experiences in their lives that sparked their interest in a subject, or pontificate about the profundity of a topic. While regaling the reader with an elaborate tale does highlight one’s interests and show off a degree of flair, it might not be the best way to present one’s qualities and expertise that research programs seek in their applicants. It is important to remember that these programs are looking for well-prepared candidates who can benefit from the program in an academic way (and you are competing with other applicants with such intentions). Therefore, it is important to not tell a personal story, but a research story.

A research story is a narrative structured around the steps you have taken to pursue a passion. It starts with the birth of an academic interest and details the tangible steps you have taken to actively explore this interest and your intellectual and personal growth in the process. The aim of this prose is to illustrate how the position you are applying for is the next chapter of your story and how it links to the skills and interest you already developed. This way, you can convince the reader that you have deliberately considered treading this path and made the necessary preparations for it. At the end of the day, research is a long process, and commitment is highly valued in the field. If you can use your research story to convey your demonstrated dedication, it will definitely aid you in your development as a scientist.
MODAFINIL: CAFFEINE 2.0

A NEUROSCIENCE INVESTIGATION INTO MODAFINIL’S COGNITIVE ENHANCING PROPERTIES

BY WONG ZHENGLONG, CLASS OF 2021

These term papers were written for Professor Ajay S. Mathuru’s course, Foundations of Neuroscience. Each student picked a topic of their choice, motivated either by prior personal interest or by developing an interest as the course progressed. The papers critically examine a topical item or question a prevailing notion by appraising it through the lens of neuroscience.

COVER
I first stumbled upon the term “nootropic” when researching about nutrition. Nootropics are substances which improve cognitive function, and there is a whole community of “biohackers” striving to optimise their mental and physical performance through different foods, supplements and drugs. This can range from something as mild as Vitamin D and Magnesium supplementation to taking combinations of pharmaceutical drugs meant to deliver a potent boost to your system. Like most, I was hesitant to even consider taking anything termed a drug without a doctor’s prescription. But my curiosity was piqued by the numerous first-hand accounts describing the dramatic benefits these drugs gave to people who were struggling to keep up with work and life. Upon deeper reflection, I also realised I was being hypocritical. If I unquestioningly take caffeine in my coffee every morning, why should I dismiss other substances which could benefit me simply because they aren’t served as a delicious drink? Amongst nootropics, Modafinil was the most frequently mentioned by students and working adults alike to improve their productivity. Rather than relying on YouTube videos and anecdotal reviews, I decided to evaluate the safety and efficacy of the drug myself through this term paper. If scientific literature agrees that Modafinil is safe and provides a substantial boost to our cognition, it may prove to be an invaluable tool to all students.

THE PANDEMIC OF SMART DRUGS

A Straits Times article published in 2017, titled “Downside of Smart drugs” [19], warns of an increasing number of Singaporean students using “smart drugs” to bolster academic performance. With no legitimate concerns raised beyond a vague list of side effects, the article betrays our innate social paranoia towards drug use. For academically competitive students, these drugs may be an invaluable tool to reach their full potential. Rather than dismissing smart drugs offhand, this paper takes a neuroscience perspective to investigate the properties of the popular study drug Modafinil, drawing on psychological and neurological studies to evaluate if and when Modafinil is an appropriate tool for students.
COGNITIVE AND ADVERSE EFFECTS OF MODAFINIL

Modafinil is a synthetic drug originally developed to treat fatigue caused by narcolepsy and obstructive sleep apnea. Outside of these clinical settings, there are accounts that it improves motivation, reduces fatigue, and improves concentration — a set of enticing properties for students. Scientific reviews on Modafinil’s cognitive effects report its impact on healthy subjects and sleep deprived subjects separately, as the drug has distinctive benefits on both groups.

For healthy non-sleep-deprived adults, there is a strong consensus amongst studies that a single dose (200mg) of Modafinil improves attention versus placebo control groups [14]. Attention is usually verified by tests measuring the reaction time of individuals to an abruptly presented stimulus [14]. However, studies have reported a mix between positive and null results for Modafinil’s effect on other cognitive measures like working memory, mood and motivation [12][14]. It may be that Modafinil has no effects on these areas or that its effect is too minute to be consistently detected in tests. Therefore, until more studies demonstrate a repeatable effect, we can only say with confidence that Modafinil enhances attention for non-sleep-deprived subjects.

In sleep deprived subjects, the range of Modafinil’s cognitive effects expands dramatically. Studies show that a single dose is sufficient to improve working memory, attention and executive function (the ability to discern between relevant and irrelevant input and take action that does not rely on habit) as compared to placebo control groups [14]. Modafinil has a remarkably powerful effect in improving wakefulness. Subjects who took Modafinil remained alert even after long hours of sleep deprivation [14]. Repeated doses only sustained wakefulness but not the other cognitive functions diminished by sleep deprivation [14]. Importantly, we should note that Modafinil’s cognitive benefits in sleep-deprived subjects are not improvements over our usual levels. Rather, Modafinil maintains cognitive function above their diminished states when we are sleep-deprived, -but this may not exceed that of rested individuals.

The reported side effects of Modafinil are weak and infrequent but include irritability, restlessness, and anxiety [12][14]. The most serious concern regarding Modafinil is its potential for abuse because Modafinil affects neurological pathways similar to addictive drugs like cocaine [17]. To better understand this risk and how it brings about its cognitive effects, we need to investigate its neurological effects on the brain.

MODAFINIL’S EFFECT ON DOPAMINERGIC PATHWAYS

Neurotransmitters are essential molecules in the brain and nervous system used to transmit information. Modafinil affects pathways related to one such molecule in the brain - dopamine. Studies have shown that Modafinil results in increased dopamine levels in the brain’s prefrontal cortex [10] which includes areas like the medial prefrontal cortex and orbital prefrontal cortex. These regions are associated with executive function, decision making, short term memory, and self-control [2][15].

Modafinil’s effect on these brain regions may account for some of its cognitive enhancing effects, particularly because other cognitive altering drugs, like d-amphetamine and cocaine, affect the brain similarly.
Modafinil does not directly increase dopamine levels in the prefrontal cortex. Instead, it blocks the action of the Dopamine Reuptake Transporter (DAT) [11], the molecule responsible for removing dopamine once it has been released. Inhibition of DAT causes an accumulation of dopamine after its release, increasing the activity of brain areas that rely on dopamine transmission. Researchers have raised concerns about Modafinil’s addictive potential because it binds to DAT in the nucleus accumbens [17] — the brain region associated with cocaine addiction — increasing dopamine levels in a manner similar to cocaine. However, a study demonstrating that Modafinil only slightly elevates dopamine levels in the nucleus accumbens compared to cocaine [3] suggests that it lacks the same addictive potential, matching the lack of virtually any accounts of Modafinil addiction.

**MODAFINIL’S EFFECT ON BRAIN REGIONS GOVERNING SLEEP AND WAKEFULNESS**

Another difference between Modafinil and cocaine is that Modafinil does not affect dopamine pathways. For instance, it may induce wakefulness by influencing brain regions associated with sleep and wake states.

Referring to Fig 1, wakefulness in humans is associated with the activation of the Tuberomammillary nucleus (TMN), the Cholinergic nuclei, the Locus coeruleus, and Raphe nuclei [13]. Conversely, lower activity in these wake-related brain regions corresponds to feeling drowsy or falling asleep [13]. These brain regions are regulated by two others: Orexin neurons and the Ventrolateral preoptic nucleus (VPLO) [13]. Orexin neurons increase activation of wake-related brain areas whilst the VPLO inhibits them and causes sleepiness [13].

Modafinil’s effect on wakefulness may be related to its impact on the TMN. C-Fos is an immediate early gene expressed in cells when they become active and thus serves as a biomarker of cell activity. A single dose of Modafinil causes TMN cells to become c-Fos positive, indicating greater activity in the TMN [16].

A study in rats also observed greater levels of histamine (the neurotransmitter involved in TMN activity) following Modafinil treatment [9], providing further evidence for increased activity. Preventing histamine production in the TMN eradicated the cognitive enhancing properties of Modafinil [6], suggesting that Modafinil cognitive effects are partly explained by histamine transmission in the TMN. Oddly, injecting Modafinil straight into the TMN does not increase histamine production or TMN activity [9], meaning that the TMN is not the immediate target of Modafinil.

Modafinil also induces c-Fos expression in Orexin neuron [11][16]. As seen in Fig 1 (by the arrows with a plus sign), activation of Orexin neurons in turn excites wake-related areas — including the TMN. Thus, the indirect of TMN by Modafinil may be the subsequent effect of its activation of Orexin neurons. A study demonstrating that Modafinil does not increase histamine in rats with their Orexin neurons removed further supports this theory [7]. However, Modafinil has no known interaction with Orexin receptors [18] and narcoleptic patients which benefit from Modafinil treatment are deficient in orexinergic pathways [8]. Like in the case of TMN activation, Orexin neuron activation partly explains Modafinil’s effect on wakefulness because it excites wake-related brain areas, but it is not Modafinil’s direct target.
Lastly, Modafinil reduces c-Fos expression in the VPLO [16] indicating decreased activity in this brain region. Lesser VPLO activity results in greater excitation of wake-related brain areas as VPLO acts as their inhibitor (as seen by the arrows with minus signs in Fig 1) [13]. VPLO inhibition by the drug also contributes to TMN activation. Studies have observed that Modafinil reduces the amount of GABA, the neurotransmitter used by the VPLO to inhibit wake-related brain areas, released by the VPLO [4]. Modafinil’s inhibitory effect on the VPLO in turn depends on its effect on another neurotransmitter: norepinephrine [5]. However, the origin of this chain effect is still not known.

To summarize, Modafinil’s effect on wakefulness may be partly explained by increased activity in the TMN and wake-related brain regions, induced indirectly through excitation and inhibition of the VPLO and Orexin neurons respectively. Activation of these brain areas may also explain Modafinil’s other cognitive effects as brain regions often contribute to multiple cognitive functions. However, the immediate target of Modafinil is still not known and it creates numerous other neurological effects on the brain not captured in this paper. Cognitive functions usually rely on several brain regions and processes, so it is likely that Modafinil’s cognitive effects are the summation of its multiple modes of action throughout the brain. Given this, it is too simplistic to lump it in the same category as notorious drugs like cocaine on the basis of a single shared pathway.

CONCLUSION

Contrary to the Straits Times article, our findings suggest that Modafinil is relatively safe for students to use, with weak sides effects and a low potential for addiction. Given its cognitive effects, Modafinil should often come in handy for students as they are frequently sleep deprived. A single dose of Modafinil mitigates the worst drawbacks of sleep deprivation, helping them pull all-nighters to meet pressing deadlines or cram for exams. Unfortunately, only the first dose of Modafinil reaps its full benefits, and staying awake using multiple doses of Modafinil will likely result in subpar work. Taken on normal occasions, Modafinil should help improve attention, which could mean better focus during study sessions. However, as this focus could just as easily be used to finish an entire season on Netflix, the discipline and motivation of the student is still essential for productivity.

Despite the label “smart drug,” Modafinil seems more analogous to caffeine, increasing our capacity to work rather than making us smarter; however, many anecdotal accounts on YouTube point to it being much more potent. Although this paper found that Modafinil should generally be beneficial with little drawbacks, the actual experience of the drug is highly idiosyncratic.

REFERENCES


Find the full list of references at https://writerscentre.yale-nus.edu.sg/newsletters/
Terminating Tau in Patients with Alzheimer’s Disease: One Step Forward or a Step in the Wrong Direction?

BY SYDNEY NUR REIBSCHIED, CLASS OF 2021

This paper will review the in-human drug trials of tau-targeting drugs, focusing on IONIS-MAPTRx. IONIS-MAPTRx is an antisense oligonucleotide, which aims to block the producing of all forms of tau, combating the tau pathology known to play a role in Alzheimer’s Disease. A short history of the tau hypothesis and its new developments following the failure of amyloid beta drug trials is discussed. The mechanism behind IONIS-MAPTRx and research supporting along with research in combat with the drug’s mechanism is examined.

BACKGROUND

Alzheimer’s Disease is the most common form of dementia [23]. Alzheimer’s Disease (AD) is a neurodegenerative disease, which progressively destroys cognitive skills such as remembering new information, the ability to communicate, problem solving, and basic functions such as walking or swallowing [19]. However, after decades of research, medicine still has not been able to win the battle against AD.

Since the 1990s, the presence of tangled bunches of fibers in the entorhinal cortex, a part of the brain known to play a key role in memory, has been identified as an early indication of Alzheimer’s Disease [25]. Years later, researchers still have not been able to pinpoint the principle cause of the symptoms seen in AD, but they have narrowed the main principal causative substance of AD to two main culprits: amyloid /3 (A/3) and tau.

Dominating the research in AD for the past 25 years, the amyloid hypothesis has been intensely interrogated. The generally accepted concept of the amyloid hypothesis is that amyloid /3 (A/3) peptides aggregate together and form clumps which eventually turn into plaques [18, 22]. Theses plaques are said to be the start of a chain of events which leads to AD: inflammation, tangled tau-fibers known as neurofibrillary tangles (NFTs), inability for the cells to communicate through synapses, and subsequently cell death [4, 5]. Despite many A/3 – targeted clinical trials in the past three decades, believing that disaggregating A/3 would stop the cascade of events causing the disease, all clinical trials have failed [12, 20, 22].

Due to the failure of A/3 treatments, researchers are starting to shift more of their focus on the tau pathology that was supposed to be in the amyloid hypothesis later in the chain of events [13, 20, 30]. In the tau hypothesis, rather than A/3 causing the chain of events, the tau protein pathology is believed to be the chief cause [20]. The tau protein when misfolded forms neurofibrillary tangles (NFTs) and threads in dendrites and axons [18, 22]. NFTs are believed to cause the cascade of damage in the transport system, cytoskeletal system, signalling system, and mitochondrial integrity of the brain of people with AD [11, 15-18, 20, 29, 30]. Advancements in research are finding that the tau pathology actually has a more direct correlation to cognitive decline than A/3 [13, 18, 30], and treatments are finally focusing on targeting tau after decades of failed research [12].
CURRENT TRIALS TARGETING TAU

There are nine major drugs which specifically target tau that are currently being investigated through in-human clinical trials [27]. Six of the nine drugs utilize the body’s immune system, telling the immune cells to inhibit the propagation or “seeding” of pathological tau [2, 5–7] and or reduce extracellular tau present [3]. The recent emphasis on drugs activating the immune system is most likely triggered by the 2018 Nobel Prize in Physiology or Medicine going to researchers for their advancements in immunotherapy. The small molecule drug types in trial work similarly: to prevent the aggregation of extracellular pathological tau and to dissolve existing aggregates [9, 10]. However, one drug stands out—IONIS-MAPTRx. IONIS-MAPTRx is an RNA based drug in trial [27], which seems to have the most potential to solve Alzheimer’s disease if the tau hypothesis is correct.

IONIS-MAPTRx: A THOUGHT-PROVOKING MECHANISM

IONIS-MAPTRx is the only drug which focuses upstream on inhibiting the production of tau in trial [4]. The idea of targeting the production of all tau is much more extreme than the other eight drugs in trial. If any of the other drugs show results, then the tau hypothesis will of course be strengthened. However, if IONIS-MAPTRx works then this drug will be groundbreaking evidence for the tau pathology having a direct cause to AD, causing neuroscience to have a need to reconsider the role of tau normally. On the other side, because it focuses on stopping all tau, including healthy tau from being produced, this is the drug which has the most capability to see defeat.

Functionally, IONIS-MAPTRx is the only drug of its kind, an antisense oligonucleotide (ASO), in trial for AD. ASO technology is by far the most interesting mechanism out of the nine drugs in trial. Starting with the approval of the very first ASO drug approvals in 2016, Nusinersen for spinal muscular atrophy and Eteplirsen for Duchenne muscular dystrophy, the use of ASOs has gained momentum. ASOs are short, synthetic single-strands of nucleic acid that are complementary to a strand of RNA that they bind to. When bound, ASOs can increase or reduce the amount of protein made from the RNA they are attached to [24]. The pharmaceutical giant IONIS Pharmaceuticals dominates the ASO market currently and is the company behind both Nusinersen and the current drug on trial IONIS-MAPTRx. ASOs are commonly said to hold the potential to be the “next frontier” [24] for neurological therapeutics resulting in pharmaceutical companies rushing to be pioneers of the field.

MECHANISM

IONIS-MAPTRx acts to reduce the initial expression of tau rather than focusing on the inhibition of seeding or reducing extracellular pathological tau through an RNA-based approach (Figure 1) [4]. Its target is the Microtubule-Associated Protein Tau gene (MAPT gene) which codes for tau protein expression [21], IONIS-MAPTRx works by binding to the mRNA transcribed from the MAPT gene (normally producing tau) and destructing it, which consequently blocks translation of the gene into all types and isoforms of the tau protein [21].

![Figure 1](image)

**Figure 1.** The mechanism behind IONIS-MAPTRx: The drug targets RNA, binds to it, and destructs it. Therefore it inhibits the formation of all types of tau protein.

IONIS-MAPTRx was first tested in mice modified to have a mutation on a spot in the MAPT gene, which leads to neurofibrillary tangles modeling AD [8]. The results showed that when treated with the ASO, there was a significant decrease of the amount of tau present, a reversal of phosphorylated tau pathology, a halt in hippocampal and neuronal loss, and a reverse seeding activity [13, 21].

In trials with nonhuman primates (cynomolgus monkeys), a mean MAPT mRNA reduction of 77% was reported in the frontal cortex, and a 74% reduction in the hippocampus was reported [21], with significant tau protein reduction in the spinal cord, frontal and temporal cortex, and hippocampus [13]. This revealed promising application of IONIS-MAPTRx in humans.
and the in-human drug trial of IONIS-MAPTRx was approved and started on June 5th, 2017 [1]. IONIS-MAPTRx is the first tau-lowering ASO to be tested in humans with AD, and the study is estimated to be completed on February 29th, 2020 [1, 21].

POSSIBLE CONSIDERATIONS

The major risk of this study concerns the effects of reducing levels of all tau, considering that non-tangled tau is necessary for normal neuronal function. IONIS-MAPTRx inhibits the production of all isoforms, not just hyperphosphorylated tau. Normally, tau is found throughout the nervous system and is well-known to serve the functions of stabilizing and assembling microtubules [26]. Tau has also been found to play an essential role in regulating intracellular pathways by interacting directly with several tyrosine kinases, and it possibly plays a role in the creation of dendritic spines — a key in synaptic plasticity [26]. In May, 2018 researchers developed a virus based technique which decreases the expression of tau similarly to the way IONIS-MAPTRx is said to work. The researchers also studied its effects on mice to understand the physiological function of tau in the hippocampus [26]. The study concluded "unambiguously" that acute tau knockdown in the hippocampus directly impaired cognitive functions of spatial learning and memory, as well as motor coordination [26]. This conclusion contradicts the findings of IONIS Pharmaceutical lead studies, which found little to no impair of normal neuronal function when tau was decreased in the hippocampus of mice [14, 23]. The results of this study could be evidence that the problem of tau in the case of Alzheimer’s disease is not that tangles occur, but that tau loses its physiological function [26].

THE FUTURE

Regarding IONIS-MAPTRx, its mechanism of inhibiting all forms of tau may not work. The 2018 study mentioned above is valid. This poses a bigger question of whether or not tau in AD contributes to the clinical manifestations through a loss-of-function, gain-of-function, or both. There still exist the possibility that the amyloid beta hypothesis may be the correct instigator of Alzheimer’s disease. A possibility for research is investigating why exactly A3 trials failed and if science has been missing something. At the present moment, continual strong support for Alzheimer’s Research is being maintained, and tau research could be the answer.

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Find the full list of references at https://writerscentre.yale-nus.edu.sg/newsletters/
“Hello dear, sorry to have kept you waiting.” Mrs Jones’ velvet voice enveloped Tania and smoothed out her anxiety. Mrs Jones had kind eyes. Their watered-down depths coupled with the creases that lined her loose skin, etching out the long years of life she had lived — 102, to be exact. Mum said that in the past, most oldies lived for only 80 years. Nowadays, 120 was the average. Tania couldn’t imagine a time when most people lost out on 40 years altogether.

Mrs Jones spoke in her gentle voice. “What do you want to eat, Tania? Japanese food, your favourite?”

This was only their fifth meeting together but each time they went out, Mrs Jones would bring Tania to a fancy restaurant which served food she and her parents couldn’t afford. She was glad to eat out. Most days, she ate Huel. Although it tasted much better than it did ten years ago,
better than it did ten years ago, real food beat gulping down powder-and-water mix any day. Nonetheless, Huel was cheap, instant, and nutritious. But the protein came from locusts, which was what made it cheap. Tania had learnt that eating insects was shunned before her grandparents’ generation. Most people in the past ate real meat... from animals. She shuddered as she imagined a world where animals were killed and eaten so freely. Nowadays, such animals could only be found in conservatories, and most of the meat they ate was cultured. Only the rich could afford to have real meat.

She was lucky to be assigned to an oldie as affluent as Mrs Jones. Any expenditure of the oldies was up to their discretion, as long as nothing was illegal. “What would you like to eat, Mrs Jones? We always go to Japanese places but you haven’t told me what you like,” Tania said.

“I like Japanese food too, Tania. The System paired us together for a reason, you know? Similar taste is one of them.” Mrs Jones eyes crinkled as she requested for a hovercar pickup.

Tania fidgeted in the restaurant chair. She tried to figure out where to place her hands and what to say. It was awkward sometimes, having to interact as complete strangers paired together by the System. But it always gets better as you go on more oldiedates. Besides, Mrs Jones was a sweet lady with a kind heart and Tania enjoyed listening to her stories. Looking at the menu, Tania went for the cheapest donburi option. “That’s all you’re getting?” Mrs Jones asked. Without waiting for an answer, she tapped on the Orderglass and selected bowls of chawanmushi, agedashi tofu, ikura, uni and matcha ice blend, in addition to her own bowl of hot soba.

“So Tania,” Mrs Jones said, “how’s your family?”

“They’re good!”

“Are your parents still working hard? How’s the art business?”

“The usual. They’re experimenting with new mediums to create more avant-garde stuff people are looking for nowadays. It’s hard to come up with something completely original and well-liked, you know what I mean?”

“Back in my day, there weren’t as many artists as there are today. There were so many different jobs. You could be a firefighter, a phone operator, a janitor... you’ve never heard of them, have you?” Mrs Jones gave a wry smile.

Tania couldn’t think of why anyone would want to be a firefighter. Apparently their job was to enter buildings on fire and put them out. That sounded way too dangerous for a job. But she knew that they didn’t have firebots back then. Tania also couldn’t think of why anyone would want to work as a phone operator or a janitor. Those jobs sounded menial and tiresome. She would go mad if she had to listen to a phone all day for months on end or clean buildings for a living.

“How is school?”

“Oh! As per usual. Learning new things every day and taking tests. We’re starting on algorithmic thinking now. It’s pretty interesting.”

“Always remember, learning comes from the heart. Do what you love and follow your passions. Life is only good for doing what you enjoy. People in my time used to chase after what earned them the most money... striving for soulless jobs they didn’t enjoy, what with bankers, consultants and fund managers. We don’t even need these people today! When blockchain and cashless ledger technology appeared, there was no longer any need for banks and the people they employed. What a time it was to be alive when those institutions collapsed. They were the ones who perpetuated the inequality in society back then. Now, there’s no longer any space for money-scammers...”

Tania smiled and nodded patiently. She didn’t always know how to respond when Mrs Jones went on her rants about the money-scaming finance industry or her melancholic bouts about Mr Jones. Tania loved hearing the smooth, warm voice of Mrs Jones, but she wondered if the oldie ever realised that she repeated these stories all the time.
MAN'S_BEST_RENT

By Alistair Ryan
Class of 2020

<sequence (1) = PARTY_DAY>

_InitlliPaws 22.0
>initiating boot sequence
>loading machine learning... DONE
>loading letter recognition... DONE
>uploading collar interface... DONE
>initiating leash response... DONE
>booting system to factory settings......

I awake. Hello world.

>DisplayLang = “English”
>func(“SetDateAndTime”) = ERROR_124:
TimeReceptorNotFound
>EnterHandler = “Garland”... APPROVED
>Awaiting instruction...

I look = two men. I see “Garland,” “Garland” is tapping my leash. He bends down. “Orwell, can you upload the party pack to Goldie? She’s got a client tonight.”

>FaceRecognised = “Orwell”

Orwell syncs my SmartCollar to the server. I wait on table. Default position.

>Receiving...
>PartyTricks.apk...100%
>Interactions.apk...100%
>AgeGroup.apk...100%
>ClientData.apk...100%

Garland is almost done, “Alright, buddy. You’re good to go again.” I see Orwell walk. Out of the room. Five minutes later, he has bowl. Inside are small brown pellets.

“Eat up, you don’t wanna be hungry tonight,” says Orwell.
“What fusion is this?” says Garland.
“CoreEnergy. For tonight’s party,” says Orwell, “with a learning booster.”
“Scrap it,” says Garland. “Give her the IntelliPack. She’s got a few assignments coming up this week and we need to speed the process up.”

Orwell exits the room. He returns with a new bowl. This time, there are small blue pellets inside. He tells me to eat. I listen. I eat. It tastes like nothing. But I eat it all. A long while later I am led outside the room.

I walk through a long, narrow corridor. It is bright. White lights. Along the corridor, other doors. At the end, there is a glass door. Sunshine is pouring through it. The floor is cold, and my paws feel cold. The air smells clean.
Finally I reach the glass door, and Orwell opens it. We are on a street. In front of the building, I see a van. On the van, it reads:

**INTELLIPAWS**

*Friends For Hire*

With it, there is a picture of a dog. When I look back at the building behind me, I see the same words on the storefront. Intellipaws. I see something else which makes me stop. But Orwell is walking quickly. He pulls my leash hard, yanking me to catch up. So I didn’t get a good look.

He leads me up into the back of the van, then ties the leash to a grill that separates me from the front. Then he goes in front and starts the van. I see him input something into the dashframe. Then he reclines his seat fully and goes to sleep. The van starts to move, but I do not. From where I am in the back I can see it very clearly now, the thing I saw on the glass door of the store front. Looking at the little mirror in the van, I see myself. And I look like the same dog on the side of the van.

When the van finally stops, a voice speaks. *You have arrived at 155 Baskerville Avenue. Travel duration: twenty three minutes. Vehicle fuel left: seventy-two percent. Parking conditions at 155 Baskervi—*

Before the message is complete, Orwell has woken up and cut the transmission by waving his hands twice. He leads me out of the van. We’re on a street. We walk up to a house. Orwell places his hands on the palmlock, and the door opens. Many people are waiting for us inside. A lady walks towards us.

“Ah! You must be Mr. Smith,” she says. “Glad you had no trouble with the palmlock, some of the guests couldn’t get in just now even though I’ve uploaded everyone’s retinas to the mainframe earlier.”

“Not a hassle at all, Ma’am,” Orwell replies. “Please, make yourself at home. And I assume this must be Goldie?”

“Ah yes, Goldie.” Orwell looks at me. “Goldie, this is Mrs. Jones, please listen to her for the evening. I will be back in four hours.”

> FaceRecognised = “Mrs_Jones”

“Thank you, Mr. Smith. Sarah and her friends will be so happy to see a dog, especially since they went extinct after the —”

“I’m sure she will, Ma’am.”

“Oh, one last thing - is her wakeword Goldie?”

“Yup. “Hey, Goldie” is the default for all golden retrievers. We’ve disabled mature reactions and programmed her for interactions with children tonight. Here’s the list of things you can make her do. Just use the leash.”

Orwell hands the instruction manual over to Mrs. Jones, as well as my leash, then leaves. Mrs. Jones leads me upstairs. She opens a room and a little girl is inside. She is sitting in the middle of the room, alone. She has a VVR headset on. The room is empty, except for four triangulators in each corner of the room.

“Here, let’s get you connected,” says Mrs. Jones. She registers my leash to the CoreEngine. Suddenly, about ten other children appear in the room. They are all projections. Sarah on the chair has disappeared. Instead, she too is a projection. I am in their VVR space now. The whole room is filled with decorations, and the children cheer when they see me. On the wall, a banner says:

**HAPPY 8th BIRTHDAY SARAH!**

The children stroke my fur and huddle around me. Although they are projections, I can feel them.

“Hey, Goldie,” I suddenly hear.

> func(Wakeword) = ”true”;

“Can you show us some tricks?”

> func(smartcollar_display) = ”What would you like to see?”

I answer back on my SmartCollar interface, as well as say, “What would you like to see?” I display a set of options as well:

> func(smartcollar_display) = ”1. Flip 2. Balancing 3. Fake Death. more...”

Sarah holds up a finger. I recognise it as one.

> Accessing “tricks.apk”... DONE

I find flip algorithm in my trick.apk pack and run it. The girls cheer. Eventually, Mrs. Jones disconnects me when my time there is up. The children and the decorations disappear, but Sarah sits in the middle of the room. She is still at her party, too busy to say goodbye. Orwell appears and brings me back to Intellipaws. ❋
DEAR LARRY...

By Lawrence Ypil, Writing Lecturer

Before diving into this issue’s edition of Dear Larry, let me thank everyone who sent in their questions about the art and craft of the writing life, which is really an excuse to talk about so much more! I also wanted to invite everyone who has a burning question to shoot me an email in time for our final issue of this school year. Email me at lawrence.ypil@yale-nus.edu.sg – I look forward to reading all your emails. Now off to the questions!

How do writers find value in rearranging words to create poetic meaning? Do we defer to the existence of a muse that merely precipitates things that have been waiting to be written all along?

In an age where it’s hip to be talking about writing schedules and habits, productivity hacks and prompts, the idea of a muse has always been something I have never fully been ever to shake off. While I’m a firm believer in ritual and habit, the need to sit down in the same place regularly in order to build a writing practice, something has to be said of those moments when struck with an idea, and there is no other choice left to make except to drop everything and write. In those special moments I return to the belief that for all our cultural obsession with control (over our schedules, our goals), there is ultimately also value in believing in being in the right place at the right time.

I like the way you put it: the muse as a precipitant, as a mere catalyst for magic to happen (or a chemical reaction if you want to be scientific about it). And that’s an important distinction to make: that the muse isn’t the topic of one’s art, not its subject matter, but that which permits the articulation of ideas and feelings that have long been “kept in” and waiting to come out. In this way, is the muse, ours and not ours, forever eluding possession or control? The muse is also temporary and transient — it leaves when the wind begins to blow in a different direction, it comes when it pleases. In an age where we want everything to go as we please, it sometimes resists our wishes. And in this way it is still magical to write.
What is an auspicious page number?

I’ve always had a soft spot for numbers that are divisible by 3: 39, 453, 12, and I suspect everyone has their own secret superstitions that tide them over for the day, a breather after every few pages, the first word only at the break of dawn. To stand up from the desk only after 25 mins, pomodoro style. To make sure the edges of one’s readings are all aligned before you start. To flip the light switch three times, before the house turns pitch dark. I wonder if one of the tragic consequences of the inevitable turn to the digital is the decrease in the material contact in which rituals are made of, anxiety needing its dogeared pages, imagination needing its soft or rough textures of felt, or steel, or page – left or right, odd or even, filled with words handwritten, or blank.

How do you overcome the fear of your own voice?

You grit your teeth and close your eyes. If you’re the type to like to hear your voice, then you’ll be fine, but chances are you don’t, so you will have to understand that hearing your own voice can feel like getting under one’s skin and the self becomes the shape of some Other that is most Familiar, like the secret you’ve always known but never told anyone, not even yourself. That you wish to find your voice, though, through writing, probably means that you are not content with the way things are usually said. That you find it necessary to see the shape of the pressure of your own voice on language and you are interested in charting and measuring and changing this imprint on words. In which case you may find, in the midst of saying what you need to say, in that voice that is yours but not yours, that you must bear the burden not of speaking but of listening. In this way will you know that you are finally beginning to write what you need to write. You will not know what will come next. But you will listen as if your life depended on it, because in many ways it does.

How does one right a moth? How does one write a moth?

I’m not too sure, but I’m sure Virginia would know.

What’s your advice for writing an advice column?

Ah! The penultimate meta of meta questions! This one is easy. It’s actually the same advice I would give to writing – delay writing it until the last minute. Give it your all, when you are finally at the desk. Be honest – with yourself, but most especially with your imagination. And never, ever, answer the question that’s been posed.
SINGPOWRIMO

In co-sponsorship with the Library. Daily collective poems written by Yale-NUS community members - all welcome to contribute!

April 1 - 30

PEER TUTOR RECRUITMENT

Writing peer tutor recruitment for AY 2019-2020 will start in early March. To apply, students must be nominated by a faculty member. Look for details on the Writers’ Centre website and FB page during Week 7!

CAPSTONE SUPPORT

EVENT 1: Capstone Writing Retreat

Led by DF Isa Peralta. Come to the Writers’ Centre for 30-minute consultations, healthy snacks, and a quiet, cozy writing space.

March 16

EVENT 2: Capstone Proofreading Workshop

Led by Prof Carissa Foo. Capstone writers are invited to bring a full draft to learn and practice tips for effective and efficient proofreading.

March 30

Want to be in the loop with Writers’ Centre events and resources? Follow our FB page at https://www.facebook.com/yalenuswriterscenter/