Role of bilingualism in neurodegenerative disease II: Beyond Alzheimer's

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Author's note

This chapter draws upon similar themes as an epistemological paper titled 'Beyond Alzheimer's Disease: Might bilingualism be a more generalized protective factor in neurodegeneration?' by Voits, Pliatsikas, Robson, & Rothman (2019). While the present chapter is a concise review of the available literature, please see the aforementioned manuscript for a more detailed discussion on neurodegenerative disease mechanisms, meticulous evaluation and linking of the parallel literatures on bilingualism, and more general research of progressive neurodegeneration, and a comprehensive roadmap drawing up a future research agenda for the field.

Abstract

Over the past decades, bilingualism has emerged as a potential factor having a significant impact on cognition and brain structure. Such research typically examines the effects of bilingualism in healthy children and adults. Conversely, the body of literature examining bilingualism effects in ageing populations remains comparatively small. This holds especially true with regards to effects of bilingualism in clinical ageing populations. Current evidence suggests that bilingualism might contribute to delaying the expression and/or progression of the symptoms of Alzheimer's dementia for as much as 5 years. To the extent bilingualism plays an ameliorative role at all, it seems reasonable to expect that it would have similar effects for other neurodegenerative disorders. Nevertheless, relevant studies examining disorders other than Alzheimer's Disease or Mild Cognitive Impairment are extremely limited. Despite compelling reasons to the contrary, the few relevant studies that do exist are not properly linked, nor appreciated as a meaningful cohort in their own right. Making links across neurodegenerative disorders and bilingualism, to the extent possible, serves both practical health-related and theoretical-oriented needs. This chapter considers whether the currently available evidence is sufficient to allow for claims of bilingualism conveying more general protective effects in clinical ageing while identifying gaps in our knowledge and recommending future work to better understand these proposed links.

Introduction

My academic background has been quite varied with distinct interests that have shifted, morphed, and spilled over into one another over time. At different points of my life I have been a student of medicine, neuroscience, linguistics, and language sciences. Some would say that these are disciplines that are difficult to bridge, even in today's scientific world of interdisciplinary research. Yet, the intersection of all of the above is what this chapter is about. This might not have been the case if it was not for the ground-breaking and pioneering research by Ellen Bialystok and colleagues (2007) that shaped this field of study and kickstarted the linking of bilingualism and clinical implications use of more than one language might have.

I first saw Ellen in person at the 2016 Society for the Neurobiology of Language (SNL) meeting in London, UK. I had recently graduated from a cognitive neuroscience undergraduate program and had developed a keen interest in the neuroscience of language. At the time, I was working at a medical college in a teaching position and had not commenced work on my doctoral dissertation yet, so I attended the meeting as a listener to get myself up to speed with the latest developments in the field, network, and engage with as many researchers as I could in those few days.

One of the central events of the SNL 2016 meeting was a debate on the consequences of bilingualism for cognitive and neural function between Ellen and Manuel Carreiras. I recall this as an extremely heated debate, reflecting the intense nature of discussions regarding this topic in the wider literature. This 1.5-hour long exchange of densely packed arguments from both discussants was formative for myself as a young researcher as it really piqued my interest in the cognitive and neural effects of bilingualism. I tried to find a moment to introduce myself to Ellen, especially after the debate. However, given her calibre, she always seemed to be surrounded by people and I never mustered up the courage to push through the crowds to talk to her. Now, four years later, things have changed. I am in the final stages of my PhD research

project on bilingualism and effects of it on brain and cognition in aging. I am privileged to be able to contribute to this volume devoted to Ellen and her foundational work on bilingualism, brain, and cognition, which has clearly been an inspiration for my own research. And, finally, I have grown as a researcher, I have grown my confidence and, if I find myself in the same scientific meeting as Ellen Bialystok, I will not hesitate to introduce myself to her anymore. Hopefully this can happen soon.

The initial findings suggesting bilingualism to be a factor that delays the onset of dementia by 4-5 years (Bialystok et al., 2007), were arguably the cornerstone of a research programme linking bilingualism with changes in clinical outcomes and have since been replicated by others (e.g., Alladi et al., 2013; Woumans et al., 2015). More recently a few large meta-analyses of relevant studies have confirmed the initial findings – while the severity of Alzheimer's Disease is not likely to be reduced in bilinguals, the onset of the disease is indeed projected to be later in life than in their monolingual counterparts (Anderson, Hawrylewicz, & Grundy, 2020; Brini et al., 2020).

The linked and parallel literature on bilingualism effects in healthy adults has produced mixed results (see Lehtonen et al., 2018 for review). This variability in results is smaller in studies looking at older populations, both healthy and clinical, suggesting a more robust effects of bilingualism in the later years of life. This is linked to the concepts of *cognitive reserve* and *neural reserve*, to which bilingualism is thought to be contributing factor leading to build-up and increase of the reserves in question (Perani & Abutalebi, 2015). The core idea is that as for a bilingual to successfully control their two (or more) competing languages and use the language appropriate for communication in a given context, languages not needed/used need to be inhibited or suppressed, while the language in active use needs to be monitored for any intrusions from the other languages (Abutalebi & Green, 2007). This feat of constant bilingual language control has knock-on effects on the corresponding cognitive control processes more

generally. Furthermore, the extensive use of executive functions involved in bilingual language control over time leads to changes in the neural substrate supporting them, manifesting as increases in neural tissue (brain reserve) or improved connectivity (cognitive reserve), making the brain more resilient when facing age- or disease-related neurodegeneration..

As a result of the above, the neuroanatomical changes to the brain as a result of constant management of more than one language can be meaningfully attributed to protection against atypical pathological decline. Bilingual experience changes the physical characteristics of the brain in areas associated with language and cognitive control (see Pliatsikas, 2019, for review). These changes to shape and volume of brain structures, white matter integrity, and grey matter density are especially relevant as neurodegeneration targets them directly (e.g., Auning et al., 2014; Gold, Johnson, Powell, & Smith, 2012; Zarei et al., 2009). Thus, if bilingualism predicates anatomical changes in the brain, increased cognitive and neural reserves, and also delays the onset of Alzheimer's dementia symptoms, we may expect these effects to be more generalisable to other progressive neurodegenerative diseases which share overlapping neural underpinnings and clinical features of Alzheimer's disease. To give a few examples, Alzheimer's disease, Huntington's disease, and Parkinson's disease are all associated with amyloid protein pathology; brain structures overlap with basal ganglia affected in Alzheimer's disease, Huntington's disease, and Parkinson's disease. The most obvious unifying factor linking all of these is the progressive nature of the disease, which commonly results dementia whichever the primary diagnosis is. With all of this in mind, we might, in fact, even ask if it is possible to *not* find similar effects for progressive neurodegeneration in general, in face of the currently established links between bilingualism and Alzheimer's Disease.

The current research on the potential clinical effects of bilingualism, however, has been mostly focussed Alzheimer's Disease and Mild Cognitive Impairment, discussed in more detail in chapter 17 of this book by Tom Schweizer (see also chapters 12 by Christos Pliatsikas and

16 by Gus Craik). Nevertheless, this should not limit the study of other neurodegenerative disorders. To build up on this discussion and these very promising initial findings, in the following sections I will discuss the evidence currently available for bilingualism effects on progressive neurodegenerative diseases other than the most common one – Alzheimer's disease –, namely, Huntington's disease, Parkinson's disease, and multiple sclerosis. Following that I will look beyond progressive neurodegeneration and discuss research revealing bilingualism to play a modulating role in non-progressive neurological outcomes as well. I will conclude this chapter with directions to further test these hypotheses more directly in future research.

Huntington's Disease

Huntington's Disease is an inherited, genetic neurodegenerative disorder with onset of symptom expression in middle age. Behaviourally, Huntington's disease usually manifests as a motor disorder, with characteristic jerky movements and impaired gait. Additional to that, Huntington's disease patients report executive functioning and cognitive disturbances (Craufurd, Thompson, & Snowden, 2001). Physiologically, Huntington's disease is associated with deposits of abnormal protein in the brain formed as a result of expression of mutant huntingtin gene (Davies et al., 1997). The slow onset of the disease is puzzling and could potentially be attributed to accumulation of the misfolded protein over decades of life. The brain regions affected the most are the striatum (encompassing the caudate nucleus and putamen) and a multitude of cortical regions, but, similarly to Alzheimer's disease, the exact mechanisms of how this results in neurodegeneration and cell death are still unknown (for a review see Walker, 2007). Clinical phenotype and expression of motor symptoms is subject to heterogeneity and depends on the cortical areas affected by grey matter thinning (Coppen, Jacobs, van den Berg-Huysmans, van der Grond, & Roos, 2018; Rosas et al., 2008; Scahill et al., 2013). Although Huntington's disease was initially thought to be '100% genetic', there is

now evidence for the role of environmental factors that slow down the expression of motor and cognitive Huntington's disease symptoms in animal models, implicating that a neural reserve and/or cognitive reserve modulate the outcome not only in Alzheimer's disease, but also Huntington's disease (see Nithianantharajah & Hannan, 2011, for a review). In support of the cognitive reserve theory, a large-scale study found that length of education is associated with an earlier estimated age of onset (which might be confounded by earlier recognition of symptoms in highly educated individuals) but less severe clinical profile (Lopez-Sendon et al., 2011). Also, there is evidence of better cognitive, neural and executive functioning outcomes in those Huntington's disease patients following a cognitively active lifestyle (Garcia-Gorro et al., 2019).

Given that Huntington's disease targets the striatum (Augood, Faull, & Emson, 1997), a brain region known to be implicated in cognitive control and 'reinforced' by bilingualism (Giavazzi et al., 2018), there are direct links for theorising and investigating whether the reported effects of bilingualism on brain structure and cognition would also mediate the course of Huntington's disease. There is some initial work done in the direction of exploring language processing mechanisms in Huntington's disease. Giavazzi et al. (2018) observed that Huntington's disease patients perform worse on a linguistic selection task than control participants, and showed that the striatum is implied in the selection of linguistic alternatives. Another recent study (Calabria et al., 2020) found a dissociation between bilingual language control mechanisms (language activation/inhibition and cross-language interference) in Huntington's disease patients. While patients exhibited impaired language activation/inhibition as evidenced by higher switch costs in a language switching task, they performed similar to healthy controls in a bilingual Stroop task, measuring cross-language interference. This can be interpreted as at least partial cognitive reserve in Huntington's disease patients allowing for some aspects of language control to remain unaffected by the disease when facing

neurodegeneration. The clear limitation of this study, however, was the lack of neuroimaging data for these patients, that would allow a more accurate picture of what cortical or subcortical areas where most affected in this small sample (n=12).

Moving from the effects of bilingualism on behaviour to its effects on brain structure and function in Huntington's disease specifically, a recent study reported bilingualism to be associated with increased grey matter volume in inferior frontal gyrus and significantly increased metabolism in an array of brain regions (Martínez-Horta et al., 2018). Although no effects were found on the structures of the brain associated with Huntington's disease the most – the striatum – bilingualism also correlated with increased cognitive functioning in Huntington's disease. This study, along with Calabria et al. (2018) provide the first direct indication of the effects of bilingualism on Huntington's disease patients, which warrants further and more detailed investigations.

Parkinson's Disease

Like dementia of the Alzheimer's type, the exact cause of Parkinson's disease is unknown, but it is thought to develop as a result of a combination of genetic and environmental factors. Parkinson's disease is a neurodegenerative disease characterised by degeneration of dopaminergic neurons on the substantia nigra and subsequent depletion of dopamine in the basal ganglia (Lotharius & Brundin, 2002). This accompanied with Lewy body presence manifests clinically as motor impairments such as muscular rigidity and rest tremor (for a review, see Jankovic, 2008). However, in addition to motor impairment, Parkinson's disease is also associated with non-motor clinical features such as cognitive and sensory disturbances (Kalia & Lang, 2015). Executive functioning is also impaired in Parkinson's disease (Kudlicka, Clare, & Hindle, 2011). Parkinson's disease is commonly concomitant with dementia (with Lewy bodies), associated with aggregation of Amyloid-β in the cortical structures and the

limbic system (Kotzbauer et al., 2012). This makes Parkinson's disease a heterogeneous disorder with commonalities to both Alzheimer's disease and Huntington's disease.

There is evidence for the cognitive reserve theory specifically related to Parkinson's disease in the literature, although the extent to which bilingualism alone contributes beneficially to the progression of Parkinson's disease is yet to be determined. From potential contributor factors to cognitive reserve, education is the only proxy that has been systematically studied in Parkinson's disease. These results suggest a better cognitive performance in highly educated individuals with Parkinson's disease (for a review see Hindle, Martyr, & Clare, 2014). While higher educational attainment does not correlate with amyloid-ß protein aggregation in Parkinson's disease patients, it does predict cognitive outcomes at similar levels of amyloid-ß deposits, showing evidence for cognitive reserve with education as a contributing factor (Lucero et al., 2015). Using cognitive lifestyle scores as a predictor for cognitive reserve, Hindle et al., (2017) found that higher cognitive reserve was not predictive of better executive functioning, but it did predict better global cognitive and also motor outcomes in Parkinson's disease.

Pertaining to language use and bilingualism, populations with Parkinson's disease have been studied to further understand the role of basal ganglia in bilingual language control (Cattaneo et al., 2015) and linguistic impairments in Parkinson's disease bilinguals (Johari et al., 2013; Zanini, Tavano, & Fabbro, 2010). This evidences the direct overlap between the areas affected by Parkinson's disease and areas involved in cognitive control. But whether bilingualism has a direct neuroprotective role in Parkinson's disease remains unclear. In a single study by Hindle and colleagues (2015) a group of English-Welsh bilinguals with Parkinson's disease showed no difference in executive functioning when compared to English monolinguals on tasks tapping mental generativity, working memory, inhibition and switching. To date this is the only available study examining the effects of bilingualism on Parkinson's

disease, and, while executive control measures were found to be the same independent of the number of languages spoken, other questions, such as any differences in brain structure and function, which could show any evidence for or against bilingualism-related cognitive or neural reserve remain unanswered. As a result, to date there is no information on whether bilingualism directly interacts with the progression of the disease and what clinical implications there might be. However, given the regions typically enhanced by the bilingual experience, and the recent evidence from bilinguals with Huntington's disease, further and systematic investigation of this particular patient group is rightly called for.

Multiple Sclerosis

Multiple Sclerosis is an autoimmune disease resulting in inflammatory neurodegeneration of white matter within the brain and spinal cord. The characteristic pathology includes axonal and neuronal loss, demyelination, and astrocytic gliosis (Lassmann, Van Horssen, & Mahad, 2012). The disorder is understood to be caused by a variety of genetic, environmental, and lifestyle factors, with environmental factors playing a bigger role than in Huntington's disease and Parkinson's disease (Olsson, Barcellos, & Alfredsson, 2016). Onset of symptoms may happen much earlier in life, with diagnosis not uncommon in early adulthood. Neurodegeneration in multiple sclerosis is not caused by misfolded protein deposits but by progressive inflammatory lesions instead. As a result, whole brain atrophy takes place at a rate of 0.5%-1.5% per year. Clinically, early multiple sclerosis is expressed via acute episodes of neurological deficits, known as relapses. They are specific to the area of the central nervous system affected and the extent of neurodegeneration (Thompson, Baranzini, Geurts, Hemmer, & Ciccarelli, 2018).

Although there are very few direct investigations linking bilingualism to multiple sclerosis directly, Giovannoni et al. (2016) outlines the paramount importance of higher brain

fitness or increased neurological reserve for preserving one's general health when facing multiple sclerosis. While they do not explicitly mention bilingualism, they call for prioritisation of activities that enhance one's cognitive reserve and, in turn, protect against cognitive impairment in the longer term. Effects of cognitive reserve in multiple sclerosis is further supported by a study utilising premorbid intelligence as a proxy for it. Here, it was found that higher general premorbid intelligence, as measured by vocabulary knowledge, predicts higher information processing efficiency in higher levels of brain atrophy (Sumowski, Chiaravalloti, Wylie, & Deluca, 2009). This suggests, as with other types of neurodegeneration, there may be bilingualism-induced cognitive reserve changes for multiple sclerosis outcomes as well. Moreover, since increased cortical lesions and decreased brain and grey matter volume are predictors of cognitive impairment in multiple sclerosis (Calabrese et al., 2009), it would be predicted that bilingualism-induced neuroplasticity in grey and white matter might contribute to a better outcome in multiple sclerosis, via a neural reserve mechanism.

Limited research directly examines the effects on bilingualism on multiple sclerosis. A recent study (Aveledo et al., 2019) looked at executive functioning, in particular monitoring and inhibition in a flanker task, in age- and sex-matched groups of monolingual and bilingual multiple sclerosis patients and healthy controls. While it was predicted that bilingual individuals should perform faster and exhibit smaller conflict costs, as measured by reaction times in the flanker task, conflict costs were reported to be the same for multiple sclerosis and control groups, suggesting no enhanced executive functioning in bilingual multiple sclerosis patients when compared to monolingual ones. However, multiple sclerosis monolingual participants made significantly more errors than control monolingual participants, while the two bilingual groups (patient and control) did not differ in that respect, hinting towards some benefit for the bilingual patients only. Another small-scale study (Soltani et al., 2018) cross-sectionally tested executive functioning in relapsing-remitting multiple sclerosis monolingual

and bilingual patients. Here, results showed significantly better non-verbal executive functioning in bilinguals, although the results were worse in verbal executive-functioning tasks in this group. In sum, these studies should be treated as initial explorations of bilingualism and multiple sclerosis and, while no conclusive effects of bilingualism on multiple sclerosis were evident, one has to be mindful of small participant groups tested (n=10 multiple sclerosis bilinguals in Aveledo et al., 2019; n=13 multiple sclerosis bilinguals in Soltani et al., 2018), which do not allow for sufficient statistical power to draw global conclusions at this time.

Non-progressive neurological disorders

Evidence reviewed so far suggests that increased brain reserve mitigates the effects of progressive neurodegeneration. This calls for more targeted research on the potential effects of bilingualism, as a contributor to cognitive and neural reserves. However, there seems to be effect on clinical outcomes in cases of other neurological disorders too, going beyond the effects of progressive neurodegeneration discussed so far. These other notable mentions include disorders such as schizophrenia, epilepsy, and stroke. Some initial evidence has indicated that the outcomes of the above can be mitigated by bilingualism. As the disease mechanisms and clinical development are quite different, this evidence only further bolsters the view of cognitive and/or neural reserve contributing to brain health when facing a neurological disorder. That is, bilingualism contributes to increased brain plasticity resulting in compensatory effects across the board, e.g. a greater ability for the brain to 'rewire' itself in a more efficient manner in light of acute, not only progressive, brain tissue loss.

The most robust evidence for modified clinical outcomes in bilinguals are linked to enhanced cognitive improvement in individuals who have suffered stroke. Stroke is a case of an acute onset neurodegeneration. This neurodegeneration constitutes stable, non-progressive neurological damage, allowing for greater reorganization of neural networks over time and

subsequent recovery. There is evidence that bilingualism is a predictive factor of post-stroke cognitive outcomes, with more bilinguals (40.5%) than monolinguals (19.6%) exhibiting intact cognitive functions post-stroke (Alladi et al., 2016). A more recent study cross-sectionally evaluated stroke recovery in monolingual and bilingual stroke patients. It was found that even if the incidence of post-stroke aphasia is the same for monolingual and bilingual individuals, bilinguals are likely to have less severe symptoms of aphasia (Paplikar et al., 2018). These results imply potential benefits of bilingualism even on the recovery of patients with acute neural tissue loss and open up even further research avenues encompassing an increasingly wider scope on interactions between bilingualism and neurological conditions.

Schizophrenia is a disorder that manifests as neurocognitive dysfunction, although there is no consensus for whether it is a result of progressive neurodegeneration – rather, it is thought to be neurodevelopmental as it does not progress after onset and it is possible experience recovery from it. There are changes in the brains of schizophrenia patients, but they are not progressive (for a review see Rund, 2009). Most studies in this area are rather looking at the effects of the disorder on the bilingual language production (Smirnova et al., 2015) or second language acquisition (Dugan, 2014). The only review paper exploring the effects of bilingualism to day (Seeman, 2016) suggests that while there is no evidence to date for or against better bilingualism-related clinical outcomes in schizophrenia, this is an important aspect to look at in terms of therapy and bilingualism. There is also evidence for better employability rates in bilingual schizophrenia patients, which leads to increased quality of life and overall satisfaction. However, the information is scarce and the research showing the benefits of bilingualism on brain and cognition might also prove to be beneficial in schizophrenia, especially in the light of suggestions that increased cognitive reserve may interact with outcomes in neuropsychiatric syndromes via either affecting the risk of

development or mitigating the symptoms (see Barnett, Salmond, Jones, & Sahakian (2006), for review).

Epilepsy – a neurological illness characterised by seizures as a result of abnormal electrical activity in the brain, namely increased neuronal excitation and reduced inhibition, causing synchronisation of seizure-inducing excitatory networks. It is the most common chronic neurological disease, with 65 million people affected worldwide, and anti-epileptic pharmacological treatments as well as surgical treatments for epilepsy are readily available (Moshé, Perucca, Ryvlin, & Tomson, 2015). There is very little evidence of research into bilingualism and epilepsy, but two studies suggest bilingualism-related benefits in epilepsy patients. First, a study compared bilingual and monolingual children with epilepsy and found significantly better working memory in bilinguals, although no other measures of executive functioning were significantly different between the two groups (Veenstra et al., 2016). This is the same trend observed in studies comparing monolingual and bilingual children without epilepsy. Thus, it is not clear that epilepsy as a separate factor brings anything to bear specifically. More to the point at hand, however, is a recent study testing bilingual and monolingual patients with temporal lobe epilepsy, a common type of focal epilepsy, associated with executive functioning impairment. While white matter exhibited reduced integrity in frontal areas of the brain in the bilingual patient group, the performance on executive functioning measures was similar to that of the other groups (Reyes et al., 2018). This serves as evidence for higher cognitive reserve in bilingual temporal lobe epilepsy patients. Indeed, this suggests that (bilingualism-induced) cognitive/neural reserve seems to be the common denominator across all the diseases/disorders discussed.

Discussion and conclusions

The interest and body of research on the effects of bilingualism on the declining brain is increasing, as evidenced by the small, but steadily growing body of literature in the recent

years. However, it is clear that the literature is quite limited, questions need to be answered and predictions tested. Having discussed the research considering bilingualism and clinical neurodegenerative populations, a few unifying points stand out.

First, it is impossible to avoid the pervasive common theme emerging from the available literature – the notion of cognitive and neural reserves and bilingualism as a contributing factor to them. It is established that bilingualism contributes to this mechanism by delaying the onset of Alzheimer's Disease symptoms, however, the discussion in the literature about attenuation of other types of neurodegeneration via the cognitive reserve mechanism is usually done via some other proxy or contributor, such as educational attainment, disregarding bilingualism - a strong candidate contributor to cognitive reserve. This applies not only to progressive neurodegeneration, such as Alzheimer's disease but to other neurological conditions too. Given that bilingualism is an established contributor to this mechanism, the absence of research directly investigating the effects of it is puzzling.

Second, there are strong parallels between the natural history of Alzheimer's disease and other types of neurodegeneration. This provides clear predictions and hypotheses to be tested, based on our current knowledge of bilingualism-related neuroprotection from Alzheimer's disease onset. Nevertheless, there is a miniscule amount of literature at this moment on bilingualism and any clinical effects it may have, beyond the literature on Alzheimer's disease. There are some initial suggestions on the positive effects of bilingualism in Huntington's disease, indication of improved executive functioning in Parkinson's disease. However, there is no literature on the wider effects of bilingualism on the disease progression in Parkinson's disease. Even if the neurophysiology of multiple sclerosis differs from other types of progressive neurodegeneration, the wider multiple sclerosis literature suggests that neuroprotective effects attributed to bilingualism could slow disease progression.

We live in a globally ageing world. 2019 marked the first year in human history when there were more people aged 30 and above in the world than those aged under 30 (Ritchie & Roser, 2020). The overall global number of people 65 year old and older is forecast to be just under 2 billion by 2050 (United Nations, 2017). With these numbers in mind, and the fact that bilingualism does delay the onset of Alzheimer's disease symptoms it is increasingly important to understand the contributions increased cognitive and neural reserves might have for global public health and economy. Given that there are no pharmacological cures to most of these disorders this research might inform public health policies around the world.

Overall, it is clear that the literature on bilingualism and neurodegeneration as a whole is extremely scarce and there is a vast amount of research to be done. This applies to both quantity and quality of future research. Not only are more studies needed, but also the links between them need to be better understood. However, at present there is a lack of a central theme or a main objective unifying the ongoing research. It would be wise to look at the effects of bilingualism not only in isolation as related to a particular disease, but study the effects of bilingualism and, by this proxy, cognitive and neural reserves, on age- and disease-related neurodegeneration in general. A more general research agenda would be welcome to allow for forging forward with common aims, questions, comparable methods and procedures.

There are definite predictions and directions for future research on clinical effects of bilingualism. The initial findings of bilingualism as a factor delaying the onset of Alzheimer's disease came from studies looking at medical records such as Bialystok et al. (2007). Since then, the field has moved on to experimental studies testing these claims and directly examining the differences between monolingual and bi- or multilingual Alzheimer's disease and mild cognitive impairment patients (e.g., Duncan et al., 2018). As a first step, it would be valuable to see similar studies to Biaystok et al., (2007) and Alladi et al. (2013), looking at medical records done for the effects of bilingualism on more closely related neurodegenerative diseases

– Huntignton's disease and Parkinson's disease. At the same time, there is a need to begin (or continue, as is the case for mild cognitive impairment and Alzheimer's disease) experimental research, directly examining clinical effects of bilingualism in patient populations – as evident from the review above, there are often few studies per disorder that cannot, in essence, provide satisfactory amount of evidence for global conclusions. And finally, we need to better understand the exact underlying mechanisms of bilingualism and its contribution to improved clinical outcomes.

Often the research community has treated bilingualism as a dichotomous variable, whereas it is an incredibly complex and multifaceted experience with many factors contributing to the bilingual spectrum (DeLuca, Rothman, Bialystok, & Pliatsikas, 2018). Therefore it is recommended to collect more detailed language background information and patterns of bilingual language, such as Language and Social Background Questionnaire (LSBQ) (Anderson, Mak, Keyvani Chahi, & Bialystok, 2018), Language Experience and Proficiency Questionnaire (LEAP-Q) (Marian, Blumenfeld, & Kaushanskaya, 2007), or the measures of one's language entropy (Gullifer & Titone, 2019). By treating bilingualism as a binary (yes/no) value, we are losing much of the detail within bilingualism such as length of immersion in one's second language environment, age of acquisition, frequency of language use and more, which can provide more insight and provide better understanding of bilingualism and its role in neuroclinical outcomes.

The initial findings show bilingualism to have a very tangible impact on the clinical outcomes in at least some types of neurological disorders. However, at this stage is it of paramount importance to remain cautious. While these findings are extremely encouraging, we are yet to reach a critical mass of literature that would support (or not) our present knowledge of the effects of bilingualism on neurodegeneration *beyond* Alzheimer's disease and mild

cognitive impairment. To do so we need to rely on joint interdisciplinary forces of biologists, cognitive scientists, language and neuroscientists, gerontologists and many more.

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