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Cycling and impaired cognition

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Abstract

Physical activity can help to prevent hypertension, heart disease, stroke and diabetes. Physical activity is associated with lower risk of mental illness and it plays an important role in the independence of older adults, for example by walking at their own speed or riding a home trainer. Two important aspects of physical activity are the psychological and neurological aspects. For this literature review about the extent in which cycling can contribute to the mobility and independence of people with neurodegenerative disorders PsycInfo is used as a search machine and the included neurodegenerative disorders are dementia, mild cognitive impairment, Alzheimer's disease and Parkinson's disease. It appears that cycling can slow down cognitive impairment, but this is not found in all studies. The results are significant after 6 months for Alzheimer's and Parkinson's, but not after 12 months. Physical activity can possibly play a protective role in the development of dementia or MCI later in life. The difference in cycling interventions and durations of the sessions appears to play an important role. When cycling is combined with a mental task (dual task performance), effects are small but significant after 6 months. But when participants stopped cycling after the intervention, results went back to before the intervention. Therefore, it appears that the effect of cycling on impaired cognition is significant in the short term and not in the long term. More research is needed including neuroimaging techniques, like MRI or CT scan, and a direction for future research is to focus more on the role of cycling for personal mobility and to search for more realistic ways to make the cycling experience more real life next to Virtual Reality.

Samenvatting

Lichamelijke activiteit kan hypertensie, hartaandoeningen, beroertes en diabetes helpen voorkomen. Lichamelijke activiteit wordt in verband gebracht met een lager risico op psychische aandoeningen en het speelt een belangrijke rol bij de onafhankelijkheid van oudere volwassenen, bijvoorbeeld door in hun eigen tempo te lopen of op een hometrainer te rijden. Twee belangrijke aspecten van lichamelijke activiteit zijn de psychologische en neurologische aspecten. Voor deze literatuurstudie, met als doel om de mogelijke effecten van fietsen op mobiliteit en onafhankelijkheid van mensen met neurodegeneratieve stoornissen te onderzoeken, wordt PsycInfo gebruikt als zoekmachine, en de geïnccludeerde neurodegeneratieve aandoeningen zijn dementie, milde cognitieve impairment, de ziekte van Alzheimer en de ziekte van Parkinson. Het lijkt erop dat fietsen cognitieve stoornissen kan vertragen, maar dit is niet in alle onderzoeken aangetoond. De resultaten zijn significant na 6 maanden voor Alzheimer en Parkinson, maar niet na 12 maanden. Lichamelijke activiteit kan

mogelijk een beschermende rol spelen bij het ontstaan van dementie en MCI op latere leeftijd. Het verschil in interventies en duur van de sessies blijken een belangrijke rol te spelen. Wanneer fietsen wordt gecombineerd met een mentale taak (dual task interferentie), zijn een aantal resultaten klein maar significant na 6 maanden. Maar als deelnemers stopten met fietsen na de interventie, gingen de resultaten terug naar vóór de interventie. Het lijkt er dus op dat het effect van fietsen op verminderde cognitie op korte termijn significant is en niet op lange termijn. Er is meer onderzoek nodig, waaronder neuroimaging-technieken, zoals MRI- of CT-scan, en een richting voor toekomstig onderzoek is om meer te focussen op de rol van fietsen voor persoonlijke mobiliteit en om te zoeken naar meer realistische manieren om de fietservaring levensechter te maken naast Virtual Reality.

1. Introduction

Physical activity refers to all kinds of movements. Synonyms commonly used are exercise and moving, and popular exercises are walking, sports, and cycling. There are different levels of physical activity and it is for everybody's enjoyment (World Health Organisation [WHO], 2010). Physical activity helps to prevent hypertension, heart disease, stroke and diabetes, is associated with lower risk of mental illness (Teychenne et al., 2021), and it plays an important role in the independence of older adults, for example by walking at their own speed or cycling on a home trainer. Maintaining independence in the ageing population will lead to better continuing favouring social relationships and mental health (Mandolesi et al., 2018), where this independence is important to maintain a sense of control about going where they prefer (Weinberg, & Gould, 2015). Physical activity can be divided into low intensity and high intensity exercise. In low intensity physical activity, participants perform about 20% of the total load, and in high intensity physical activity they perform on roughly 80% of their total capacity (Singh et al., 2005). By performing physical activity at a low intensity level for two times per week, older adults could stay longer independent than when they are not physically active (Pereira, Baptista, & Cruz-Ferreira, 2016). Other research shows that regular physical activity in older adults can result in coping more easily with instrumental activities of daily living (ADL). As a result, they can stay independently and self-sufficient for longer (Crevenna, 2020). Instrumental activities of daily living are activities that allow an individual to live independently in a community. These are not necessary for functional living, but it can significantly improve quality of life (Arcoverde, Deslandes, Rangel, et al., 2008). Some examples are cooking, transportation, cleaning, laundry and managing finances (Guo, & Sapra, 2021). Besides psychological benefits and increasing independence, physical activity also improves physical performance, mental status and general health (Mahalakshmi, Lee, & Kumar, 2020). It blunts stress activity and therefore protects against potentially behavioural and metabolic consequences of stressful events and possibly preventing many chronic diseases (Silverman & Deuster, 2014).

Physical activity can influence a number of factors, whereby two important factors are the psychological and the neurological effect (Mandolesi et al., 2018). The first are the psychological effects. One of these, with the most benefits, is wellbeing (Cavill, Kahlmeier, Rutter, Racioppi, & Oja, 2008; Oja, et al., 2011; Willis, Manaugh, & El-Geneidy, 2015). D'Cunha et al. (2020) showed that older people living in a care facility improved quality of life, well-being and cognition when they could participate in activities outside the care facility such as wheelchair cycling and horse riding. In wheelchair cycling, participants sat in a

wheelchair that was attached to a bicycle. Another possible effect is that physical activity changes neurotransmitter levels and therefore improves wellbeing (Mandolesi et al., & Monteiro-Junior et al., 2015). These changes on neurotransmitters take place in the white and grey matter of the brain and losses of these matters are part of the normal ageing process. These losses are seen in the prefrontal cortex, insula, anterior cingulate gyrus and the inferior parietal lobe. These areas are connected to the limbic system and this plays an important role in cognitive processes like attention, working memory and the control of behaviour (Ohnishi et al., 2001). Neural cells can adapt or succumb to these changes. When they succumb, it leads to neurodegeneration and then one may speak of abnormal ageing (Mattson, Chan, & Duan, 2002). Neurodegeneration is a process of progressive loss of selectively populations of neurons, which results in extrapyramidal and pyramidal movement disorders and cognitive or behavioural disorders (Dugger, & Dickson, 2017). In this case, physical activity plays a protective role in this process of neurodegeneration. When physically active, someone may counteract or stop the process of neurodegeneration (Mahalakshmi, Lee, & Kumar). One possible mechanism is that physical activity promotes neuroplasticity and decreases neuronal apoptosis. Another possible explanation for this protective role is that exercise improves cognitive function by increasing cerebral vascular blood flow and thereby increasing cell regeneration and volume in brain regions which are critical for cognitive function, including the hippocampus (Leyland, Spencer, Beale, Jones, & van Reekum, 2019). It appears that six months of walking at an increasing intensity increased grey and white volume matters in healthy adult controls, and therefore it can be stated that even relatively short periods of physical activity can begin to restore some of the losses in brain volume associated with normal ageing (Colcombe et al., 2004).

One of the most used forms of physical activity in the Netherlands is cycling (Stoffers, 2012). Cycling can be used for different goals, like exercising and mobility, and it may be an alternative way for people with impaired cognition if, for example, driving a car is no longer an option. Cycling is also a healthy process and combines mobility, physical activity and is environment friendly but it is not without risk and may lead to conflicts, difficulties or crashes. An increased risk for a bicycle crash is related to cognitive and physical decline (Reurings, Vlakveld, Twisk, Dijkstra, & Wijnen, 2012). Cycling technology is nowadays advanced with the rise of electrical bicycles (e-bikes). This makes the option to take a bicycle more attractive for more people, which means that traffic is also becoming more crowded, and so does the number of crashes in which people are involved (Haustein, & Møller, 2016). Van Cauwenberg, Schepers, Deforche, and de Geus (2022) showed that cycling can be beneficial for older adults, whereby the life expectancy of Dutch people can be a half-year longer compared to Flemish

people due to cycling. Cycling is a dual task interference. This means that an individual must perform two different tasks i.e., in this case riding a bike/keeping balance and looking at the surroundings. This is an important factor because the environment is constantly changing.

Michon (1985) composed a model about driving behaviour. This model is used for driving a car, but it can be applied to riding a bicycle. According to the model, cycling can be divided into three levels. The first level is the operational level. This level includes the motor skills required to ride a bicycle, like getting on and off the bike, extending your hand and keeping balance. The second level is tactical and consists of the manoeuvres of the cyclist. An example is crossing the road, overtaking and turning. Finally, there is the strategic level. This includes the choices about which route to take (the busy crossroad because the route is shorter versus the longer route without a busy crossroad). Beside these three levels, there are also important skills used when cycling. One of them is hazard perception. Hazard perception is about recognizing, detection and prediction of danger in time. Another skill is status awareness. Road users should estimate their own ability to control the hazard mentioned before.

All different kinds of people participate in traffic. Road accidents or injuries occur in all age groups, but the most important group are old people, because damage is more severe and recovery can take much longer, if recovery takes place. Due to muscle problems, slow reaction times and osteoporosis, the impact of an accident is much higher and the recovery time and period much longer in comparison to other age groups (Azami-Aghdash, Aghaei, & Sadeghi-Bazarghani, 2018). This is supported by Engbers et al., (2018), which shows that the risk of older people sustaining an injury in a cycling accident is three times higher than middle-aged people and that this injury risk increases with age. Busy arterial roads, intersections and distributor roads have the highest share of fatal crashes for cyclists, whereby the most accidents occur on intersections. When looking at the overall cycling accidents, the most accidents happen in built-up areas (Reurings, Vlakveld, Twisk, Dijkstra, & Wijnen, 2012). People with impaired cognition may already have a difficult time in traffic because of distractions in the environment and because decline in cognitive skills is associated with an increased risk of accidents. There is, however, little known about people with neurodegenerative disorders regarding cycling (Reurings, Vlakveld, Twisk, Dijkstra, & Wijnen, 2012).

The goal of the current literature study is therefore to reveal the current knowledge about effects of cycling on impaired cognition, and how cycling may be used to support people with cognitive impairments such as dementia, mild cognitive impairment (MCI), Alzheimer's and/or Parkinson's disease. The following research question is stated: To what extent can cycling contribute to the mobility and independence of people with

neurodegenerative disorders. It is expected that cycling has a positive effect on neurodegenerative disorders, because it may slow down or stop cognitive decline due to exercising. It is also expected that cycling has a positive effect on well-being, because it can lead to staying independent for a longer period of time.

2. Method

2.1 Search machines

PsycInfo is used as search machine in the current study.

2.2 Search strategy

The key search words included ‘cycling OR bicycling OR bike riding OR cyclist OR road cycling’ AND ‘Parkinson OR Alzheimer OR dementia OR cognitive impairment’. There are search terms used for every neurodegenerative disorder in specific. This included ‘cycling OR bicycling OR bike riding OR cyclist OR road cycling’ AND ‘Alzheimer’s disease’, ‘cycling OR bicycling OR bike riding OR cyclist OR road cycling’ AND ‘Parkinson’s disease’, ‘cycling OR bicycling OR bike riding OR cyclist OR road cycling’ AND ‘dementia’, and last ‘cycling OR bicycling OR bike riding OR cyclist OR road cycling’ AND ‘mild cognitive impairment’.

Figure 1 shows a schematic overview of the search strategy.

2.3 Selection criteria & data extraction

All the included studies met the following selection criteria:

- Randomised controlled trials or experimental designs
- Including participants with dementia, mild cognitive impairment, Alzheimer’s or Parkinson’s
- The intervention has to use cycling as an exercise form
- No duplicates
- Cycling has to be on a bike or home trainer.

The first step, identification, led to a total of 166 results. Four of these were duplicates and therefore excluded, which led to 162 results (see table 1). After this, the studies are screened and only studies were included with patients with one of the four neurodegenerative disorders mentioned above (n=144). Studies about the effect of cycling at cell level, like leukocytes and other neurotransmitters were excluded. Cycling has a different meaning than cycling on a hometrainer or bike in these articles and therefore they were excluded. The next step was screening the articles abstracts and keywords if there was a match between the keywords and the words used in the search strategy. If this was the case, the abstracts were read and if the articles were about one of the four neurodegenerative disorders and cycling on a hometrainer or bike, they were included. If not, the articles were excluded. The next step is about eligibility. All articles were sorted on the inclusion criteria and divided into one of the four

neurodegenerative disorders. If they did not meet inclusion criteria, they were excluded. This led to the inclusion overview for every neurodegenerative disorder.

Figure 1. Flow chart including search strategy and exclusion and inclusion criteria.

| | | | | | |
|-----------------------|--|--|--|--|-----------------------------|
| Identification | Primary search: PsycInfo | | | | Duplicates removed: n= 4 |
| | Records located: n= 166 | | | | |
| Screening | Dementia n= 162 | MCI n= 162 | Alzheimer's disease n = 162 | Parkinson's disease n = 162 | |
| | Titles & abstracts screening: n= 47 | Titles & abstracts screening: n = 6 | Titles & abstracts screening: n = 47 | Titles & abstracts screening: n = 62 | |
| Included | Articles fitting the inclusion criteria: n = 5 | Articles fitting the inclusion criteria: n = 2 | Articles fitting the inclusion criteria: n = 6 | Articles fitting the inclusion criteria: n = 5 | |

3. Results

3.1 Dementia

After implementation of the inclusion and exclusion criteria, 5 studies were identified that investigated the effect of cycling on people with dementia. Table 1 shows participant data.

Table 1

Participant data for the dementia studies

| Study | Participants | Age | Gender (%F) | Severity as inclusion criteria | N | Severity of disorder |
|--------------------------------|---------------------------------------|---------------|-------------|---|-----|--|
| Sacco et al., (2016) | Patients with MCI | 72.3 (SD=2.3) | 37,5% | MMSE score higher than 22 | 8 | |
| Bowen (2012) | Dementia | 81.6 | 69.3% | TICS score <2 SD below the mean | 277 | |
| | No dementia | 75.4 | 52.9% | - | 531 | |
| Hörder et al., (2018) | Healthy women between 38 and 60 years | 50.2 (SD=7.0) | 100% | - | 191 | Psychiatric examinations and medical records |
| Buettner, & Fitzsimmons (2002) | Patients with dementia and depression | - | - | MMSE score lower than 24 and GDS score +4 | 70 | |
| van Santen et al., (2022) | Patients with dementia | 79 (SD=6.0) | 46,4% | Mean MMSE score of 18.75 | 112 | |
| | Informal caregivers | 66 (SD=12.5) | 74% | - | 200 | |

Note.: – means that there is no information about this data.

3.1.1 Inclusion and exclusion criteria

No contradictions to participation in physical activity (Sacco et al., 2015; van Santen et al., 2021) and a clinical diagnosis of dementia were used as inclusion criteria in 4 of the 5 studies. Only Hörder al., (2018) included healthy women. A possible diagnosis of dementia was given at the end of the study and therefore it was no inclusion criteria. The Minnesota Mental State Exam was used as an inclusion method in two studies. Severity of dementia was based on MMSE or GDS scores. Included patients are shown in table 1. Patients with a comorbid psychiatric disorder other than dementia were excluded (Sacco et al. 2016; van Santen et al., 2022). Sacco et al., (2016) is considered a dementia study because of the MMSE severity score,

whereby a score of 26/27 can be considered as MCI and below as dementia (Hoops, 2009).

Bowen (2012) and Van Santen et al., (2021) included community dwelling adults, but they did not have to live there for a specific time like in the study by Buettner and Fitzsimmons (2002), which only included participants who had been in a facility for at least a month. Van Santen also included participants who attended the day care activities at least two times per week and participants needed a caregiver who was willing to participate. Because their intervention lasted six months, participants were excluded if they were admitted to the hospital or a nursing home in the following six months. Bowen (2012) used healthy adult samples from a larger database (Health and Retirement Study [HRS]). The sample is from a longitudinal design. They used every participant, except the ones who did not record any physical activity information. In the study by Hörder et al., (2018) they also used a sample of healthy participants from a larger dataset, but they looked specifically at one month of birth and selected their sample based on that. Van Santen, Meiland, Dröes, van Straten, & Bosmans (2021) used a clustered randomised controlled trial. A clustered randomised controlled trial is a randomised controlled trial in which pre-existing groups (clusters) of individuals are randomly assigned to treatment conditions.

3.1.2 Interventions

Sacco et al. (2015) assigned each participant random to one of two conditions. In both conditions, participants did three months of cycling on a home trainer two times per week for 20 minutes. In the first condition, participants only performed cycling on a home trainer. In the second condition, participants also cycled on a home trainer, but did some cognitive enrichment tasks in addition. These participants had a screen in front of them with two different cognitive tasks: a go-no-go task and a simple reaction time test. They did these tasks while cycling. The intervention lasted for 3 months and after these 3 months, all participants did nothing for three months. After these three months, both groups did the intervention they had not performed yet. Results show that participants in the second condition improved their reaction time during the go-no-go task, but this improvement was back to baseline one month after the intervention. It is possible that the improvement only happens when cycling and performing cognitive enrichment tasks at the same time. But they did not include a control group who performed no cycling, so it is possible that cycling combined with cognitive enrichment tasks leads to improvement. It also indicates that cycling may have a positive impact on reaction time, because when the intervention stops, results were back to baseline. But they do not compare the results with a group who did not perform cycling.

Bowen (2012) used data from an existing data set. Participants in this dataset reported their physical activity at baseline, in 2000 and 2002 by asking if they participated in activities such as cycling, swimming, hiking and walking three or more times a week. Cycling is used as a form of measurement of physical activity and therefore included. Hörder et al., (2014) also used data from an existing dataset, known as the Prospective Population Study of Women (PPSW). In their sample, participants cycled on a home trainer to maximal workload. Maximal workload is based on the results of previous subtests with the goal of achieving a workout time of 6 minutes before fatigue. They started with a warming-up followed by a break for five minutes. After the break, every participant had to cycle as fast as they could for six minutes. In this case, cycling is also used as a measurement tool for physical fitness. All participants received neuropsychiatric examinations by a psychiatrist and by experienced psychiatric nurses to make a diagnosis of dementia or not. From 1968 until 2012, every participant was tested six times for dementia. Bowen (2012) included demographics, genetic risk factors, health conditions and behaviour as covariates. Hörder et al., (2014) do not mention anything about additional information about participants or their cognition. They only used the diagnosis of dementia, and this was based on medical records. Results showed that in participants who performed high on fitness, the risk of dementia could decrease with 88%. This could mean that physical activity can delay the onset of dementia. Both studies had much drop out, but this did not have a significant effect on the outcome.

Buettner et al., (2002) used a wheelchair bicycle to investigate the effects of this way of cycling on long-term care dementia patients. Participants took place in the wheelchair and another person sat behind them and did the cycling. They experienced the cycling experience, but they did not perform the cycling themselves. The authors do not mention the surroundings, only what kind of wheelchair bike is used. The intervention consisted of two phases. In phase one, participants performed wheelchair cycling five times a week for one hour and for a total duration of two weeks. After these two weeks, the intervention lasted but at maintenance level. This included wheelchair cycling two times per week with a family or staff member instead of five times and is called phase two. There is no control group. Results show that participants reported higher quality of life and less depression. This could indicate that only the experience of cycling can improve quality of life, even without performing the actual cycling activity. So, despite the fact that participants did not ride an actual bike, only the experience of cycling was enough to increase quality of life and decrease depression rates. Despite these results, there were no neurological indications that the intervention stopped or slowed down the depression. This result relies on self-report only. Depression rates were significantly lower after the

intervention. Another important point for further research could be to investigate whether the decrease in depression and increase in quality of life can lead to stabilisation of dementia and how this works.

Last, Van Santen et al., (2021) included patients with dementia and assigned them to one of two groups. The first group did interactive cycling on a stationary bike, two times a week for six months. Their route was presented on a screen in front of them which made the experience more like real life cycling compared to cycling on a home trainer without a screen. This was the exergaming group. The second group was the control group and they took part in day care activities like singing, cooking or hiking, but not cycling. They included the MMSE to measure cognitive functioning and the GDS for the screening of depression before the intervention. The Cohen-Mansfield Agitation Inventory (CMAI) was conducted after the intervention to measure agitation. Results show that there were no differences between both groups at the 3-month period in cognition, but after these 3 months the financial costs of the intervention were higher for the exergaming group. But this difference was not significant after 6 months (the two periods of three months combined). The authors mention a possible social aspect, whereby walking in a group is more beneficial than cycling individually. Quality of life was the same for both groups after 6 months, so there is no improved quality of life. This is contradictory to Buettner et al., (2002), which showed an improved quality of life. The difference is that Buettner et al., (2002) used wheelchair cycling with another person and in Van Santen et al., (2021) every participant cycled individually. The exergaming group said that their quality of life was lower than the control group, the social costs were higher and the effects were smaller. So, cycling on a home trainer, two times a week for six months does not have a significant effect on quality of life, physical activity. After three months, costs were higher for the exergaming group.

3.1.3 Limitations

Hörder (2018) and Bowen (2012) both used an existing, longitudinal sample. A lot of drop out, which is a common problem with this kind of data, was a problem only reported by Hörder et al. Sacco et al., (2015) did not use a control group, but only an experimental group. So, they say that cycling improves reaction time, but only in people with dementia.

Another limitation is that the severity of dementia is different in every study. This could mean that in one study the patients had more severe dementia than in another study and therefore influence the results.

3.2 Mild Cognitive Impairment (MCI)

When looking at mild cognitive impairment, two studies are used (McEwen et al., 2018; Anderson-Hanley et al., 2014). Table 2 shows participant data.

Table 2

Participant data for the MCI studies

| Study | Participants | Age | Gender (%F) | Severity as inclusion criteria | N | Severity of disorder |
|--------------------------------|---|----------------------|-------------|--------------------------------|----|----------------------|
| McEwen et al., (2018) | Older adults with subjective memory impairments | 66.2 (± 4) | 69.3% | - | 55 | |
| Anderson-Hanley et al., (2012) | Older adults | 78.55 (± 16.1) | 78.75% | - | 79 | |

3.2.1 Inclusion and exclusion criteria

Inclusion criteria were not clearly mentioned, but Anderson-Hanley et al., (2012) showed that participants had to score -1,5 SD on three domains on the neuropsychological battery measuring memory, attention, language, visuospatial functioning and executive functioning (Jak et al., 2009). Exclusion criteria were no neurological disorders or physical limitations. This is contrary to McEwen et al. (2018), which mentioned no specific inclusion and exclusion criteria, only that neurological disorders or physical limitation was not limited to functional independence, health conditions and medications.

3.2.2 Interventions

McEwen et al., (2018) and Anderson-Henley et al., (2014) both used a randomised clinical trial. McEwen et al., (2018) used two different conditions. The first condition is the simultaneous (SIM) group. In this group, participants did some stretching in the first hour and in the second hour, they learned new memory training strategies while cycling sedentary for 20 minutes. This group practised these strategies while they were performing stationary aerobic cycling. The second condition is the sequentially group (SEQ). In this group participants did aerobic cycling in the first hour. In the second hour they also learned new memory training strategies while being sedentary for 20 minutes, but they practised these new strategies while they were still sedentary and did not cycle. The training content was identical for both conditions. Both groups

cycled on a stationary cycle. They also did a warming up and cooling down of 10 minutes. Sessions were weekly and lasted for two hours. The intervention lasted for about four weeks. Additionally, they conducted non-verbal memory, visual memory, finger tapping, symbol digit coding, Stroop task, shifting attention, continuous test performance and non-verbal reasoning test to assess cognitive function at baseline and the end of the study. Results show that both groups (SIM and SEQ) had less subjective memory impairments after the intervention, but this was non-significant. This means that there is less impairment, but this is not enough to cause a memorable effect. Memory is a subjective measure. It is possible that there was not enough time for cognition to improve due to a short intervention period. Both groups showed improved verbal memory and shifting attention. Executive function improved in both groups, but the improvement was greatest for the SEQ group. So, this could mean that cycling improves executive function in both groups. Memory improved more in the SIM group compared to the SEQ group. This means that cycling before the cognitive tasks could improve the performance of executive function.

Anderson-Hanley et al., (2014) used two conditions. The first condition was stationary cycling and the other condition was interactive stationary cycling. In the second condition, an additional VR screen was present and participants interacted with a virtual bike tour. Their intervention lasted 45 minutes, was divided over five days and cognitive function was measured at baseline, after one month and after three months. In the first 3 months, participants were randomly assigned to one of the two conditions. After the 3-month intervention, participants got to choose in which group they wanted and stayed in this group for another month. This was the naturalistic group. The authors do not mention differences due the stationary versus interactive group, only the difference is that in the interactive group a tv screen was present. Additionally, they conducted the Stroop task to measure cognitive function. They also measured self-efficacy using the Self Efficacy for Physical Activity Survey (SEPAS). Their degree to which participants saw barriers and benefits in exercise was measured with the Exercise Benefits/Barriers Scale (EBBS). Social support was measured with the Social Support and Exercise Survey (SSES) and motivation with the Motives for Physical Activities Measure-Revised (MPAM-R). The authors looked at the period after the intervention if participants continued cycling or not. Participants with declining executive function at the start of the naturalistic window condition exercised more frequently compared to the group which already made executive function improvements. This shows that motivation can play an important role. Earlier research by the same authors suggests that exergaming while stationary cycling can serve as a buffer against cognitive decline (Anderson-Hanley et al., 2012). They used the Stroop

task to measure cognitive function. There was a significant relation between motivation to exercise and exercise adherence, namely the higher the motivation, the more active participants took part in the activity after the intervention.

3.2.3 Limitations

Both studies do not mention participants' MCI severity. There are different stages of MCI (Anderson, 2019) and it is possible that one of the studies had more severe MCI than the other and therefore the results are different. Both studies do not mention any reasons for why they choose their outcome measures. Apart from this, they measured cognitive function with only the Stroop task and no other tasks. The Stroop task measures aspects of attention, but not all cognitive domains included in MCI.

3.3 Alzheimer's disease

There were six studies related to Alzheimer's disease. Participants data is shown in table 3.

Table 3

Participant data for the Alzheimer studies

| Study | Participants | Mean age | Gender (%F) | Severity as inclusion criteria | N | Severity of disorder |
|---------------------|---------------------------|---------------------|-------------|-------------------------------------|----|----------------------|
| Yu et al., (2011) | AD patients | 81.4 (± 3.58) | 62.5% | +11 MMSE score | 8 | Mild-moderate-severe |
| Yu et al., (2015) | AD patients | 78 (± 8) | 62% | 12-24 MMSE score | 26 | Mild-to-moderate |
| | Primary family caregivers | 64 (± 12) | 80% | - | 26 | |
| Yu et al., (2021) | AD patients | 77.3 (± 6.3) | 47% | 15-26 MMSE score or 0.5-2 CDR score | 59 | Mild-to-moderate |
| Yu et al., (2021) | AD patients | 77.4 (± 6.8) | 45% | 15-26 MMSE score or 0.5-2 CDR score | 96 | Mild-to-moderate |
| Ayed et al., (2021) | AD patients | 69.6 (± 0.99) | 65.38% | 10-19 MMSE score | 79 | Moderate |
| Sakhare (2021) | Younger adults | 25.9 (± 3.7) | 45% | - | 20 | - |
| | Older adults | 63.6 (± 5.6) | 50% | - | 20 | - |

3.3.1 Inclusion and exclusion criteria

All articles included participants who can understand and speak English. Five articles only included participants aged >60. All studies used participants which lived in a community house or another non-institutionalized environment (Yu et al., 2011; 2015; 2021a; 2021b., Ayed et al., 2021., & Sakhare, 2021). Four of the six studies conducted the MMSE as indication if participants met the criteria for Alzheimer's. Medical clearance from the primary care provider and a clinical diagnosis of Alzheimer's disease were required (Yu et al., 2011; 2015; 2021a; 2021b). Yu et al., (2021a) and Yu et al., (2021b) used a CDR score between 0.5 and 2, and Yu et al., (2015) used a cut off score between 1 and 3. Yu et al., (2015) also used more than 100 heart beats per minute as inclusion criteria to ensure exercise safety. More than one-month stable use of Alzheimer medication was an inclusion criterion used by Yu et al., (2021a) and Yu et al., (2021b), while Ayed et al., (2021) only included participants who did not use any drugs and used it as an exclusion criterion. Yu et al., (2021) included caregivers and they were screened that they were the primary care provider at that moment and if they were qualified for enrolment. Additionally, Ayed et al., (2021) included participants with normal or corrected-to-normal vision and participants who could walk independently.

Five of the six articles also excluded participants with a neurological or psychiatric disorder other than Alzheimer's disease, only Yu et al., (2011) did not mention this. Ayed et al., (2021) additionally excluded participants with cardiovascular and orthopaedic problems and Yu et al., (2015) measured depressive symptoms. If participants had a high score of >5 on the Geriatric Depression Scale Short Form, they were excluded. Four of the articles excluded participants with unstable medical conditions in their history or in the past 6 months (Yu et al., 2011; Yu et al., 2013; Yu et al., 2021; Yu et al., 2021). Yu et al., (2021) also looked at MRI abnormalities. When these were present, participants were excluded. Abnormalities in the cycler-ergometer were also used as excluding criteria by Ayed et al., (2021). Both Yu et al., (2021a) and Yu et al., (2021b) used a resting heart state between 50 and 100 as an inclusion criterion. Sakhare (2021), studied both a group of older and younger adults who were physically capable of cycling. The younger adults were approximately 20 years younger than the older adults. A study by Yu et al., (2015) used the same design, but with a caregiver instead of younger adults. These were, on average, 14 years younger than the participants. The study used cycling as a measurement form physical fitness and was therefore included (Sakhare, 2021).

3.3.2 Interventions

Five of the articles used stationary bicycles and one article used an additional VR display next to stationary cycling (Sakhare, 2021). In four of the articles, participants did a warming up before the intervention, a cooling down after the intervention and the total duration of 6 months with cycling for three times a week. Two studies did not say anything about the duration of the intervention (Sakhare, 2021; Ayed et al., 2021). Differences were in the duration of the cycling sessions. Yu et al., (2021), Yu et al., (2011), and Yu et al., (2021) sessions lasted between 40 and 60 minutes, and Yu et al., (2015) fluctuated between 15 and 45 minutes. Ayed et al., (2021) included one session of 20 minutes, but no information is given about measurement points or the total duration of the intervention. It is possible that they only did one session, but that is also not mentioned. Five of the articles used individualised, moderate intensity cycling (Yu et al., (2011); Ayed et al., (2021); Yu et al., (2015); Yu et al., (2021a) & Yu et al., (2021b) and one did not mention anything about intensity (Sakhare, 2021). During moderate intensity cycling, participants use 60-75% of their total power. This is established with heart rate reserve (HRR) and a score of 12-14 on the Borg Ratings of Perceived Exertion (RPE) scale.

Yu et al., (2011) and Yu et al., (2015) performed a single group design. Participants were older adults with mild-to-moderate Alzheimer's disease and there was no control group. Yu et al., (2011) showed that cardiorespiratory fitness, gait and balance did not improve after 3 or 6 months of cycling three times a week. The moderate intensity cycling did not have an effect. This does not apply to the study by Yu et al., (2015), which showed slower cognitive decline compared to the normal course of the disease. A possible explanation for this difference is the sample size. Yu et al., (2011) had 8 participants and Yu et al., (2015) had 52 participants. Because of this difference, it is possible that the difference is found in larger groups and not in small groups. Additionally, they measured caregiver distress and there is a significant decrease in caregiver distress when AD patients did moderate intensity cycling three times a week for 6 months. It is possible that AD-patients experienced less depression and more quality of life and therefore there was less caregiver distress. Additionally, they measured global cognition with the ADAS-cog, ADL with the Disability Assessment of Dementia (DAD) and they used the NPI-Q to measure BPSD (behavioural and psychological symptoms of dementia), and showed that cognitive decline was slower in their participants compared to the mean trajectory of Alzheimer's. There was no increase in the DAD or NPI-Q score, which means that the possibility to perform ADL's is not improved and that participants did not have less or more disturbed perception and thoughts, mood, affect and behaviours associated with Alzheimer's

after the intervention.

Two studies used one control group and one intervention group. In this case, one group did moderate-intensity cycling and the other group did light and low-intensity stretching (Yu et al., 2021a, & Yu et al., 2021b). Yu et al., (2021a) looked at neurological and cognitive variables. They measured neurological outcomes like hippocampal volume and cortical thickness. Cognitive outcome measures were global cognition measured with the ADAS-cog and the MMSE. Results showed that hippocampal volume and cortical thickness decreased at both time points (6 and 12 months), but not as quickly as in the control group who performed low-intensity stretching. They also found a negative correlation between hippocampal volume and ADAS-Cog in the 6-month intervention group but this correlation was not found in the 12-month group. The authors concluded that cognitive decline is slower in the intervention group compared to the control group and this is partly due to a slower decrease in hippocampal volume and cortical thickness. So, the global cognition became worse over the duration of the intervention, but this was slower in the cycling group compared to the control group.

Yu et al., (2021b) measured specific cognitive components. Just like Yu et al., (2021a), they used the ADAS-cog to measure global cognition. Additionally, they conducted tests which measured episodic memory, executive function, attention, language and processing speed. They also measured premorbid intellect with the Wechsler test of adult reading. Just like Yu et al., (2015), they measured behavioural and psychological symptoms of dementia with the Neuropsychiatric Inventory but then the caregiver variant (NPI-C) and ADL with DAD. BMI was measured additionally. It is possible that they used the same participants, but they do not mention it. Results showed that, after 6 months of moderate-intensity cycling, the cognitive decline in patients with Alzheimer's is reduced when compared to the normal development of the illness. This finding was not found 12 months after the intervention, which means that the decline is slowed down until 6 months and after this the decline will be stable or get worse. Participants stopped cycling after the 6-month intervention period. In the first six months, the decline is slowed down but after these it will continue like before six months. So, stretching and cycling does not stop cognitive decline and there is no significant difference in cognitive decline whether you are stretching or cycling. It may be that if participants kept cycling after the intervention period, the results were different. But nothing can be said about this and therefore this is an important topic for future research.

Ayed et al., (2021) studied three groups. The first group performed cycling, the second group did not perform any exercises (control group) and the third group cycled and resolved cognitive tasks simultaneously. All groups performed three tasks. One regarding attention

(Stroop test), another one about problem solving (Tower of Hanoi) and the last one was about memory (Digit Span task). These were measured before and after the intervention. They also conducted the MMSE, episodic verbal memory with a recall task, visuo-constructive disorders using the clock test, verbal fluency with a lexical fluency task, mood with the GDS, and QOL with the WHOQOL BREF for all participants. The results showed that AD-patients in the first and third group improved their performances on the Stroop and Digit Span backward task compared to the control group. The first and third group did not differ in their improved performances and therefore there is no dual task interference effect. The execution time with the Tower of Hanoi and the Digit Span forward was less in the third group compared to the other groups. But the first group did also perform better than the control group. This means that the combined third group needed less time to succeed in these tasks than the other two groups. Ayed et al., (2021) mention that the control group performed worse in overall cognitive domains compared to the other two groups and this could mean that the significant findings in the first and third group were a direct effect of the exercise and not a learning effect. But, as mentioned above, there is no information about the duration of the intervention or the number of sessions and, therefore, no information about the duration of the effect.

Sakhare (2021) used two different groups: healthy younger and older adults. Both groups completed four trials of cycling and wore a device on their head which allowed them to navigate through a virtual reality park environment. They had to locate and catch lost animals in the park. They had to cycle one route a day and if they saw an animal, they had to bring it back to the sanctuary before starting the next search and rescue. The goal was to motivate older adults in general in engaging in aerobic exercise and cognitive tasks through VR. They measured mood, simulator sickness before and after the intervention, motion sickness and heart rate. Results showed that both groups showed enjoyment and low levels of stress. They emphasise the importance and possibilities to use VR for engaging in physical and cognitive activity in older adults.

3.3.3 Limitations

All studies have some limitations. One of the most mentioned limitations is a small sample size. Different reasons are mentioned. One is that the participants are old and have Alzheimer's, and that can cause restrictions of participation during the intervention. If someone falls, they cannot cycle anymore and have to be excluded from the study. Another one is that a diagnosis of Alzheimer has to be specific in terms of a MMSE-score. If someone has Alzheimer's, but their score was too high or low they were excluded. This made the sample very homogeneous. Yu et

al., (2011) and Yu et al., (2015) only used an intervention group and no control group. So, they cannot compare their results to healthy older adults, but they can compare it to AD-patients. This makes generalizability to normal older adults hard, but easier for AD-patients.

3.4 Parkinson's disease

The last topic is about Parkinson's disease. There are a total of 5 studies about cycling and Parkinson's disease found. In these articles, data are reported about 158 participants in total. Table 4 includes participants data.

Table 4

Participant data for the Parkinson studies

| Study | Participants | Age | Gender (%F) | Severity as inclusion criteria | N | Severity of disorder |
|---------------------------|--------------|------------------|-------------|---|----|---|
| Jonas (2018) | PD patients | 66.1 | - | Diagnosis of idiopathic Parkinson's and stage 1,2,3 on the Hoehn and Yahr scale | 22 | Mean UPDRS-difference score: 1.1250 (SD= 2.031) |
| Ault (2016) | PD patients | 70 (\pm 7) | 44% | Diagnosis of idiopathic Parkinson's and stage 1,2,3 on the Hoehn and Yahr scale | 16 | Mean UPDRS-score: 14.26 (SD=2.1) |
| Hazamy et al., (2017) | PD patients | 66.23 (SD= 8.54) | - | Diagnosis of idiopathic Parkinson's and stage 1-3 on the Hoehn and Yahr scale | 39 | Mean UPDRS-score: 34.87 (SD= 10.91) |
| | HOA | 72.86 (SD= 8.95) | - | - | 21 | |
| Hazamy et al., (2019) | PD patients | 65.45 (SD= 9.95) | 38.4% | Diagnosis of idiopathic Parkinson's and stage 1-3 on the Hoehn and Yahr scale | 38 | Mean UPDRS-score: 34.04 (SD=10.69) |
| | HOA | 72.74 (SD= 9.33) | 28.6% | - | 21 | |
| Gratkowski et al., (2017) | | 56 | 0% | Motor symptoms on the right side | 1 | |

Note. HOA means healthy older adults.

3.4.1 Inclusion and exclusion criteria

Four of the five studies used a diagnosis of idiopathic Parkinson's disease, a score between 1 and 3 on the Hoehn Yahr scale and no exercise contradictions that prohibit participants from cycling. Hazamy et al., (2017) and Hazamy et al., (2019) both included participants with a

stable reaction to antiparkinsonian or psychotropic medication. But they also used inclusion and exclusion criteria for their other control group: the healthy older adults. They had to be neurologically healthy and aged between 30 and 80 years. The patients with Parkinson's were excluded if they had a history of encephalitis or other neurological signals and an MRI scan with proof of brain atrophy. If participants or the healthy older adult group had a history of falls, they were excluded which reduced the chance of drop out. Additionally, four studies used exclusion criteria like neurological and psychiatric disorders, dyskinesia, uncontrolled movement or other aspects that prohibit someone from cycling.

3.4.2 Outcome measures

Both studies by Hazamy et al., used the same outcome measures. They measured processing speed, controlled processing, working memory and executive function. Additionally, Hazamy et al., (2019) looked into emotion and word choice. The Parkinson Fatigue Scale (PFS) and the Intrinsic Motivation Index (IMI) were conducted by Jonas (2018). The PFS measures the level of perceived fatigue, and the IMI measures the subjective experience of intrinsic motivation. Ault (2016) measured gait and freezing with the kinesia ONE, mobility with the timed up and go and balance with the modified clinical test of sensory interaction in balance. Jonas and Ault do not measure any cognitive domains: cycling is used as a measurement method.

3.4.3 Interventions

Four of the five articles used randomised controlled trials (Jonas, 2018; Ault, 2016; Hazamy et al., 2017; Hazamy et al., 2019). Information about participants is shown in table 4. In the article of Gratkowski et al., (2017) they describe an experimental approach to bicycling in Parkinson's. In five studies, participants were randomly assigned to one condition. All groups did a 5-minute warming-up before the intervention and a 5-minute cooling down after the intervention.

Jonas (2018) compared a static cycling group and a dynamic cycling group. In the static condition, participants were asked to cycle statically (at the same speed) for 30 minutes on a home trainer and in the dynamic condition they had to cycle at a dynamic speed on a home trainer (ascending speed until 90% of their maximal workload) also for 30 minutes. Ault (2016) did something comparable, but instead of a static cycling condition, they used a stretching group and compared them with the dynamic cycling condition. The stretching group performed upper and lower body stretching exercises. The intervention lasted 6 weeks and included dynamic cycling or stretching three times per week for 40 minutes. Jonas showed that participants in the dynamic cycling condition reported less fatigue and tension and a decrease in motor symptoms

compared to the static condition. This could mean that people had less motor impairments and were less fatigued when dynamic cycling. So, cycling speed is an important factor when looking at these results. Maximum workload leads to increased blood flow and heart rate and that could be a possible mechanism behind less fatigue and a decrease in motor symptoms. Maybe it is possible that fatigue plays an important role.

Ault (2016) showed an improvement in gait and mobility. Participants in the dynamic cycling condition improved more compared to the stretching group. This improvement was already noticeable after three sessions. In this context, mobility means keeping balance while cycling. Ault (2016) also showed that mobility improved more after every session compared to the session before, which could mean that the more they cycled, the better their mobility became. An interesting, but unexpected result was while looking at balance, participants in the dynamic condition had less of a tremor than the participants in the static condition (Jonas, 2018). The authors do not mention a possible explanation because they did not have one. This is an interesting topic for future research. Both studies show that participants in the dynamic cycling condition had less fatigue and decreased motor symptoms (Jonas, 2018) and improved mobility (Ault, 2016) compared to the static cycling group or the stretching group.

Hazamy et al., (2017) and Hazamy et al., (2019) investigated cognition while cycling in Parkinson's. In both studies, the first group performed a single task session and a dual task right after. In Hazamy et al., (2017), the second group did a dual task first and thereafter performed a single task session. The single task consisted of cycling on a home trainer at a comfortable tempo for two minutes and after this, they performed 12 different neurocognitive tasks on a laptop at a desk. The second group did the same 12 different cognitive tests but performed these while they were cycling at a comfortable speed. There was a large screen in front of them on which the cognitive tasks were shown. Between the tasks, they did not cycle. In Hazamy et al., (2019), every participant did a 3-minute discourse task, where they looked at different grammatical aspects. A discourse task is about a topic which has value messages attached to them (Dimbleby, & Burton, 2020). The single task consisted of only the 3-min discourse task on a laptop and in the dual task participants performed the 3-min discourse task while they were cycling stationary. In both conditions, participants had to respond to one of the four sentences (prompts) and they could take all the time they needed. Hazamy et al., (2017) showed that cycling speed in both groups was faster during the easiest tasks, but the speed never came below participants' own baseline, not even during the hardest tasks. Participants also responded faster in the dual task condition than the single task, which could mean that the more cognitive load, the faster the reaction time while cycling, but cycling speed went down. Overall, healthy older

adults responded faster and were more accurate than participants with Parkinson's. This could be expected, because Parkinson's can lead to brain atrophy and one of the core elements of brain atrophy is decreased processing speed. So, cycling may improve reaction time in both groups, but only when participants were cycling during the cognitive tasks and not when they cycled first and did the neuropsychological tests after this.

Gratkowski et al. (2017) describes an experimental approach to bicycling in Parkinson's. The goal of the research was to measure the cortical and subcortical activity in patients with Parkinson's while cycling. In this case, cycling is used as a measurement method and not as an intervention method. They used an experimental single case study of a 56-year-old male with deep brain stimulation (DBS) electrodes. The participant had to cycle on a modified home trainer and EEG signals were measured through a battery-powered amplifier worn by the patient on a belt. Then the participant had to cycle at a self-paced speed for 30 minutes at intermittent rest and pedalling periods guided by a sound. At the start and at the end the participant heard a sound and this was his sign to start or stop. There were 10 seconds between the rest and pedalling phases. The results showed that measuring the effects of cycling on Parkinson's at a neurological level could give a clear and detailed overview of the cortical activity and the blood flow of the brain. This intervention is non-invasive, which makes it easier to apply for more people and the costs are lower.

3.4.4 Limitations

Most of the studies had a small sample size. The biggest sample size was 39 and the smallest sample size was 16. Because of this, generalisation is difficult, and it can cause a lack of power. Hazamy et al., (2019), Jonas (2018) and Ault (2016) used self-report questionnaires. These are prone to bias, so they had to be careful with interpreting the results. They do mention this in their research, but they do not control for them. An alternative is to use observation techniques or performance-based measures (Schmitter-Edgecombe, Parsey, & Cook, 2011).

4. Discussion

The goal of this literature study was to investigate the possible roll of cycling on impaired cognition in four neurodegenerative disorders: dementia, MCI, Alzheimer's and Parkinson's. It appears that cycling on a home trainer in a controlled environment could lead to a slower reduction in cognition; however, this improvement was mostly not statistically significant in all studies. The potential effects of cycling on cognition in patients with dementia, MCI, Alzheimer and Parkinson appear to be different, also for the short and long term. No effects were found after 12 months, but some small, non-significant and significant effects were present after 6 months in all four neurodegenerative disorders. After 12 months, there was no effect for MCI, Alzheimer's and Parkinson's, but a small effect for dementia. The research question 'to what extent can cycling contribute to the mobility and independence of people with neurodegenerative disorders', cannot fully be answered based on the current literature used in this study. With caution, it can be said that cognition cannot be improved by cycling, but that cognitive decline may possibly be slowed down. So, the hypothesis that cycling has a positive effect on neurodegenerative disorders, because it slows down or stops cognitive decline due to cycling, is partly supported by this literature study. The results vary across the different neurodegenerative disorders and are mentioned one by one below.

When looking at dementia, results show that cycling two times a week for 20 minutes may improve cognition in dementia patients but this improvement was not found after 1 month follow-up (Sacco et al., 2015; Pereira, Baptista, & Cruz-Ferreira, 2016). A possible explanation is that cycling leads to more neuroplasticity, but as soon as people stop cycling, this process stops (Leyland, Spencer, Beale, Jones, & van Reekum, 2019). There was no difference in quality of life and mobility after 6 months in the cycling group compared to the stretching group. This could mean that there is only a significant effect on the short term and not on the long term (Sacco et al.,). Results showed that high fitness possibly reduced the risk of dementia with 88%. A decrease in depression rates after wheelchair cycling was shown by (Buettner, & Fitzsimmons, 2002). They mention that this decrease is because of the cycling experience. Going outside has a positive effect on quality of life and depression rates went down. This is a very promising result that cycling can contribute to more quality of life and less depression rates. Depression is measured with the GDS, a self-report questionnaire. Differentiating between depression and dementia is a common problem in the field of psychology because dementia patients often appear to be depressed and depressed patients can also appear demented (Lezak, 2012). Depressed participants often somatize their distress, which can have a negative effect on the validity of the results of the GDS. It could be that the decrease is present because

there was no depression in the beginning but only dementia.

One article related to cycling and MCI suggest that there is no relationship between cycling and decrease in dementia or cognitive decline (Anderson-Henley et al., 2014). McEwen et al., (2018) showed a positive relationship between cycling and MCI. Cycling can significantly improve general cognitive function in the condition of aerobic exercise (cycling) and memory training combined. In this memory training, participants repeated memory words for 40 minutes while they continued cycling. So, dual task interference could improve general cognitive function. Both studies used the same measure for cognitive function: the Stroop task. A possible explanation for the difference in findings is that Anderson-Henley et al., (2014) measured executive function as one concept with the Stroop task, while McEwen et al., used eight measures of executive function. Executive function is not an unitair concept (Stuss, & Alexander, 2000), and that is maybe the reason why Anderson-Henley did not find significant results. They measured a part of the executive functions, but not all. Another possible explanation that both studies found different effects is that they do not differentiate between early and late MCI or how MCI is diagnosed. In both articles, MCI is diagnosed based on the score on a single episodic memory task and subjective cognitive complaints. Edmonds et al., (2019) showed that there is high susceptibility to false-positive diagnostic errors in this way of diagnosing MCI. This means that people will get the diagnosis of MCI when the cognitive impairments are part of the normal ageing process. So, results should be interpreted with caution. Another possible explanation is that both studies used different kind of cycling tasks, whereby McEwen et al., (2018) did not use any form of VR unlike Anderson-Henley et al., (2014), which used a VR screen in the interactive stationary cycling condition.

The articles related to Alzheimer's showed that cycling can slow down or decrease cognitive decline, but this depends on intensity and duration of the intervention. A decrease in cognitive decline was present after 6 months (Yu et al., 2013; Yu et al., 2021a), but not after 12 months at moderate intensity cycling. Cardiorespiratory fitness (Yu, Savik, Wyman, & Bronas, 2011), independence, attention and problem solving was improved (Ayed et al., 2021). This could decrease the risk for a bicycle crash, which is increased with cognitive decline (Reurings, Vlakveld, Twisk, Dijkstra, and Wijnen, 2012). It can also lead to a better physical condition and reduced risk of hypertension and diabetes (Teychenne et al., 2021). Yu et al., (2021a) and Yu et al., (2021b) showed a decrease in cognitive decline in the cycling group compared to the stretching group. But the cognitive decline was still present and did not stop. They showed that after 6 months of cycling, the cycling did not have a significant effect on the cognitive decline like before the intervention. The process of neurodegeneration is not stopped, but cognitive

decline is slowed down to a minimum amount. After six months, this effect was no longer present. A decrease in hippocampal volume, cortical thickness and white matter is present in both groups, but the decrease was smaller in the cycling group. Ayed et al., (2021) showed that acute intensity cycling in combination with a mental task could lead to significant cognitive improvements. This dual task interference is also shown in patients with MCI. However, there is no information about a follow up, so, nothing can be said if the effects are lasting. It appears to be that the positive effect of cycling is mainly present in the short-term (up to 6 months) and not in the long-term (after 12 months).

After cycling, a sample of patients with Parkinson's displayed a decrease in motor symptoms only in a dynamic cycling condition (increasing speed) and not in the static (the same speed) cycling or stretching condition (Jonas, 2018, & Ault, 2016). A possible explanation is that cycling increases cerebral blood flow and therefore increases volume and cell regeneration in brain regions which are critical for cognitive function and motor skills, in this case the basal ganglia. But no information is found about follow-up. Therefore, in the first 6 weeks, cycling has a positive effect on motor symptoms, but nothing can be said about the long term. Ault (2016) found an improved gait in the dynamic cycling condition after cycling 40 minutes, three times a week for six weeks. A possible explanation is that cycling can contribute to more activation in cortical brain regions (which control motor movements), which will possibly lead to increased sensory information and improved motor function like gait. So, activation of cortical brain regions plays an important role, like previous literature suggested (Mandolesi et al., & Monteiro-Junior et al., 2015; Dugger, & Dickson, 2017; Leyland, Spencer, Beale, Jones, & van Reekum, 2019). The positive effect of a dual task interference is also present in patients with Parkinson's (Hazamy et al., 2017; Hazamy et al., 2019), which showed improved cognition due to cycling only when participants were cycling on a self-paced tempo and simultaneously got a mental task from the researcher. Because of this dual task, cerebral blood flow is increased and there is more activation in brain regions like the basal ganglia, which could be a possible explanation for the short-term effects and not the long-term effects. So, the positive effect of cycling on cognition can possibly be traced back to increased blood flow. A limitation is that their patients with Parkinson's were significantly older than the healthy older adults. Patients with Parkinson's performed more poorly than healthy older adults on all cognitive tasks, but both groups improved on visual tasks. So, cycling may improve cognition in patients with Parkinson's, but also in healthy older adults. This is an optimistic result.

When taking the information all together, it appears to be that cycling can have a significant effect on cognition, but mainly in the short-term. After six months, participants

stopped cycling and after that, the effects are no longer present. Participants stopped cycling in the follow-up period. In dementia, cycling may play an important role in a delayed onset, but because cycling is not the only form of physical activity, nothing can be said about cycling in specific. Physical activities are not divided into different categories like cycling, swimming etc, but all together in one category. It can be stated that cycling may delay the onset of dementia, but so may swimming or other rigorous physical activity. So, it seems that exercise is the determining factor and that it is not limited to cycling.

Cycling combined with a mental task like memory training, appears to be superior to cycling alone and a mental task after the cycling session in participants with MCI, Alzheimer's and Parkinson's, but not all results are significant. Participating in traffic might also be considered a mental task. In this case, cycling through traffic might also have an effect on cognition. All studies included cycling in a non-real life setting and not in real-life traffic. Therefore, it is a recommendation for future research. There are methodological differences between the studies that could account for the differences in results, such as medication use and using a home trainer with a tv-screen or VR-glasses versus only a home trainer. It appears to be that the experience of cycling could improve quality of life in patients with dementia. But this was only measured one time and not after 6 months. So, nothing can be said about the long-term effects. Long-term effects of physical activity on cognition are shown by Hörder et al., (2014) and can possibly lead up to a delayed onset up to eleven years.

4.2 Limitations

There are some limitations worth mentioning. The first one is about ethics. At this point in time, there is no practical, risk-free way to let people with neurodegenerative disorders participate on a bike in real life traffic, despite it happening in the real world. It is not possible to prohibit someone from cycling, even if they have a neurodegenerative disorder. Most studies are limited to cycling on a home trainer and not cycling in real life. Authors try to make cycling during the intervention more like real life by using a screen or VR-glasses (Sakhare, 2021; Anderson-Henley et al., 2014), but it is still a controlled environment and very different from the real-world experience of cycling. Because of this, statements about the effect of real life cycling on cognition and mobility in people with neurodegenerative disorders cannot be given, but statements about the possible effect of cycling on cognition in these patients can be. It remains important to investigate the effect of cycling on people's mobility, because mobility plays an important role in independence (Crevenna, 2020) and quality of life (Arcoverde et al., 2008). A way to investigate this role further could be by differentiating between which cognitions and

skills are needed when cycling compared to driving a car and the effect on people's lives if these are no longer possible because of ageing or another factor.

4.3 Strengths

Next to the limitations mentioned above, there are a couple of strengths worth mentioning. One of them is that all studies only included participants with medical clearance from a healthcare provider to participate in the study. This limits the chances of dropping out and it gives a reliable diagnosis. Another one is that this is the first literature study, to our knowledge, looking at the effect of cycling on cognitive impairment.

4.4 Directions for future research

Directions for future research are to focus on finding ways to make the environment more like a real-life experience of cycling instead of watching a screen or VR-glasses. But this is difficult considering ethical guidelines. A possible way to make cycling more like real life is to create a circuit and then adapt to make it safe for participants, like cycling with training wheels or wearing a protective suit. In this way, participants will have real-life world experience, only in a safer environment with less distractions and risks. Lastly, use of screenings techniques like MRI could be helpful to differentiate between brain activity before and after the intervention to measure cerebral blood flow. This appears to play a protective role by increasing cell regeneration and volume in brain regions which are critical for cognitive function (Leyland et al., 2019; Yu et al., 2021).

4.5 Conclusion

It appears that cycling could have a positive effect on cognitive decline in the first six months, but this effect is not present after 12 months. The differences in study design and results make it hard to generalise, but despite this it looks promising to investigate the effect of cycling on impaired cognition and to focus more on the role of mobility. Not all studies have the same results and this is partly due to methodological differences like testing at different moments and measurements as baseline, and the brain pathology of the four neurodegenerative disorders. It appears to be that cycling can lead to less memory impairments in Alzheimer's, dementia and MCI. It is possible that the duration of the cycling sessions plays an important role and this is a notable point that future research could focus on. Another possible explanation is that brain regions are more stimulated through cycling which increases dopamine levels and blood flow and therefore could lead to less motor symptoms in Parkinson's and less memory impairment

in dementia, MCI and Alzheimer's. Cycling combined with a mental task might lead to less cognitive decline in Parkinson's, but this finding was not replicated and significant.

In conclusion, there may be a decrease in cognitive decline, but cognitive impairment because of dementia, MCI, Alzheimer's disease and Parkinson's disease will proceed and not stop due to cycling. More research about cycling and impaired cognition including functional screening techniques like MRI or fMRI is preferable. More real-life cycling experiences and interventions are needed, because it appears that there are other factors that play an important role in cycling independently, like keeping balance and heart rate. It also appears that cycling combined with a mental task (dual task interference) could lead to a better performance, but not every study found the same results.

References

- Anderson, N. D. (2019). State of the science on mild cognitive impairment (MCI). *CNS spectrums*, 24(1), 78-87. doi:10.1017/S1092852918001347
- Anderson-Hanley, C., Arciero, P. J., Barcelos, N., Nimon, J., Rocha, T., Thurin, M., & Maloney, M. (2014). Executive function and self-regulated exergaming adherence among older adults. *Frontiers in human neuroscience*, 8, 989. <https://doi.org/10.3389/fnhum.2014.00989>
- Arcoverde, C., Deslandes, A., Rangel, A., Rangel, A., Pavão, R., Nigri, F., ... & Laks, J. (2008). Role of physical activity on the maintenance of cognition and activities of daily living in elderly with Alzheimer's disease. *Arquivos de neuro-psiquiatria*, 66(2B), 323- 327.
- Ault, D. (2016). *The effects of dynamic cycling on motor function, gait, mobility and balance in individuals with Parkinson's disease* (Doctoral dissertation, Kent State University).
- Ayed, B., Castor-Guyonvarch, I., Amimour, N., Naija, S., Aouichaoui, S., Ben Omor, C., Zouhair, T., & El Massioui, F. (2021). Acute exercise and cognitive function in alzheimer's disease. *Journal of Alzheimer's Disease*, 82(2), 749-760. doi: 10.3233/JAD201317.
- Azami-Aghdash, S., Aghaei, M. H., & Sadeghi-Bazarghani, H. (2018). Epidemiology of road traffic injuries among elderly people; a systematic review and meta-analysis. *Bulletin of Emergency & Trauma*, 6(4), 279. doi: 10.29252/beat-060403
- Bowen, M. E. (2012). A prospective examination of the relationship between physical activity and dementia risk in later life. *American journal of health promotion*, 26(6), 333-340. <https://doi.org/10.4278/ajhp.110311-QUAN-11>.
- Buettner, L. L., & Fitzsimmons, S. (2002). AD-venture program: therapeutic biking for the treatment of depression in long-term care residents with dementia. *American Journal of Alzheimer's Disease & Other Dementias®*, 17(2), 121-127.
- Colcombe, S. J., Kramer, A. F., Erickson, K. I., Scalf, P., McAuley, E., Cohen, N. J., & Elavsky, S. (2004). Cardiovascular fitness, cortical plasticity, and aging. *Proceedings of the National Academy of Sciences*, 101(9), 3316-3321.
- Crevenna, R. (2020). Health-enhancing physical activity, exercise and sports—a never-ending success story. *Wiener klinische Wochenschrift*, 132(5), 113-114. <https://doi.org/10.1007/s00508-020-01640-x>.
- Dimbleby, R., & Burton, G. (2020). *More than words: An introduction to communication*. Routledge.

- Dugger, B. N., & Dickson, D. W. (2017). Pathology of neurodegenerative diseases. *Cold Spring Harbor perspectives in biology*, 9(7), a028035. doi: 10.1101/cshperspect.a028035.
- D'Cunha, N. M., Isbel, S., McKune, A. J., Kellett, J., & Naumovski, N. (2020). Activities outside of the care setting for people with dementia: a systematic review. *BMJ open*, 10(10), e040753. <http://dx.doi.org/10.1136/bmjopen-2020-040753>.
- Edemekong, P. F., Bomgaars, D. L., Sukumaran, S., & Levy, S. B. (2021). Activities of daily living. In *StatPearls*. StatPearls Publishing.
- Edmonds, E. C., McDonald, C. R., Marshall, A., Thomas, K. R., Eppig, J., Weigand, A. J., Delano-Wood, L., Galasko, D., Salmon, D., Bondi, M., & Alzheimer's Disease Neuroimaging Initiative. (2019). Early versus late MCI: Improved MCI staging using a neuropsychological approach. *Alzheimer's & Dementia*, 15(5), 699-708. <https://doi.org/10.1016/j.jalz.2018.12.009>.
- Engbers, C., Dubbeldam, R., Brusse-Keizer, M. G. J., Buurke, J. H., De Waard, D., & Rietman, J. S. (2018). Characteristics of older cyclists (65+) and factors associated with self-reported cycling accidents in the Netherlands. *Transportation research part F: traffic psychology and behaviour*, 56, 522-530. <https://doi.org/10.1016/j.trf.2018.05.020>.
- Geokas, M. C., Lakatta, E. G., Makinodan, T., & Timiras, P. S. (1990). The aging process. *Annals of internal medicine*, 113(6), 455-466.
- Gratkowski, M., Storzer, L., Butz, M., Schnitzler, A., Saupe, D., & Dalal, S. S. (2017). Braincycles: experimental setup for the combined measurement of cortical and subcortical activity in Parkinson's disease patients during cycling. *Frontiers in Human Neuroscience*, 10, 685. <https://doi.org/10.3389/fnhum.2016.00685>
- Guo, H. J., & Sapra, A. (2020). Instrumental activity of daily living. In: *StatPearls*. StatPearls Publishing, Treasure Island (FL).
- Haustein, S., & Møller, M. (2016). E-bike safety: individual-level factors and incident characteristics. *Journal of Transport & Health*, 3(3), 386-394. <https://doi.org/10.1016/j.jth.2016.07.001>
- Hazamy, A. A., Altmann, L. J., Stegemöller, E., Bowers, D., Lee, H. K., Wilson, J., Okun, M.S & Hass, C. J. (2017). Improved cognition while cycling in Parkinson's disease patients and healthy adults. *Brain and Cognition*, 113, 23-31. doi: 10.1016/j.bandc.2017.01.002
- Hazamy, A. A., Horne, S. A., Okun, M. S., Hass, C. J., & Altmann, L. J. (2019). Effects of a Cycling Dual Task on Emotional Word Choice in Parkinson's Disease. *Journal of*

- Speech, Language, and Hearing Research*, 62(6), 1951-1958.
doi: 10.1044/2019_JSLHR-L-18-0428.
- Hindle, J. V. (2010). Ageing, neurodegeneration and Parkinson's disease. *Age and ageing*, 39(2), 156-161. <https://doi.org/10.1093/ageing/afp223>.
- Hoops, S., Nazem, S., Siderowf, A. D., Duda, J. E., Xie, S. X., Stern, M. B., & Weintraub, D. (2009). Validity of the MoCA and MMSE in the detection of MCI and dementia in Parkinson disease. *Neurology*, 73(21), 1738-1745.
doi: 10.1212/WNL.0b013e3181c34b47
- Hörder, H., Johansson, L., Guo, X., Grimby, G., Kern, S., Östling, S., & Skoog, I. (2018). Midlife cardiovascular fitness and dementia: a 44-year longitudinal population study in women. *Neurology*, 90(15), e1298-e1305.
<https://doi.org/10.1212/WNL.0000000000005290>.
- Jak, A.J., Bondi, M.W., Delano-Wood, L., Wieranga, C., Corey-Bloom, J., Salmon, D.P., et al. (2009). Quantification of five neuropsychological approaches to defining mild cognitive impairment. *Am. J. Geriatric Psychiatry*, 17, 368-375. doi: 10.1097/JGP.0b013e31819431d5.
- Jonas, J. C. (2018). *Acute Effects Of Cycling On Sensory And Motor Function In Parkinson's Disease* (Doctoral dissertation, Kent State University).
- Leyland, L. A., Spencer, B., Beale, N., Jones, T., & Van Reekum, C. M. (2019). The effect of cycling on cognitive function and well-being in older adults. *PLoS one*, 14(2), e0211779. <https://doi.org/10.1371/journal.pone.0211779>
- Mahalakshmi, B., Maurya, N., Lee, S. D., & Bharath Kumar, V. (2020). Possible neuroprotective mechanisms of physical exercise in neurodegeneration. *International Journal of Molecular Sciences*, 21(16), 5895. doi:10.3390/ijms21165895.
- Mandolesi, L., Polverino, A., Montuori, S., Foti, F., Ferraioli, G., Sorrentino, P., & Sorrentino, G. (2018). Effects of physical exercise on cognitive functioning and wellbeing: biological and psychological benefits. *Frontiers in psychology*, 9, 509. <https://doi.org/10.3389/fpsyg.2018.00509>.
- Mattson, M. P., Chan, S. L., & Duan, W. (2002). Modification of brain aging and neurodegenerative disorders by genes, diet, and behavior. *Physiological reviews*.
- McEwen, S. C., Siddarth, P., Abedelsater, B., Kim, Y., Mui, W., Wu, P., Emerson, N.D., Lee, J., Greenberg, S., Shelton, T., Kaiser, S., Small, G.W., & Merrill, D. A. (2018). Simultaneous aerobic exercise and memory training program in older adults with

- subjective memory impairments. *Journal of Alzheimer's Disease*, 62(2), 795-806. doi: 10.3233/JAD-170846.
- Michon, J. A. (1985). A critical view of driver behavior models: what do we know, what should we do?. In *Human behavior and traffic safety* (pp. 485-524). Springer, Boston, MA.
- Moeller, J. R., Ishikawa, T., Dhawan, V., Spetsieris, P., Mandel, F., Alexander, G. E., Grady, C., Pietrini, P., & Eidelberg, D. (1996). The metabolic topography of normal aging. *Journal of Cerebral Blood Flow & Metabolism*, 16(3), 385-398.
- Monteiro-Junior, R. S., Cevada, T., Oliveira, B. R., Lattari, E., Portugal, E. M., Carvalho, A., & Deslandes, A. C. (2015). We need to move more: Neurobiological hypotheses of physical exercise as a treatment for Parkinson's disease. *Medical hypotheses*, 85(5), 537-541. <https://doi.org/10.1016/j.mehy.2015.07.011>.
- Moore, A. R., & O'Keefe, S. T. (1999). Drug-induced cognitive impairment in the elderly. *Drugs & aging*, 15(1), 15-28.
- Ohnishi, T., Matsuda, H., Tabira, T., Asada, T., & Uno, M. (2001). Changes in brain morphology in Alzheimer disease and normal aging: is Alzheimer disease an exaggerated aging process?. *American Journal of Neuroradiology*, 22(9), 1680-1685.
- Park, J., & Cohen, I. (2019). Effects of exercise interventions in older adults with various types of dementia: systematic review. *Activities, Adaptation & Aging*, 43(2), 83-117. <https://doi.org/10.1080/01924788.2018.1493897>.
- Pereira, C., Baptista, F., & Cruz-Ferreira, A. (2016). Role of physical activity, physical fitness, and chronic health conditions on the physical independence of community-dwelling older adults over a 5-year period. *Archives of gerontology and geriatrics*, 65, 45-53. <https://doi.org/10.1016/j.archger.2016.02.004>.
- Rethorst, C. D., Wipfli, B. M., & Landers, D. M. (2009). The antidepressive effects of exercise. *Sports medicine*, 39(6), 491-511.
- Reurings, M. C. B., Vlakveld, W. P., Twisk, D. A. M., Dijkstra, A., & Wijnen, W. (2012). Van fietsongeval naar maatregelen: kennis en hiaten. *Leidschendam: Stichting Wetenschappelijk Onderzoek Verkeersveiligheid*.
- Ridgel, A. L., Kim, C. H., Fickes, E. J., Muller, M. D., & Alberts, J. L. (2011). Changes in executive function after acute bouts of passive cycling in Parkinson's disease. *Journal of aging and physical activity*, 19(2), 87-98.
- Sacco, G., Caillaud, C., Ben Sadoun, G., Robert, P., David, R., & Brisswalter, J. (2016). Exercise plus cognitive performance over and above exercise alone in subjects with

- mild cognitive impairment. *Journal of Alzheimer's Disease*, 50(1), 19-25. doi: 10.3233/JAD-150194.
- Sakhare, A. R. (2021). *A Virtual Reality Exergaming System to Enhance Brain Health in Older Adults at Risk for Alzheimer's Disease* (Doctoral dissertation, University of Southern California).
- Schmitter-Edgecombe, M., Parsey, C., & Cook, D. J. (2011). Cognitive correlates of functional performance in older adults: Comparison of self-report, direct observation, and performance-based measures. *Journal of the international neuropsychological society*, 17(5), 853-864. doi: 10.1017/S1355617711000865
- Silverman, M. N., & Deuster, P. A. (2014). Biological mechanisms underlying the role of physical fitness in health and resilience. *Interface focus*, 4(5), 20140040. <https://doi.org/10.1098/rsfs.2014.0040>.
- Stoffers, M. (2012). Cycling as heritage: representing the history of cycling in the Netherlands. *The journal of transport history*, 33(1), 92-114. <http://dx.doi.org/10.7227/TJTH.33.1.7>.
- Stuss, D. T., & Alexander, M. P. (2000). Executive functions and the frontal lobes: a conceptual view. *Psychological research*, 63(3), 289-298.
- Teychenne, M., White, R. L., Richards, J., Schuch, F. B., Rosenbaum, S., & Bennie, J. A. (2020). Do we need physical activity guidelines for mental health: What does the evidence tell us?. *Mental Health and Physical Activity*, 18, 100315. <https://doi.org/10.1016/j.mhpa.2019.100315>.
- Van Cauwenberg, J., Schepers, P., Deforche, B., & de Geus, B. (2022). Effects of e-biking on older adults' biking and walking frequencies, health, functionality and life space area: A prospective observational study. *Transportation research part A: policy and practice*, 156, 227-236.
- van Santen, J., Meiland, F. J., Dröes, R. M., van Straten, A., & Bosmans, J. E. (2022). Cost-effectiveness of exergaming compared to regular day-care activities in dementia: Results of a randomised controlled trial in The Netherlands. *Health & Social Care in the Community*, 30(5), e1794-e1804. doi: 10.1111/hsc.13608.
- Weinberg, R. S., & Gould, D. (2019). *Foundations of sport and exercise psychology*, 7E. Human kinetics.
- Willis, D. P., Manaugh, K., & El-Geneidy, A. (2015). Cycling under influence: summarizing the influence of perceptions, attitudes, habits, and social environments on cycling for

- transportation. *International Journal of Sustainable Transportation*, 9(8), 565-579.
<https://doi.org/10.1080/15568318.2013.827285>.
- Winters, M., Sims-Gould, J., Franke, T., & McKay, H. (2015). "I grew up on a bike": Cycling and older adults. *Journal of transport & health*, 2(1), 58-67.
<https://doi.org/10.1016/j.jth.2014.06.001>
- Yu, F., Savik, K., Wyman, J. F., & Bronas, U. G. (2011). Maintaining physical fitness and function in Alzheimer's disease: a pilot study. *American Journal of Alzheimer's Disease & Other Dementias*®, 26(5), 406-412. doi: 10.1177/1533317511414861.
- Yu, F., Thomas, W., Nelson, N. W., Bronas, U. G., Dysken, M., & Wyman, J. F. (2015). Impact of 6-month aerobic exercise on Alzheimer's symptoms. *Journal of Applied Gerontology*, 34(4), 484-500. doi: 10.1177/0733464813512895.
- Yu, F., Mathiason, M. A., Han, S., Gunter, J. L., Jones, D., Botha, H., & Jack Jr, C. (2021). Mechanistic Effects of Aerobic Exercise in Alzheimer's Disease: Imaging Findings From the Pilot FIT-AD Trial. *Frontiers in aging neuroscience*, 13. doi: 10.3389/fnagi.2021.703691.
- Yu, F., Vock, D. M., Zhang, L., Salisbury, D., Nelson, N. W., Chow, L. S., Smith, G., Barclay, T.R., Dysken, M., & Wyman, J. F. (2021). Cognitive effects of aerobic exercise in Alzheimer's disease: a pilot randomized controlled trial. *Journal of Alzheimer's Disease*, 80(1), 233-244. doi: 10.3233/JAD-201100.