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## ***“The role of Cognitive Reserve on cognitive and psychological well-being”***

*Doctoral dissertation:*

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## Introduction

In the present Ph.D. dissertation, a comprehensive look around the concept of Cognitive Reserve (CR) has been conducted, with a specific focus on healthy older adults first and then on clinical sample, considering cardiovascular disorders (CVDs).

To this aim, the present work is divided in three chapters. The first one provides a theoretical background concerning the description of the construct of CR, its evolution starting from the primordial concept of *reserve* and how it has been measured and quantified over the years, reviewing and describing some of its main indices (i.e., education, work and leisure activities; Nucci et al., 2012). After that, research on neuroanatomical basis related to CR and on cognitive abilities involved was explored to better understand its crucial implications on the cognitive sphere. In addition, as greater CR allows individuals to recruit a variety of resources using alternative brain networks and cognitive strategies (Stern, 2002, 2011, 2014) helping them to face new or critical situations, a review about its impact on psychological well-being (PWB) has also been explored.

After the description of the most studied CR indices over time, a focus on creative thinking has been provided in the second chapter. Starting from describing the evolution of creativity, its multidimensional nature and some of the theoretical models from the cognitive neuroscience literature, Divergent Thinking (DT) has been considered. In accordance with Guilford's definition (1956), it is nowadays conceived as one of the most indicative proxies of creative thinking and a measure of individuals' creative potential (Runco & Acar, 2012). Moreover, as it implies the use of different cognitive abilities such as memory, attention and in particular executive functions (EFs), it has also been considered a proxy of CR in recent years (Palmiero et al., 2016; Colombo et al., 2018). The chapter results from the premise that the population over 65 years old is rapidly increasing and that research on healthy aging has become one of the priorities in the research community, looking for a cost-effective method to prevent or delay symptoms of cognitive decline; for this reason, the first experimental study is provided in this chapter. In accordance with the concept of CR highlighted by Stern (2002, 2006, 2009) and on evidence indicating its beneficial role both on cognitive functioning and on the psychological sphere (Sneidere et al., 2024), the study aimed at exploring the effects of a DT training on these two spheres of a healthy older adults' sample. In addition, it wanted to better clarify if CR had an impact on any improvement, in order to reach consistent practical and clinical implications about the aging health.

In the third paragraph, the concept of CR has been considered in the clinical field of CVDs. Firstly, a brief theoretical background about cardiovascular disorders was provided, along with related

issues that has to do with bad CVDs' implications such as poor adherence to treatment. As poor adherence to treatment may have important implications on individuals' PWB and quality of life (QoL), this chapter aimed to understand if CR may have a protective role on this. Since recent literature (Pucci et al., 2024) have identified novel forms of reserve taking place in the motor system including a motor reserve (MR) and given the importance that the physical component plays on CVDs, two studies are provided in this chapter. The first one is a state-of-the-art review aimed at exploring and looking for a direct link between CR, MR and its potential beneficial effects on adherence to treatment and on QoL in patients affected by CVDs. Afterwards, an experimental longitudinal study has been conducted to understand the relationship that these two constructs, CR and MR, may have with physical and PWB, with adherence to treatment and related factors (such as illness perception and self-care behaviors) in patients affected by CVDs.

## CHAPTER 1. COGNITIVE RESERVE AND WELL-BEING IN HEALTHY AGING

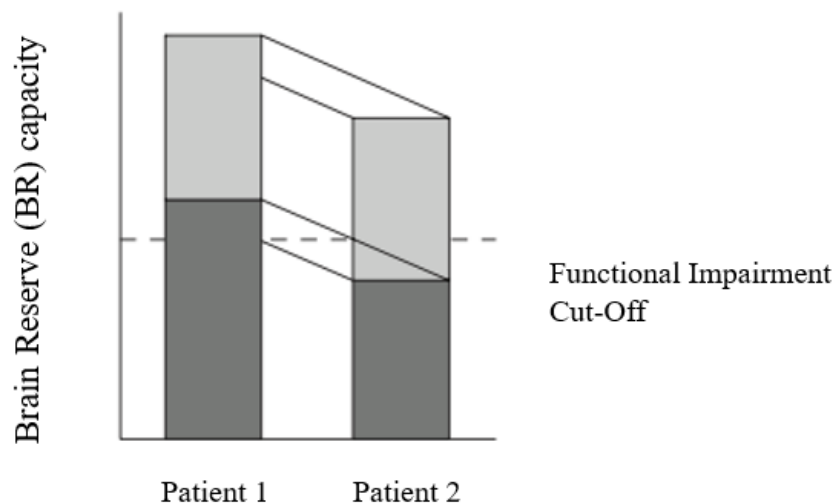
### 1.1. What is Reserve?

Brain aging is characterized by important interindividual differences, which are not only found at the structural, metabolic and chemical level of the brain, but also on the ability to compensate for losses associated with brain damage due to the normal aging process (Cabeza et al., 2002) or to the onset of degenerative diseases (Grady et al., 2003).

Since the end of the 1980s, some studies (Stern, 2002; Evert et al., 2003; Kesler et al., 2003; Mortimer et al., 2003) have demonstrated that there is no direct relationship between the degree of brain damage's severity (whether acquired, due to aging, or the onset of degenerative diseases) and its clinical manifestations, that, on the contrary, it is possible not to manifest any cognitive or behavioral symptom in the presence of brain lesions and, again, that it is possible to present different clinical manifestations between individuals. This has led researchers to introduce and develop the complex and multidimensional concept of *reserve* (Chicherio et al., 2012), which allows to understand how individual differences lead some people to cope better than others with the consequences of brain damage or pathologies (Colombo et al., 2018). According to the concept of *reserve*, this would be due to differences in cognitive and neural processes as well as to biological differences (this will be discussed in the next paragraph). Thus, those who have a greater reserve are able to optimize or maximize performances through the differential recruitment of neural networks which, most likely, reflect the use of alternative cognitive strategies (Stern, 2002). In this regard, it is interesting to note that Stern (2009) also emphasized that the concept of reserve is relevant not only in cases of subjects affected by dementia or other neurological conditions, but also for normal aging, since it allows the population to deal more effectively with the changes due to the passing of time and to counteract cognitive decline.

The concept of reserve as it is defined in this work emerged from the development and combination of mainly two different models over time. Firstly, the so-called *passive models* of reserve and *threshold models* (Kazman, 1993; Staz, 1993) conceived reserve as a passive process defined in terms of “the amount of damage that can be sustained before reaching a critical threshold”; from this point of view, the brain reserve (BR) capacity would depend on the number of neurons and synapses and on the brain size, which bring later clinical manifestations following brain damage. This means that for the same brain damage, if the threshold is exceeded, it produces the same outcome in each individual and that the differences between individuals in clinical manifestations are due to the global reserve capacity of the brain (Chicherio et al., 2012). Accordingly, a

significant brain damage can produce a clinical or functional disorder in a patient with less BR capacity if this exceeds the aforementioned critical threshold; conversely, a subject with a larger BR capacity can maintain a level of functionality for a longer period of time since the damage does not reach the critical threshold (Figure 1)



*Figure 1: Brain Reserve (BR) model and critical threshold concept (adapted from Stern, 2002). For two individuals with different amounts of brain reserve (black colored space), a determined brain damage (gray colored space) leads to clinical evidence only for patients with less BR (patient 2), as the amount of altered tissue exceeds the critical threshold causing clinical manifestations. At the same time, patient 1, who has more BR, remain preserved from the brain damage (Chicherio et al., 2012)*

Otherwise, when following the *active model* (Stern, 2002; 2009), Stern developed the Cognitive Reserve (CR) concept, which is not something predetermined as the BR capacity, but it can be described as the accumulation of brain resources during an entire lifespan (Cabeza et al., 2018) that helps the brain to actively cope with or compensate for brain damage. This second model, therefore, refers not only to the structure but rather to the functional benefits that the brain may enjoy under certain conditions.

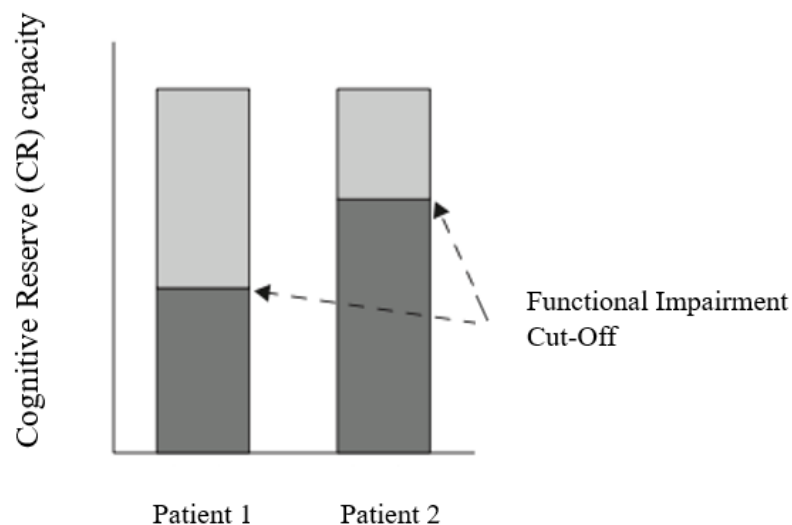
## **1.2. The Cognitive Reserve hypothesis**

As we've already reported in the previous paragraph, the concept of reserve was first developed following the observation of a non-linear relationship between brain pathology, or physiological decline, and its clinical manifestation, as well as a means to explain the inter-individual differences

in how the brain responds to pathology. Thus, it is relevant when we refer to situations that imply the involvement of the brain in sustaining damage (Stern, 2002).

According to the cognitive reserve (CR) hypothesis conceptualized by Stern (2002; 2009), CR represents the “ability to optimize or maximize performance through differential recruitment of brain networks, which perhaps reflects the use of alternate cognitive strategies”. In other words, it describes the ability of the brain to use alternate paradigms to solve problems when the standard approach is no longer available (Stern, 2012).

According to different evidence, it denotes a cumulative improvement in neural resources resulting from the interaction of innate individual differences (i.e., genetics factors) and environmental factors (i.e., experiences in life), mitigating the effects of physiological neural decline or caused by age-related diseases (Cabeza et al., 2018; Scarmeas & Stern, 2003). Thus, subjects who have proven to be more active, seem to have a greater CR. This is demonstrated by the fact that two individuals with the same brain reserve can differ in the way they react to a brain injury (Chicherio et al., 2012; Figure 2).



*Figure 2: Cognitive Reserve (CR) model (adapted from Stern, 2002).*

*It shows two individuals with the same amount of brain reserve: patient 1, using more efficient processing mechanisms, has a greater CR than patient 2. Patient 1 can therefore tolerate a larger damage better than patient 2 before a possible functional incapacity occurs (Chicherio et al., 2012).*

CR allows individuals to optimize their performances thanks to a more adaptable functional brain process (Stern et al., 2018), reflecting their ability to recruit differential brain networks and alternative cognitive strategies (Stern, 2002; 2011; 2014). For this reason, CR is not fixed and immutable, but several and relevant lifetime exposures could influence this construct (i.e.,

intelligence, education, occupation, leisure activities, social engagement, motor and physical exercises, Stern et al., 2018).

Taking in consideration the division into *passive* and *active* models of reserve above explained, it is crucial to consider that those models would not be mutually exclusive; more recently, researchers have assumed that they should be considered complementary, as they provide complementary explanations of different forms of functional plasticity (Stern, 2002). It can be said that BR may be seen as the hardware, while CR as the software of the brain, and both are currently considered essential components of what is defined as global reserve.

Delving into this aspect, to better understand the complexity of the construct, three different concepts have been highlighted over time corresponding to interrelated CR perspectives (Cabeza et al., 2018): *Reserve* (i.e., BR and CR), which has been already defined; *Brain Maintenance*, which considers the development of age-related brain changes variability (physiological or pathological) due to genetics or lifestyle, in contrast with BR, as it refers to the neurobiological capital at any point in time (Stern et al., 2018), that occurs throughout the lifespan and become critical in the old age (Cabeza et al., 2018); *Compensation*, which refers to the recruitment of neural resources in response to a consistent cognitive demand.

Literature discussed also the neural dimension related to CR, which refers to the inter-individual variability in the brain networks (Stone et al., 2018). According to Stern and colleagues (2003), changes in neural activity among individuals are, in fact, strongly related to different levels of CR, thereby helping to explain the individual differences in the capacity to cope with age-related changes or pathologic conditions. In this field, neuroimaging techniques offered a methodological facility to investigate the neural implementation of variables that are assumed to reflect reserve. Different experiments using both functional (i.e. PET, fMRI) and structural (mainly MRI) imaging is available in the aging literature, confirming that subjects engaging in more leisure activities can clinically better tolerate brain pathology (Scarmeas & Stern, 2003), leading to the possibility to conceptualize reserve as a reflecting indexes of brain plasticity (Bartre's-Faz & Arenaza-Urquijo, 2011).

In addition, according to a more comprehensive point of view, there is another line of research that conceives reserve as a mechanism of pure defence expressed by the organism during evolution, which is what is meant when talking about “acquired resilience”. This study postulates that reserve has a simple tissue basis: it is the result of an evolved system of cellular mechanisms that allow mammals to use everyday stresses (e.g., exercise or caloric restriction) as stimuli to increase the resilience of tissues (Stone et al., 2018) (this would also include a brain-level reserve).

### 1.2.1. Measurement of Cognitive Reserve

As emerges from the literature overviewed, CR is a dynamic and multifactorial construct that is not directly observable. It is quite complex to reach a quantitative measure of CR, as it is influenced by many variables, including intelligence (Alexander et al., 1997; Satz et al., 2011) longer education (Stern et al., 1994; Kukull et al., 2002; Roe et al., 2011), the complexity of profession carried out during life and the years spent in the profession (Qiu et al., 2003; Andel et al., 2005; Kröger et al., 2008; Karp et al., 2009), greater physical activity (Prakash et al., 2015), reading and literacy (Manly et al., 2005; Brewster et al., 2014), socio economics factors (Koster et al., 2005; Ouvrard et al., 2016; Rusmaully et al., 2017), social interaction and participation in demanding leisure activities (Fabrigoule et al., 1995; Scarmeas et al., 2001; Scarmeas & Stern, 2003; Fancourt et al., 2018), bilingualism and nutrition (Wöbbing-Sánchez et al., 2020). In the last decades, it emerged that variables such as the level of literacy and the engagement in high-level cognitive activities, which had an impact on CR (Larson et al., 2013; Malek-Ahmadi et al., 2018), remain dynamic throughout life even after the completion of formal education, actively contributing to CR (Malek-Ahmadi et al., 2018; Thow et al., 2018). On the one hand, this is positive, since it allows CR to be always strengthened throughout life, but, on the other hand, variables such as those mentioned might be strongly influenced by socio-cultural and interindividual aspects (Jokinen et al., 2016; Van Hek et al., 2016). It leads to difficulties in conducting studies aiming to compare various countries and cultures objectively and thus have generalizable results.

To counteract limitations, scientific literature reveals three general approaches to the measurement of CR: (i) the *residual approach*, which examines the difference between individuals' cognitive functioning and what would be expected based on their brain status and demographic factors (e.g., age, education, sex); in this approach, CR is inferred from the "residual" or unexplained variance in cognitive performance after controlling for these variables. (ii) The *neuroimaging approach* is based on the identification of functional activation brain networks that may underlie CR. Finally, the method based on (iii) *sociobehavioural proxies* looks at indirect indices assumed to covary with and contribute to the development of CR (Stern et al., 2018).

Traditionally, attempts to operationalize and measure objectively the CR construct have been made through the measurement of different proxies (like those above mentioned). Measures of CR, in fact, vary from instruments that use one single proxy, like education (Chapko et al., 2018), to tools that include several proxies and convert them into a total score (Nogueira et al., 2022). Since the approach of using one single proxy risks to disregard important components of a complex construct as the CR, most studies have focused on the combinations of some proxies. Life-course studies, in fact, showed that measures of education, occupation and engagement on cognitively stimulating

activities synergically interacted with each other (Dekhtyar et al., 2015; Jefferson et al., 2011). Taken together, these findings are in favour of an assessment of CR based on multiple indirect indicators that can provide both a comprehensive representation of individual life experiences and a lifelong pattern based on the interactions of lifestyle factors (Kartschmit et al., 2019; Pettigrew & Soldan, 2019). Education, occupation and leisure activities are the most frequently used (Jones et al., 2010; Nucci et al., 2012). For this reason, in the course of the current paragraph, these are the proxies of CR that will be reviewed and discussed.

One of the first indicators of CR was IQ or pre-morbid IQ (Alexander et al., 1997; Satz et al., 2011); this indicator considers the correlation between intelligence and CR, which is a correlation supported by the literature (Nucci et al., 2012). However, it is important to consider that CR is not equivalent to IQ. Sternberg (1982) claimed that intelligence represents an adaptive goal-directed behavior, so its focus is on the resulting performance (which obviously depends on the individual's cognitive status) (Montemurro et al., 2021) and not on cognitive resources storage as CR does. For this reason, IQ was excluded from the CR indicators despite their unquestionable correlation (Nucci et al., 2012). Afterwards, processing resources and executive functions have been taken into account as two of the most commonly used indicators of CR (Siedlecki et al., 2009; Satz et al., 2011), together with performance on vocabulary tests and education (Scarmeas et al., 2004).

A significant number of studies in the literature have focused on this last indicator, considering education as the number of years of completed study or the degree of literacy. Several studies in the field were conducted on normal aging, but most literature was born from patients affected by neurodegenerative diseases such as Alzheimer's disease (AD). They have shown a more rapid cognitive decline in individuals with lower educational attainment (Albert et al., 1995; Butler et al., 1996), as well as greater levels of CR in AD patients with higher education, acting as a protective factor against cognitive decline (Stern et al., 1994; Alexander et al., 1997). Accordingly, it has been advanced by Stern (2009) that CR may mediate between AD and its clinical expression.

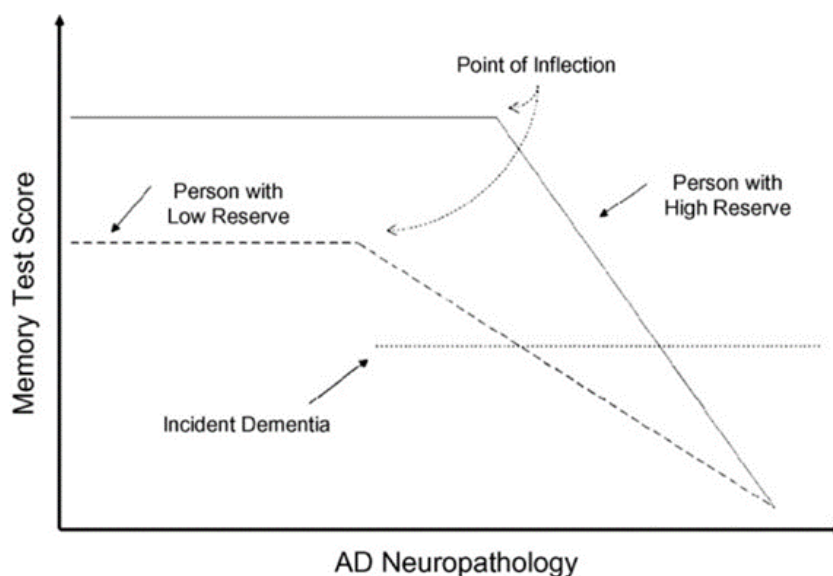


Figure 3: “AD Neuropathology” on the X-axis represents the progressive deterioration of the pathology over time. “Memory Test Score” on the Y-axis represents individuals’ performance on a memory task. Assuming that AD pathology increases over time at the same rate in two patients with high and low CR, the following predictions can be made for the subject with greater CR: (i) the point of inflection, where cognitive functioning begins to be affected by AD, occurs later; (ii) clinical manifestations of AD will be reached when the pathology is more severe; (iii) at each level of memory performance, AD will be more severe; (iv) after the inflection point, cynical progression will be more rapid (Stern, 2009).

However, educational attainment as a proxy for CR presents several limitations and its importance is debated in the literature, as it might be particularly influenced by sociodemographic and cultural factors (Jokinen et al., 2016; Van Hek et al., 2016). We ought to remember, in fact, that as age increases, a multitude of factors contribute to compromise cognition in older adults (Netz et al., 2019). According to the study by Mondini and colleagues (2022) aimed at investigating the effects of demographic factors (age and sex), the presence of comorbidities and CR indicators (education and occupation) on a continuum ranging from healthy to pathological aging, it has been shown that education can be considered the only variable that continues to predict performance over time. A peculiarity that emerged from the study revealed that the explanatory protective role of other predictors seemed to progressively weaken over time. The same research group (Montemurro et al., 2022) also studied whether the CR indicator linked to life experiences could be a better predictor of performance than education in healthy controls. Results reinforced the importance of taking into account interindividual differences due to various potentially beneficial activities in adulthood (in addition to demographic data such as age and sex and education), but not the same level of education. A possible explanation can be found in their characteristics: education is acquired during a period of highly plastic development and involves intensive and systematic learning (Ramey et al., 1984); life experiences represent the accumulation of cognitively stimulating experiences during

adulthood in a less structured and more heterogeneous way. Therefore, the prominent effect of education even during the advanced stages of decline, may indicate that the contribution of education to CR is more resilient to brain damage (Montemurro et al., 2021). Accordingly, recent studies agreed in defining education as a factor in setting a threshold, rather than having longitudinal impact (Cadar et al., 2017; Wilson et al., 2019; Nyberg et al., 2021).

Afterwards, also work complexity has been considered as a proxy of CR: different occupations require varied levels of mental demands, thereby providing heterogeneous forms of mental exercise that differently support brain functions (Andel et al., 2005; Kroger et al., 2008; Karp et al., 2009). Along with all these factors, it is logical to expect that other lifetime exposures could also be beneficial in increasing CR. Pre-morbid engagement in leisure activities seemed to play a pivotal role in the construction of CR: intellectual, social and physical activities have been considered as part of leisure-time activities (Stern, 2009; Nucci et al., 2012).

Despite the attempts made thus far to operationalize and measure CR, it is important to consider that much of the literature agreed that CR is not a fixed factor (Cabeza et al., 2018); therefore, it can continuously be modified by life experiences (i.e., through indicators previously mentioned or those that are a consequence of cognitive stimulation), even when the brain is already affected by neuropathology (i.e., through rehabilitation trainings, Liberati et al., 2009; Stern, 2012; Schwartz et al., 2016) and the main instruments adopted thus far for its measurement are not very sensitive to longitudinal changes.

Over the years, some studies showed a possible relationship between CR and another potential proxy, which is creative thinking, highlighting that these constructs have some common basic cognitive aspects, particularly the concept of cognitive flexibility and fluidity of thought (Antonietti and Colombo, 2013, 2016; Colombo et al., 2018). According to recent evidence, in fact, divergent thinking abilities developed by Guilford (1956) may be considered as an indicator of CR (Palmiero et al., 2016; Colombo et al., 2018; Colautti et al., 2023; Fusi et al., 2024): it will be discussed in detail in the next chapter.

### 1.2.2. Challenges in measuring Cognitive Reserve

The difficulties in evaluating CR stem from various sources. One major issue lies in the definition of the construct, as early theorists proposed definitions of CR that were similar but not identical, complicating efforts to guide construct validation studies. Another challenge in assessing CR is that it refers to something not directly observable. In this view, despite attempts to achieve the most precise objective measurement possible, we ought to consider that CR proxies, such as educational

attainment, are affected by contextual and social factors. Between them, gender differences in educational attainment have received abundant attention in prior research on the field; for example, it emerged that the gender gap in the completion of tertiary education in European countries is widening and in the advantage of women (Van Hek et al., 2016). Moreover, this gap has developed over time and differs between countries, indicating that both individual factors and contextual circumstances in a person's upbringing might be relevant for an individual's educational attainment (Van Hek et al., 2016).

In this view, even if proxies offer several advantages when quantifying CR, there is a parallel need for a comprehensive measure derived from standardized tools. There are widely recognised instruments developed to provide a more rigorous and replicable assessment of CR; they bring the advantage of uniformity in measurement across diverse populations, allowing researchers to compare results across studies and draw more robust conclusions. Two recent systematic reviews (Kartschmit et al., 2019; Landenberger et al., 2019) have identified six published questionnaires: the Cognitive Reserve Index questionnaire (CRIq; Nucci et al., 2012), the Cognitive Reserve Questionnaire (CRQ; Rami et al., 2011), the Cognitive Reserve Scale (CRS; Leon et al., 2011), the Lifetime of Experiences Questionnaire (LEQ; Valenzuela & Sachdev, 2007), the Premorbid Cognitive Abilities Scale (PCAS; Apolinario et al., 2013), and the Retrospective Indigenous Childhood Enrichment (RICE; Minogue et al., 2018). All the questionnaires assess two or more experience-based proxies of CR.

In the light of the reasons and limitations reported, striking a balance between the understanding gained from proxies and the precision afforded by a standardised measure is crucial for advancing our comprehension of CR dynamics in diverse populations and contexts. Ideally a CR measure should incorporate a variable that captures the moderation of the relationship between life course-related brain changes and cognitive changes. The accuracy of CR measurement improves when additional measures are included, such as: (i) assessments of anatomical changes (e.g., brain imaging), (ii) measures of cognitive function (e.g., cognitive performance and daily functioning), and (iii) a CR proxy, which refers to variables influencing the relationship between (i) and (ii) (Nogueira et al., 2022).

In conclusion, the assessment of CR remains a topic of debate. Currently, it is largely based on proxy indicators. It seems that using multiple indicators is the most effective approach, with several tools available, though they would benefit from further validation. Other methods, such as residual and imaging approaches, may become more accessible as brain measurement techniques improve.

A CR that is shaped by experiences, thus modifiable, and protective of cognitive function holds great promise for an aging population, making it crucial that we gain a deeper understanding of it.

### 1.3. Cognitive Well-Being

Even more and more studies showed the role of CR as a means of prolonging the functionally healthy years of older adults (Livingston et al., 2020). It is proven that the decline in cognitive function due to aging or to a pathological process (i.e., neurological diseases such as AD) is associated with diminished psychological well-being (PWB, Llewellyn et al., 2008; Wilson et al., 2013). As we previously saw, greater CR allows individuals the recruitment of a variety of resources depending on their capacity to use alternative brain networks and alternative cognitive strategies and abilities (Stern, 2002; 2011; 2014), acting on cognitive functioning and, to a wider range, to individuals PWB. In order to better understand how it happens, researchers wondered about neuronal correlates of CR and tried to explore if there were stable patterns; findings are discussed in the following paragraph.

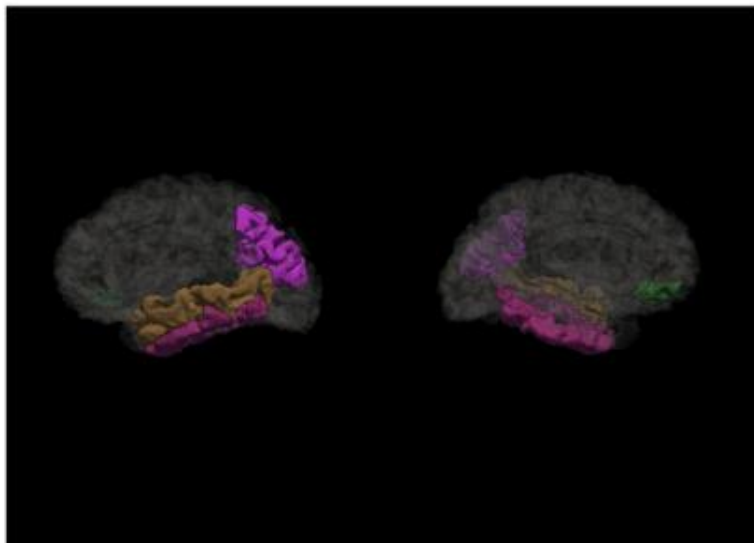
#### 1.3.1. Cognitive Reserve and Brain Functioning

At the empirical level, CR is currently operationalized thanks to brain imaging studies, highlighting individual differences in connectivity patterns between different regions, as well as the way these differences are associated with CR indicators. In other words, it is currently hypothesized that CR is related to a generic functional connection network that is not specific to the task performed, and that can be solicited in various tasks (Chicherio et al., 2021).

Considering the most used proxies of CR (i.e., education, occupation and leisure activities), some studies have focused on the relationship between *formal education* obtained and modifications of the cortical volume, in particular of the right hemisphere superior temporal gyrus, left hemisphere insular cortex, bilateral anterior cingulate gyrus (Arenaza-Urquijo et al., 2013), as well as transverse temporal cortex and the insula (Liu et al., 2012). Regarding *occupation complexity*, along with the claim that being employed brings a lot of benefits (i.e., developing new skills, social engagement, daily routine and so on, Vance et al., 2016) allowing individuals to develop specific cognitive domains associated to specific occupational demands (Spreng et al., 2011), several studies have also considered its relationship with brain cortical measures. It emerged that more complex physical occupations could be associated with higher cortical thickness in the primary motor and somatosensory cortex (Lenhart et al., 2021). *Leisure activities* can be considered the most challenging proxy, due to the difficulties encountered by researchers to reach a consensus regarding

the type of activities included, the regularity and when during life-time these activities have to be carried out. For these reasons, even if previous studies have indicated relationships between lifestyle measures and cortical volumetry, it is difficult to develop homogeneous conclusions.

Following this line, a recent experimental study by Sneidere and colleagues (2024) tried to better explore the relationship between CR lifestyle socio-behavioral proxies and cortical regions in a healthy adult sample, indicating a potential interaction between them. They used an MRI scanner to measure the cortical volumetry. In particular, results regarding occupational activities that require higher professional competence as well as work responsibility, showed larger cortical volume in the left middle temporal gyrus (region which is associated with verbal intelligence, Heyer et al., 2021), the bilateral inferior temporal gyrus (highly associated with visual processing, Marques et al., 2016) and the left inferior parietal lobule (one of the functional rich hubs in the brain, Oldham & Fornito, 2019). Moreover, the same cerebral regions showed a positive relationship also with the composite index score, indicating the sum of all socio-behavioral proxies of CR (that includes educational achievement, occupation and leisure activities).



*Figure 4: Regions associated with CR proxies (Sneidere et al., 2024). The colored cortical regions are associated with occupational CR and with the total score, indicating the sum of all socio-behavioral proxies considered in the study (educational achievement, occupation and leisure activities).*

Complementary, the study conducted by Conti and colleagues (2021) didn't show an association between temporal and parietal regions and greater global CR (measured by a composite score consisting of leisure activities, verbal IQ and education). Rather, they found that a higher CR was associated with the middle frontal gyrus, the supplementary motor area and the cerebellum of the

left hemisphere. The sum of the recent evidence completes the results provided by studies previously developed, that mainly focused on clinical samples affected by AD. According to them (Pettigrew et al., 2016; 2017), in fact, parietal and temporal regions have been considered vulnerable regions to AD, showing that CR may be related to the same regions and support a potential protective effect against the pathology. Growing evidence, nowadays, is focusing on other clinical samples (i.e., Parkinson disease, PD) showing a modulatory effect of CR on functional connectivity in basal ganglia and executive-attentional fronto-parietal regions (Di Tella et al., 2023), as well as a positive effect of CR on the longitudinal progression of mild cognitive impairment (MCI) in PD (Gu & Xu, 2022). It demonstrates that broadening the scope of investigation into other clinical samples could help researchers to reach a clearer overall picture.

### 1.3.2. Cognitive Reserve and Cognitive Functioning

In accordance with what is provided by the literature about brain functioning related to CR, most literature also proved that CR fosters cognitive efficiency, both during middle-aging and during later adulthood (Ferreira et al., 2017; Cattaneo et al., 2022; Jin et al., 2023). It has been quantified using a variety of mechanisms that interact with brain structures and contribute to cognitive performance (Stern et al., 2020). It emerged that each CR proxy has the potential to alter the relationship between brain integrity and cognitive abilities, and that's why a composite CR proxy that combines multiple proxies may be a better choice for avoiding biased measurements (Jin et al., 2023). Moreover, it is important to remember that the effects of CR proxies on brain integrity and cognition varied depending on brain integrity indicators considered, cognitive domain, age group, as well as on the proxy used (Porricelli et al., 2024).

However, although significant age-related changes in the brain structure and cognition are present in old age (Ferreira et al., 2017; Salthouse, 2019), CR may already buffer the effect of cortical thinning on cognitive abilities, such as memory or executive functions (Panico et al., 2023) with protective and compensatory actions. According to Porricelli and colleagues (2024), it has been highlighted that early fluid intelligence had the most significant impact on both the main and moderating effects of cognitive outcomes among the individual CR proxies. Fluid intelligence represents an innate cognitive ability that does not necessarily depend on prior training or experience (Schmidt et al., 2020, Sun et al., 2021), and it has been positively associated with executive function, emotional recognition, and theory of mind (Salas et al., 2021). As reported by the systematic review of Panico and colleagues (2023), a positive relationship between singular CR proxies, composite indexes or standardized scales and almost all the explored cognitive domains has

emerged, indicating a well-known association between greater CR and a better cognitive performance in adulthood. However, they couldn't achieve homogeneous conclusions and it might be due to the scarcity of available studies and the need for definite methodological improvements and the use of standardized scales for CR, in order to reduce inconsistencies among studies.

#### **1.4. Psychological Well-Being in the Lifespan**

Due to the ongoing demographic transition, the population of older adults is growing; this phenomenon is bringing new challenges and the need for increased understanding of the aging process (Martin-Maria et al., 2021). For this reason, an overall understanding of mental well-being in old age would be necessary for health outcomes, reducing disability and increasing autonomy, as well providing important information for public health endeavours (Steptoe et al., 2015).

Mental well-being in older age has been found to be both dynamic and multi-dimensional (Lara et al., 2020), including dimensions such as the evaluative one, which refers to overall satisfaction with life (Diener et al. 1985); the hedonic dimension, which includes aspects such as positive and negative affect (Kahneman et al. 2004); and the eudemonic dimension (Ryff et al. 2004), which relates to the realization of human potential and psychological functioning. It has been associated with better physical health and longevity (Boccardi & Boccardi, 2019; Chei et al., 2018).

Previous research showed that older adults tended to experience greater positive emotions despite lower levels of life satisfaction compared to younger (Lawton et al., 1992; Deaton, 2008). This has been related to a stronger focus on the positive aspects of life in older age, finding a possible explanation on the *Socioemotional Selectivity Theory* (Carstensen et al., 2003) and on the *Strength and Vulnerability Integration Model* (SAVI, Charles, 2010). The first states that older adults appreciate their time as limited and therefore prioritize short time goals in relation to social connections and regulate emotional states to optimize mental well-being. The SAVI model supports the higher perceived PWB in older adults due to their accumulated life experience, which allows them to develop powerful cognitive and behavioral control strategies. In line with the latter model, it is important to highlight the hypothesized existence of an emotion–cognition interaction mechanism that involves both emotional processing and emotional regulation, together with cognitive control mechanisms and strategies. This link relies on strong cognitive functioning bases, but to better understand it, it is necessary to deepen the relationship between cognitive functions and PWB.

The PWB construct is defined by Riff (1995) as a multidimensional construct concerning personal development and growth, as the realization of individual potential. Research revealed that it plays a

key role in older adults' health by both exerting a significant risk reduction in chronic diseases and promoting longevity (Ryff, 2014; Kubzasky et al., 2018; Kim et al., 2019).

Consistent with this complexity, several variables can also affect the relationship between PWB and age, including cognitive functioning (Reed & Carstensen, 2012; Tomaszczyk & Fernandes, 2013). More in detail, studies found that measures of global cognitive status were positively associated with PWB in older people samples (Charles, 2010; Scheibe & Carstensen, 2010). However, this evidence has not considered the possible role of specific cognitive abilities; in this vein, other recent studies suggested the specific role of executive functions (EFs) in PWB (Kim et al., 2021; Fusi et al., 2022).

Some specific models pointed out that PWB might depend not only on past experiences and interpersonal comparison, but also on the intervention of complex cognitive abilities for the balance between subjects' personal aspirations and payoffs (Steptoe et al., 2015), requiring the intervention of higher cognitive functions such as EFs. In accordance, previous studies showed that cognitive control strategies (depending on executive abilities) support adaptive psychological processes such as self-reflection, emotion regulation, and convergence of cognitive, motivational, and emotional goals (Nelis et al., 2011; Jebb et al., 2020). This is not surprising given that cognitive control plays a key role in emotion regulation (Fastame et al., 2023). Additionally, some research showed that the decline in executive control processes, such as perceptual speed or working memory, was associated with a decline in some components of PWB (Allerhand et al., 2014). It follows that age-related changes in the cognitive functioning (especially in the executive functioning such as working memory, inhibition and shifting abilities, Nyberg & Pudas, 2019) can lead to a consequent decline in those dimensions of PWB that are more cognitively demanding; the ability to inhibit automatic responses, for example, emerged to be pivotal in the context of successful aging, allowing individuals to better adapt to their changing abilities and environments. Higher inhibitory abilities were found to be associated with the perception of higher personal growth of PWB (Allerhand et al., 2014).

Thus, tailored preventive interventions aimed at enhancing specific cognitive domains (i.e., inhibition skills) appear to have potential significant clinical implications for older adults by improving their PWB and their quality of life in the long-term, also mitigating the potential development of chronic or neurodegenerative diseases (Fusi et al., 2022).

#### 1.4.1. The Selection, Optimization and Compensation (SOC) Model

Lifespan psychology took care of underlying that the aging processes are accompanied by gains, losses and a more general reorganizations of resources that are important for successful development (Baltes, 1997). It follows that individual self-regulatory and life-management behaviors are necessary to efficiently allocate available resources, being the major determinants of successful aging (Baltes, 1997; Freund, 2008; Kooij, 2015).

Within this context, the Selective Optimization with Compensation model (SOC; Baltes & Baltes, 1990) has stimulated lifespan research on successful aging. According to this model, goal setting and goal striving are crucial factors for individuals' successful development; in order to achieve maximum success, people should pursue fewer goals at the same time, allowing to invest more resources in each goal and achieve a sufficient level of functioning in each domain (Freund & Baltes, 2000). More in dept, it states that the use of three action strategies is needed to manage resource losses and to conserve valuable resources throughout the lifespan: the *selection* of fewer but important goals, which allows the individual to *optimize* their resources to pursue them, and applying adequate *compensatory* means to overcome internal or external barriers (Baltes, 1997).

In reference to the SOC model (Baltes & Baltes, 1990), well-being depends on how the individual adapts to the growing limits related to health and on how they evaluate the consequences of such limits in daily life. McKee-Ryan and colleagues (2005) differentiate the physical aspects of well-being from the psychological ones; the first refers to the subjective evaluations on how much health limits mobility and precludes the performance of any type of activity in daily living. The second refers to the subjective evaluations concerning how much individuals feel satisfied with their life, also considering any limitations due to the clinical condition.

In this regard, this model allows to develop two main considerations. Firstly, it paves the way for the growing recent literature about the importance of the physical component for both, cognitive functioning and CR and for the psychological sphere (as it will be discussed in the third chapter). According to Ihle and colleagues (2017; 2020), in fact, CR may possibly also be beneficial for physical well-being. Secondly, it is strongly connected to individuals' higher cognitive abilities, as it requires the use of effective evaluation processes (that mainly recall effective executive functioning). It helps us to clearly understand the existence of the implicit relationship between an intact cognitive functioning and PWB (Clarke et al., 2002; Llewellyn et al., 2008; Wilson et al., 2013; Cutler et al., 2017).

#### 1.4.2. The impact of Cognitive Reserve on Psychological Well-Being

As already mentioned, an intact cognitive functioning is of crucial importance for well-being in old age (Clarke et al., 2002; Cutler et al., 2017). Therefore, the gerontological and mental health research tried to identify the factors that help to preserve well-being despite suffering from constraints in health and cognitive abilities in old age.

Among those factors, CR has been considered crucial for preserving cognitive functioning and well-being in old age (Cullati et al., 2018, Ihle et al., 2020). According to Cullati and colleagues (2018), vulnerable individuals (defining “vulnerability” as a weakening process and as a lack of resources in one or more life domains, according to Spini and colleagues, 2017) who own a little reserve, should thus have greater difficulty to deal with threatening situations such as lower cognitive abilities, that consequently affect their well-being. In other words, less vulnerable individuals that have accumulated greater CR over the life course, should be able to better deal with the negative aftereffects of low cognitive abilities on well-being. In line with this conceptual view, most empirical evidence suggests that greater CR can be associated with better PWB (Brunborg & Ytrehus, 2014; Cedervall et al., 2015; Lee et al., 2017). However, some limitations are to be underlined: firstly, this evidence has focused on the role of CR for older adults’ PWB only within clinical samples suffering from cognitive impairments (i.e., dementia and stroke). Secondly, the aforementioned studies they all used different CR indices: health literacy (Brunborg & Ytrehus, 2014), physical exercise and a general active lifestyle (Cedervall et al., 2015), as well as social interactions (Lee et al., 2017); moreover, they focused on late-life reserves, neglecting a comprehensive examination of key proxies of cognitive reserve. Thirdly, prior studies considered the psychological well-being dimension, neglecting physical well-being (according to the SOC model which integrate the two dimensions). Those limitations highlight the need for further investigation in this field.

A more recent study by Ihle and colleagues (2020) tried to explore the relation between CR, cognitive functioning and PWB in healthy older adults trying to fill the gaps in knowledge already mentioned. They found a significant relationship between lower values in several proxies of CR (such as education, cognitive level of job, cognitively stimulating leisure activities and regularly speaking different languages) and lower psychological and physical well-being, in line with prior findings on PWB (Cedervall et al., 2015; Joo et al., 2017; Ku et al., 2016). Moreover, they showed that the relation of cognitive abilities to both physical and PWB in old age was attenuated in individuals with higher values of CR. This is in line with the SOC model: sustaining well-being despite health constraints in old age strongly depends on the ability to continue a cognitively stimulating active life (contributing to cognitive reserve in old age; Wilson et al., 2013).

Another recent study by Porricelli and colleagues (2024) confirming the association between CR and mental health in middle aged and older adults, tried to explore the relationship between CR and mental health in healthy adults. They found that a higher CR corresponded to fewer mental health reported symptoms. In particular, a higher CR reflecting professional activities was associated with lower stress levels, suggesting that engaging occupations may help maintain a robust mental health, especially by reducing stress symptoms during middle age.

Those findings have important implications that need to be taken into account for future studies in the field. Firstly, it would be important to consider also the physical aspects of well-being, as CR seems to be a crucial resource to deal with low cognitive abilities. Moreover, further investigation may allow public prevention policies and intervention programs targeting mental health and well-being in the aging population to consider multiple reserve domains accumulated over the life course, such as CR.



### 2.1. Creativity

“*Creativity defies a precise definition*” is the assumption of Paul Torrance (1988, p. 43), one of the most known researchers in the field of creativity and divergent thinking. This assumption gives the idea of the complexity of this term, which has been studied during the past decades by a lot of professionals and from different disciplines, ranging from pedagogy, philosophy, sociology, neuroscience to psychology. However, despite its importance, literature on creativity is fairly recent and raises many open questions, given the complexity and the extent of this construct (Zeng, Proctor & Salvendy, 2011).

The evolution of studies about creativity began at the end of the 19th century and saw a considerable boost from the mid-twentieth century, before in the USA and then in Europe, bringing to a change, also in Italy, to the conception of creative thinking (Cinque, 2010).

Starting from its etymology, the term creativity was firstly linked to the religious concept of the origin, the starting point from which everything was born. As time goes by, the idea of creativity as an adjective related to humans developed in the 20th century, indicating the use of those skills necessary to produce something new (Oxford Dictionary, 2002), filling itself with connotations that make it synonymous with “productive”. In the meantime, however, in some contexts it has taken on a deteriorating meaning, as it was related to something that is contrary to logic and rationality (Cinque, 2010). This highlights once again the complexity of the construct and the countless connotations that can be attributed to it.

From a scientific point of view, in the second half of the 19th century and starting from Darwin’s first and then Galton’s studies about genetics (*Hereditary Talent and Character*, 1865), studies on creativity focused mainly on biological and hereditary basis. Afterwards, with the development of the psychoanalytic current, creativity became a trait of some particularly brilliant people called *geniuses*; those individuals, however, were often conceived as mentally ill, considering their creative trait as something related to the irrational part of the psyche, dominated by impulses.

During the following decades, this individual trait took on a totally positive connotation, considered as a talented characteristic of those individuals. Studies by Lewis Terman, for example, focused the attention on those factors that may influence creativity (*Genetic Studies of Genius*, 1979), contrasting the hypothesis of a possible direct link with the IQ. For a long period of time, in fact, creativity was identified with intelligence. It was Guildford’s address to the American Psychological Association in 1950 that helped motivate researchers to explore this puzzling topic:

he emphasized the huge lack of research on creativity stressing the need to extend the psychological knowledge on this field (Kurtzberg & Amabile, 2001). Over the last 70 years, in fact, the amount of research dedicated to this topic has increased exponentially and it has been investigated by various disciplines and points of view. Despite the growing interest in the field, the construct is still surrounded by an aura of mystery: it is clear that a number of controversies still exist and are yet to be clarified (Zeng, Proctor & Salvendy, 2011), thus providing a definition that is definitive and exhaustive is hard. The etymon of the word creativity comes from the Indo-European roots KAR or KER (to create, to make) and implies an action that generates results as something original and new, presupposing the use of previously existing resources to generate new ones (Cavallin, 2015). From this, most authors who deepened this topic have pointed to two main criteria: novelty and usefulness (Runco & Jaeger, 2012). Among the authors who have adhered to this approach, Sternberg and Lubart (1999) proposed one of the most recognised definitions in the field of creativity, according to which creativity is *the ability to produce responses that are both novel* (i.e. original, rare and unexpected) *and suitable* (i.e. adaptive and useful according to task limitations).

#### 2.1.1. Models of Creativity

With the aim of investigating processes underlying creativity as a human faculty, several models have been developed over the years. Between them, we can find the *factorial models*, which belong to the cognitivist sphere: according to cognitivist theories, an individual is no longer considered as a passive element whose behavior is shaped by the environment; he now becomes an active presence in his world (Cinque, 2010).

According to factorial models, creative thinking is a complex unit that can be broken down into various factors, which can be analyzed with statistical surveys. Two of the most known models in this field are those by Guilford (1956) and by Torrance (1988).

##### *Guilford's Theory*

Contrary to the common belief at that time that creativity was equated with intelligence, Guilford emphasized that creativity and creative production go far beyond the domain of intelligence. The tools designed to measure intelligence, in fact, respond to the need for objectivity and the assignment of a score, which is something that goes far from Guilford's conception of creativity: asking subjects to provide answers by choosing from multiple choices prevents himself from showing his ability to find original and alternative answers (Guilford, 1950). According to the researcher, in fact, creativity doesn't depend on a single process but rather derives from a set of different components and skills (Guilford, 1957).

In 1956 Guilford published his famous work “*The Structure Of the Intellect*”, assuming that the best way to explore the human intellect was through a factorial research design, allowing him to outline a complex model composed by several factors. As we can see in Figure 5, the amount of factors proposed by the researcher can be grouped into two main domains: the “*memory*” and the “*thinking*” factors.

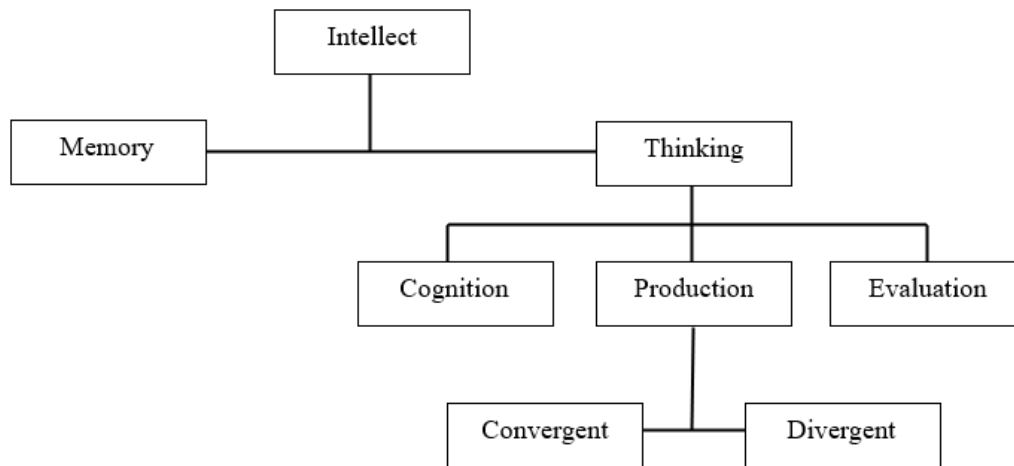


Figure 5: Diagram of the major categories of intellectual factors and their relationships (Guilford, 1957).

Into the first domain, the *memory factor*, we can find different memory abilities that have to do with the associative connections between contents, the contents themselves and its nature (i.e., rote memory, auditory, visual memory and so on). The second domain, the *thinking factor*, has a three-fold division: (i) cognition, (ii) production and (iii) evaluation. According to cognition, (i) this factor concerns the ability of becoming aware of mental demands and tasks that an individual faces; production (ii) considers our own production starting from such awareness and can be divided again in two factors, *divergent* and *convergent thinking*; evaluation (iii) is related to the judgmental sphere which considers the skills involved in assessing the thinking processes’ results. Guilford supports the idea that all the three factors mentioned are involved in a total creative act.

Going deeper into the second factor, we can produce different ways of thinking from different types of tasks; on the one hand, “convergent thinking” (CT) considers a unique and correct solution to a problem or a request, representing a way of thinking that is channeled in one specific direction and so in one determined answer. On the other hand, “divergent thinking” (DT) comes into play when an open-ended problem or situation needs to be analyzed and solved. It consists of a problem that

may require more than one correct solution and represents a way of thinking which is not controlled; it, conversely, requires the exploration of a variety of directions, possibilities and novel associations between conceptual spaces (Acar & Runco, 2014, 2015; Guilford, 1957).

Even if CT and DT may appear as independent ways of thinking where the presence of one excludes the other, Guilford (1957) highlighted that they can also occur together, bringing to a total act of problem solving. Moreover, the researcher claimed that some components of creative productions could be considered more creative than others, assessing the following indices: fluency, flexibility and originality. Starting from those indices, a lot of DT tasks have been developed with the aim of measuring these qualities of idea productions (e.g., Torrance Test of Creative Thinking - TTCT and the Alternative Uses Tasks - AUT). Fluency has to do with the production of a certain number of ideas meeting determined criteria; the second concerns the ability to vary in the conceptual categories of the responses and to switch from a category to another, while the third represents the unusual, uncommon content of the idea production, allowing the individual to make remote associations. In the end, in some instruments, also *elaboration* was considered among indices, which considers the amount of details used to embellish an idea.

#### *Torrance's Contribution*

Twenty years later, Paul Torrance made a significant contribution in the differentiation between intelligence and creativity, developing tools to measure both IQ and creativity more precisely. His contribution has to do mainly with the prediction of creative development in children aged five and up. He started from the indices advanced by Guilford to develop one of the most known and reliable tests of creative thinking, the *Torrance Test of Creative Thinking* - TTCT. From the description and composition of the instrument, Torrance's factorial proposal clearly emerges, according to which the creative process requires four components: fluency, flexibility, originality and elaboration. The tool measures the ability to provide different, original and accurate answers that combine heterogeneous elements (Torrance 1988).

#### *The ACR Model of Creativity*

A final mention to the WCR model of Creativity (Antonietti et al., 2011) describes the dynamics of creative thinking. Over the years, numerous models have been proposed that divide its development into multiple phases, demonstrating that the construct is not monolithic and unitary but composed of multiple faces in which each idea, if necessary, can be questioned and modified at any time (Colautti & Antonietti, 2018). The ACR model inserts into cognitive psychology's studies and defines three mechanisms of creativity: widening, connecting and reorganizing. The first mental

operation is theorized starting from the factorialist conception and, in particular, from Guilford's theories which associate creativity with the amount of uncommon ideas produced; in order to reach this aim, it is necessary to operate in a broad field of action that allows the identification of all components of the surrounding reality in which one operates. Connecting consists in establishing relationships between different realities to find analogies and to summarize the elements taken into consideration; reorganizing represents the readiness to change one's point of view and thus the reorganization of the mental field, allowing to reach new and unexpected meanings and interpretations.

## **2.2. Divergent Thinking**

Considering the factorial models from which the concept of DT arises, conceived as a factor belonging to the human intellect, it is clear that DT is not a synonym of creativity (Runco, 2008; Runco & Jaeger, 2012) even if the concept has been erroneously considered as a direct assessment of creative ability over time (Piffer, 2012).

Most research mainly focused on DT as one of the most consistent thought processes underlying creative cognition (Maysless, Aharon-Peretz & Shamay-Tsoory, 2014). Nowadays, it is considered as one of the most indicative proxies of creative thinking, in particular it is recognized as a measure of the *creative potential* (Runco & Acar, 2012). With this term we refer to the ability to produce original ideas that have a value for the specific context in which they are required (Lubart & Thornhill-Miller, 2019). The first author expressing this idea could be considered Wallach, as in 1970 he described DT tasks as predictors of creative performance rather than criteria. Moreover, DT tasks, as well as being considered as estimates of the potential for creative problem solving (Runco & Jaeger, 2012), have been shown to predict creative achievements concerning other variables (e.g., intelligence or "Openness to Experience" personality trait) (Kim, 2008; Vertanian et al., 2018b). Accordingly, DT assessment represents the most widely-used assessment for creative potential (Runco et al., 2017).

### **2.2.1. Divergent Thinking and cognitive processes involved**

The association between DT and cognitive functioning has been highly explored and it continues to be considered attractive for a few main reasons. Firstly, DT is believed to involve cognitive processes that trigger the generation of creative responses (Barbot et al., 2019) and the production of original ideas (Runco et al., 2017). Secondly, due to DT tasks' ease of administration, they lend

to being involved in neuroimaging and neuropsychological research protocols, representing approximately 51% of creativity assessments in neuroscience research (Benedek et al., 2019).

In recent decades, even if considerable progress has been made in uncovering the neural and psychological bases of creative cognition (Lloyd-Cox, Chen & Beaty, 2022), cognitive science is still far from a precise understanding of how creative cognition derives from neurocognitive processes. On one hand, approaches to creativity have been not easily accessible, being a construct which is hard to objectify and quantify; thus, due to its complex nature, neuroscience research's endeavors about creativity have often been undertaken separately by researchers within the different sub-disciplines of psychology (Zhang, Sjoerds & Hommel, 2020). On the other hand, one of the main gaps in knowledge concerns how and which different brain regions contribute to creative cognition and how their contribution works at different stages of the creative process, such as the generation and evaluation of ideas (Beaty et al., 2016).

To address this issue, some authors have started from the study of basic mechanisms and normal brain functioning, highlighting that three brain mechanisms allow us to deal quickly and efficiently with new situations in our environment and to face them: *The path of least resistance* is the mechanism that brings us to respond quickly to the new situation choosing the answer that is available faster (Hangura et al., 2017); *Repetition suppression* effect consists on the diminished neural activation when a stimulus is presented repeatedly (Henson & Rugg, 2003), reflecting our survival ability to adapt to our environment; and *Pattern recognition*, representing the mechanism to form mental representations of what we are facing, so that we only need to reactivate the pattern stored in our brains when we face something with the same characteristics. As a result, these three mechanisms tell us that we are programmed to find the quickest and automatic response at first, so the initial responses to stimuli will usually not be the most creative, while responses' originality increases during the exposure to the tasks (Acar & Runco, 2014; Barbot, 2018). During DT tasks, in fact, people are required to inhibit automatic responses to find novel and original answers. Starting from these promises, some researchers tried to answer questions like: how does the brain face new situations? How does it act when we try to find original solutions? Different cognitive functions and their network correlates have been reported to be correlated and connected with DT.

The role of *memory* in creative thinking is clear if we simply think that the production of uncommon ideas requires the manipulation of prior knowledge (Nickerson, 1999). Throughout our lives, in fact, we accumulate semantic representations of the objects, actions and concepts we become aware of, that are naturally stored in neural networks of our brain (Collins & Loftuss, 1975). Both behavioral and neuroimaging research has supported the involvement of episodic and

semantic memory in DT tasks (Abraham and Bubic, 2015; Beaty et al., 2020), demonstrating that creative cognition is built on both memory processes.

Concerning episodic memory, Gilhooly and colleagues (2007) were the first to propose and to prove, thanks to their experiments, the involvement of episodic memory in DT tasks. They administered to participants an Alternative Uses Task (AUT), asking them to produce as many alternative uses as possible of a specific object. Researchers found that initial responses were based on a strategy of retrieving the object's uses from long-term memory stores, rather than involving any personal-psychological creativity. Beaty and colleagues (2015) then explored dynamic interactions between brain regions during AUT tasks through a whole-brain functional connectivity analysis, identifying a network of brain regions associated with DT that included regions of the Default, Control and Salience networks. Figure 6A shows functional connectivity of the brain during a DT task; as we can see in Figure 6B, posterior cingulate cortex increases its connectivity with Control regions (i.e., dorsolateral prefrontal cortex, DLPFC) and with the Salience network (i.e., insula) during these tasks.

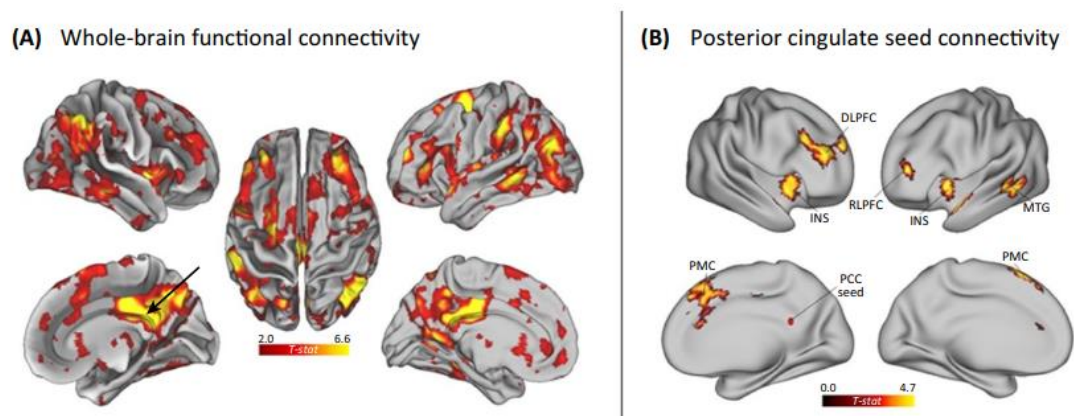


Figure 6: (A) Functional connectivity patterns activated during DT. (B) Connectivity between posterior cingulate cortex (PCC) with control regions (dorsolateral prefrontal cortex, DLPFC) and salience network (bilateral insula, INS) during a DT task. Abbreviations: ACC, anterior cingulate cortex; ANG, angular gyrus; IPL, inferior parietal lobule; MTG, middle temporal gyrus; PMC, premotor cortex; RLPFC, rostralateral prefrontal cortex; STG, superior temporal gyrus (Beaty et al., 2016, adapted).

Moreover, it has been shown that during DT tasks, brain structures involved in episodic memory were active, such as hippocampus (Beaty et al., 2016) and parahippocampal and medial prefrontal cortex (mPFC) (Mullally & Maguire, 2014).

In addition to episodic memory, semantic memory also plays a crucial role in the creative process (Benedek & Fink, 2019); semantic memory refers to the stores of concepts and facts, regardless of time or context, which is responsible for the storage of semantic categories (Vallar & Papagno, 2018). The role of semantic distance between concepts in creative cognition is used in experimental research through the idea that the further an individual moves away from a concept in a semantic space, the greater the possibility of generating original and creative ideas, going beyond knowledge constraints imposed by the semantic structure of knowledge (Abraham et al., 2012). Accordingly, it has been demonstrated that creative ability is associated with a flexible structure of semantic memory (Kenett et al., 2018). From a structural point of view, it is supported by literature that showed the role of the Semantic Control Network, crucial for flexible retrieval of stored knowledge (Cogdell-Brooke et al., 2020), and of the the Default Mode Network (DMN) (Beaty et al., 2016; 2018) during DT tasks, highlighting their central role in the creative process (Ovando-Tellez et al., 2019) as it is shown in Figure 7.

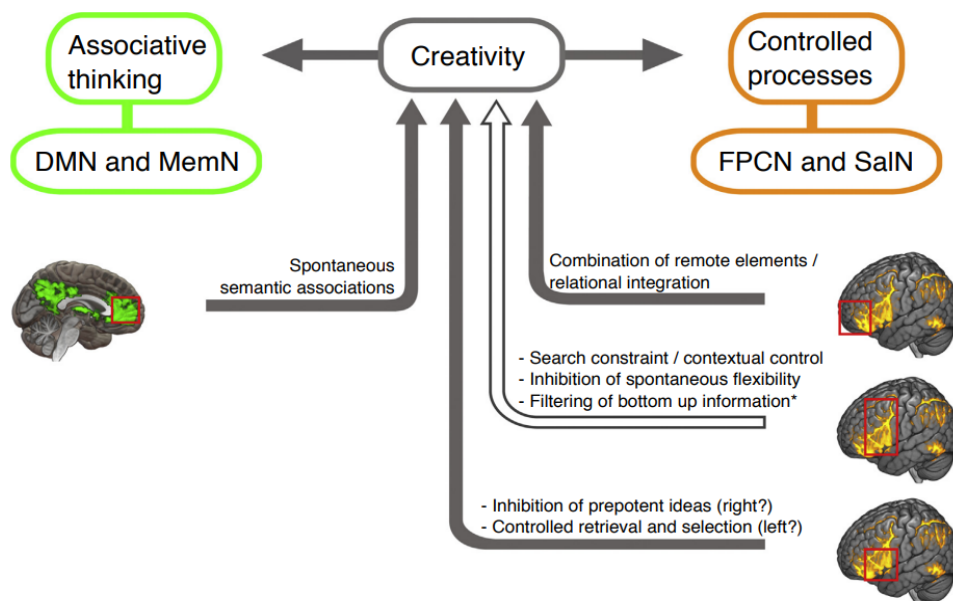


Figure 7: Tentative summary of mechanisms and network damages that can impact creativity, caused by brain lesions. Plain arrows represent the decrease, empty arrows the increase of creative performance after a damage: they are hypothetical processes that, when affected, can explain these effects. Abbreviations: DMN, default mode network; FPCN, frontoparietal control network; MemN, semantic and episodic memory networks; SalN, salience network (Ovando-Tellez et al., 2019).

Furthermore, in order to produce something new and original, it is necessary not only to recall information from our memory, but also to recombine those concepts that are distant from each

other, in an efficient way. Mednick (1962) helped the scientific community to better understand the importance of “associative processes” in creative thinking. He claimed that creative individuals, having a more flexible organization between concepts in their semantic memory, would efficiently activate remote ideas and build new ideas combining different concepts.

Finally, as memory is a reconstructive process (Schacter et al., 1998), it is important to highlight also the association between DT and future episodic thinking, so as with the ability to generate detailed episodic simulations (Addis et al., 2016). Although imaging a detailed scenario relies on mnemonic factors, such as the retrieval of episodic details, DT is fundamental in processing future episodic thinking. Accordingly, it has been postulated that detail retrieval and episodic simulation can contribute to open-ended problems such as DT (Sheldon et al., 2011).

A lot of literature emphasized that the processes before mentioned must interact with other functions in creative cognition, such as attention and different types of cognitive control functions, in order to produce new and creative ideas (Beaty et al., 2019).

Regarding *attention*'s involvement in creative thinking, research in this area is controversial. Studies pointed out that different aspects of creativity are associated with different types of attention (Benedek and Fink, 2019). Attentional functions are systems organized in a hierarchical manner, allowing us to maintain our attention for a long period of time, to react to stimuli around us and to select relevant information and exclude irrelevant ones in a given situation (Vallar & Papagno, 2018). Many researchers tried to understand what type of attention is the most involved in creative cognition. A lot of them showed that “*leaky*” attention is one of the most used by creative individuals, who succeed in collecting information and details that may be irrelevant to most people (Zabelina, 2018). It is undoubtedly useful on one hand, but on the other this modality can be also disadvantageous: people may experience a greater intrusion of irrelevant information and make more errors during typical attentional tasks (Rawlings, 1985). Other studies, on the contrary, claimed that the creative process mainly depended on focused attention: in order to produce novel and original products, creative individuals need to pay attention to details and to focus their attention on the task, even at a long-term (Nusbaum & Silvia, 2011). Further studies suggested that an integrated perspective allows individuals to be more creative, switching between various attention modalities (focused and broad) and showing a “*flexible attention*” (Vartaniam et al., 2007; Zabelina & Robinson, 2010). Spontaneous transitions between analytic or associative modes of thought, in fact, have been shown to be necessary for creative production (Gabora, 2010). Moreover, according to Martindale (1999), creative people may be able to adapt their attention to the tasks demands: a broader attention could be useful at the first steps of the creative process, when the new situation is still not so clear; during this phase, the seemingly irrelevant information may

turn out to be essential components for the solution. However, the broad attentional focus may slow the elaboration process in the long-term and the focus attention could be advantageous in the next steps of the creative process, when the idea is developed and assessed (Martindale, 1999; Vertaniam et al, 2007).

Neuroscience has also emphasized the importance of “*internally directed attention*”, showing that creative cognition is not so concerned with sensory perception, but it seems to rely more on imagination, requiring to pay attention to self-generated thought processes (Benedek, 2018); this is in line with neuroimaging studies that assign a crucial role to the DM network. The role of this type of attention may be relevant in the first phases of the process of generating ideas.

To sum up, despite the controversial evidence in the field of attention, it appears to be quite shared that during DT tasks, people rely more on selective attention and good cognitive control (Zabelina, 2018) and therefore on the ability to focus and switch attentional resources instead of having a leaky attention (Benedek & Fink, 2019).

Recent evidence suggested that DT tasks seemed to involve a top-down type of control of attention and cognition (Beaty et al., 2019), thus including the intervention of *executive functions* (EFs). Growing literature, in fact, confirmed a link between executive functions and creativity (Benedek et al., 2014c). Executive functions represent basic cognitive processes that control both thought and action; they are closely linked to the neural substrates of the prefrontal cortex and thus responsible for cognitive control. Furthermore, they are believed to be involved in all types of higher-order cognition (Miller & Cohen, 2001). More specifically, they include several processes and the most studied in the field of DT are: updating, shifting and inhibition abilities, strongly interconnected with each other and operating in synergy (Friedman et al., 2006; Miyake et al. 2000). *Updating* refers to the ability to monitor and revise incoming information, reviewing the contents of working memory by replacing obsolete information with new ones; *shifting* indicates the ability to switch flexibly between different tasks or between different information to find the most appropriate way to face a new situation (Beaty & Schacter, 2018); *inhibition* is defined as the ability to suppress dominant response tendencies that are irrelevant to the current task (Friedman & Miyake, 2004). According to Benedek and colleagues (2014c), the three processes are strongly involved in creative thinking. Firstly, the association between updating and creativity depends largely on working memory, which supports the active maintenance of relevant information to solve the task and the controlled search in memory (Unsworth & Engle, 2007); thus, a greater working memory facilitates a more effective memory search, brings to restore semantic concepts that are useful to the development of original ideas and to maintain active objectives during the execution of the tasks (Benedek et al., 2014). Secondly, also the inhibition is crucial in the creative process: in the context

of original idea generation, dominant responses reflect the most common and salient ideas but not the most original ones; the ability to suppress those responses allows the individual to selectively restore and facilitate the generation of new ideas (Benedek et al., 2012a). Thus, to sum up, inhibition reflects the ability to reject interference from semantically close concepts, facilitating the activation of more remote concepts (flexibility); high updating ability facilitates controlled search and manipulation of large numbers of concepts (Benedek et al., 2014).

Moreover, Benedek and colleagues (2014b, 2019) proposed a neurocognitive framework of creative cognition, reflecting a model that integrates creative cognition with specific cognitive functions such as memory, attention and cognitive control. Cognitive control is closely related to EF and to creativity, since research has highlighted how people may generate new and original ideas using goal-oriented strategy and not by producing ideas randomly (Benedek & Fink, 2019). In addition, cognitive control seems to require two processes, the generation and evaluation of ideas, that lead to maintain the balance between the quantity and quality of products (Groborz and Necka, 2003). Neuroimaging studies supported these findings, showing that the Executive Control Network (ECN) and the DMN are associated with controlled and evaluative processes (Zabelina & Andrews-Nanna 2016). During a DT task, early stages (i.e., flexible flow of thoughts, detecting useful information potentially derived from long-term memory) involve increased coupling between DMN and the Salience Network regions (SN), while later stages (i.e., honing in, elaboration, and evaluation of the solution) exhibit increased coupling between DMN and ECN, or Frontoparietal Control regions (FPN), deputy for deliberate attentional control (Beaty et al., 2015).

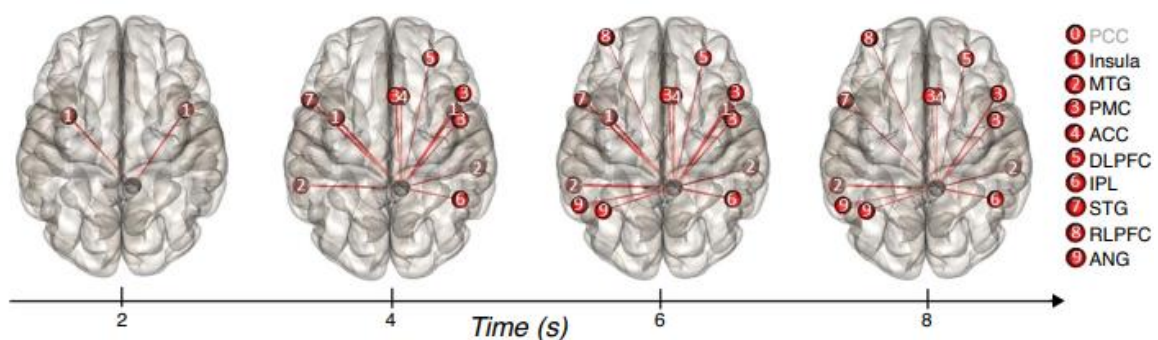


Figure 8: Time-dependent Posterior Cingulate dynamic connectivity. Early stages of a DT task (generating possible solutions to an open-ended problem) shows increased coupling between DMN and SN regions; later stages exhibit increased coupling between DMN and FPN regions (Beaty et al., 2015).

Again, other studies highlighted that the connection between the DMN and the ECN reflects the goal-directed recovery process used to search strategically in the memory, to select and to combine elements regarding past experiences during DT tasks (Beaty et al., 2018a).

However, not all literature agreed on the role of EF on the creative process. In the recent review of Palmiero and colleagues (2022), in fact, they highlighted contrasting results about the relation between DT and EF. Starting from Beaty and colleagues' study (2021b), they showed that individuals with a high cognitive control supported by high inhibition ability, working memory and cognitive flexibility, do not necessarily show high DT capacities. Rather, the contribution of EF seems to depend on the extent to which different cognitive mechanisms are used. For example, a low inhibition leads to broadening the focus of attention in the early stages of DT, while a high inhibition is necessary to narrow the focus of attention to be able to filter out irrelevant information in the next stages (Palmiero et al., 2022).

During the years, studies on creativity and DT and their association with cognitive functions, brain areas and networks involved have gradually moved considering not separate areas but broader brain networks in interaction with each other in different stages and in different manners (Vartanian et al., 2018). According to latest evidence, the interplay between three pivotal networks emerges: the Default Mode Network (DMN), the Executive Network (EN) and the Salience Network (SN).

DMN is a hub mainly involved in situations requiring an internal focus of attention and in spontaneous cognition (Andrews-Hanna, 2012) and it shows a deactivation when an external task is presented (Raichle et al., 2001). It is divided into three major subdivisions: the ventral medial prefrontal cortex (vmPFC), the dorsal medial prefrontal cortex (dmPFC) and the posterior cingulate cortex (PCC); the entorhinal cortex has been associated with the DMN, too (Raichle, 2015).

ECN (or Frontoparietal Network - FPN), of which a crucial node is the dorsolateral prefrontal cortex (DLPFC) as well as lower anterior parietal regions, is implicated in working memory, inhibition ability, task switching and DT tasks (Beaty et al., 2015). Some literature, interestingly, reported that DMN and ECN are negatively correlated; it means that when one is active, the other is inactive (Goldberg, 2018). However, they seemed to cooperate during DT tasks: the ability to come up with creative ideas involves a cooperation between brain regions associated with controlled (ECN) and spontaneous cognitive processes (DMN) (Beaty et al., 2015; 2016).

SN, on the other hand, is responsible for the relocation of attentional resources towards salient environmental events (Bressler & Menon, 2010) and has a crucial role in the dynamic switch between DMN and ECN (Beaty et al., 2015). The three brain systems described, dynamically interact to support creative performance: DMN seems to support idea generation, ECN is involved

in the ideas evaluation and SN contributes to the identification of relevant stimuli facilitating the transition between the two previous networks (Zabelina and Andrews-Hanna, 2016).

### **2.3. Divergent Thinking and Cognitive Reserve**

According to the literature that focused on cognitive processes involved in DT and considered the CR construct as “*the ability to optimize performance through differential recruitment of brain networks, reflecting the use of alternate cognitive strategies*” (Stern, 2002, p. 451), recent evidence tried to explore the relationship between DT and CR (Palmiero et al., 2016; Colombo et al., 2018; Colautti et al., 2023; Fusi et al., 2024).

This relationship can be speculatively inferred by reflecting on the proxies commonly used to measure CR, that are needed since CR cannot be directly measured. During the years, in fact, it has been estimated through different approaches and a variety of proxies; most of the studies suggested that educational, occupation and leisure activities are the most frequently used proxies of CR (Jones et al., 2010); for this reason, it is commonly assessed indirectly by evaluating experiences and activities that are believed to increase it (Colombo et al., 2018). A good example of the integration of these proxies can be found in the critical evaluation of the Cognitive Reserve Index questionnaire (CRI-q) developed by Nucci and colleagues (2012). Afterwards, more specific proxies have been proposed that have to do mostly with cognitive functioning (i.e., visuo-spatial abilities, episodic memory, working memory, processing speed, integrity of social networks, personality variables and so on; Satz et al., 2011; Fratiglioni et al., 2000; Wilson et al., 2007), as we reviewed in the first chapter. Accordingly, the meta-analysis by Opdebeeck and colleagues (2016) supports the idea that the indices of CR are related to cognitive functioning in different domains and that creativity might be one of these functions. Many of the proxies used to assess CR, in fact, indirectly refer to the flexibility of thought, which is something necessary in the creative process as we saw in the last paragraph. In the study carried out by Colombo and colleagues (2018) on a healthy aging sample, for example, they evaluated CR using three subtests from the WAIS (vocabulary, similarities and digit span), along with the years of education, occupation complexity and the number and frequency of leisure activities. They assessed individual levels of creativity through an AUT task and the generation of acronyms. Results demonstrated an heterogeneous influence of the CR proxies on performances on creative tasks: higher scores in the Vocabulary subtest were correlated with more original responses when inventing new synonyms and with more alternative uses of empty water bottles. The frequency of leisure activities was the proxy with a more significant positive effect on creative performances, demonstrating that diversifying everyday leisure activities could help individuals to generate many different ideas and to frequently change mental perspectives. These

results are in line with the conception of CR as the capacity to recruit different networks to optimize performances, reflecting the use of alternate cognitive strategies (Roldàn-Tapia et al., 2012) or alternate processes to approach tasks when standard approaches are no longer available (Palmiero et al., 2016).

In addition, literature shed light on the fact that the skills required for using alternative strategies appear to be similar to those that characterize the creative process. Accessing and applying alternative strategies require the ability to keep an open mind, to establish new and unusual relationships and to change the perspective when it is needed; these are all mental operations used to define a comprehensive creative process, as explained by the WRC model described in the previous paragraph (Antonietti & Colombo, 2013; 2016).

Nevertheless, it has rarely been placed in relation to the construct of creativity; only Christensen and colleagues (2007) did that, but testing the brain reserve hypothesis. However, starting from the premise that creativity is generally correlated with intelligence (Jauk et al., 2013), it can also represent a good indicator of CR (Palmiero et al., 2016). According to this, Palmiero and colleagues (2016) claimed that verbal creativity could be considered as another proxy indicator of CR, and open to the hypothesis that verbal creativity enhances CR and sustains active aging (Palmiero et al., 2016). From their analysis, in particular, general creativity was firstly correlated to cognitive reserve but when they divided the creativity index in two composite scores (verbal and visual creativity scores), only the composite scores of the verbal creativity positively correlated with CR. This means that CR can also be defined as a multi-dimensional construct that involves different types of information processing, such as those involved in basic verbal intelligence and verbal creativity (Palmiero et al., 2016).

Therefore, assuming that CR can be continuously modified by life experiences, even when the brain is already affected by neuropathology (Liberati et al., 2012), activities that involve verbal creativity can also actively help older people to cope with cognitive decline. Following this line, the study by Colautti and colleagues (2023) confirmed the strict relationship between DT and CR in a sample of healthy older adults. It showed that, even if DT undergoes an age effect, especially the visual component of DT which requires more cognitive control mechanisms respect to verbal DT (Colautti et al., 2023), subjects can sustain it by adopting compensatory mechanisms (i.e., recruiting to a greater extent crystallized abilities and prior knowledge rather than relying on declining control processes). Such results shed light on the potential role of DT, similar to CR, in counteracting possible cognitive impairments, allowing the recruitment of cognitive abilities that allow to perform goal-oriented behaviors and satisfy cognitive demands (Colautti et al., 2023).

### 2.3.1. The relation between DT-CR and Well-Being during the Lifespan

As we highlighted in the previous paragraph, CR can also be defined as a multi-dimensional construct that involves different types of information processing (Palmiero et al., 2016). Therefore, assuming that CR can be continuously modified by life experiences (Liberati et al., 2012) and considering results from recent evidence which confirmed the association between DT and CR (Palmiero et al., 2016; Colombo et al., 2018; Colautti et al., 2023; Fusi et al., 2024), activities involving DT abilities could help individuals, especially older people, to actively cope with physiological and pathological cognitive decline, developing useful and flexible cognitive strategies, as well as more efficient utilization of brain networks (Palmiero et al., 2016). Along with age, in fact, some cognitive abilities are more susceptible than others to life changes and to the consequent physiological decline (Mather, 2010). In particular, these are the cognitive mechanisms associated with fluid intelligence and supporting cognitive control, like executive functions, compared to the cognitive functions that pertain to the crystallized intelligence domain, which are mainly more preserved (Verhaeghen, 2003; Oswald et al., 2019).

In recent decades, increasing evidence reported that creative thinking, and in particular DT, may be preserved in aging (Fusi et al., 2021) and may support cognitive functioning, with beneficial effects on both healthy and clinical populations (Colautti et al., 2018; Fusi et al., 2020; Fusi et al., 2022; Colautti et al., 2023). According to this evidence, it has been hypothesized that cognitive stimulation aimed at supporting active aging or reducing the risk of cognitive decline should also rely on creativity, becoming a pivotal protective factor against cognitive decline (Palmiero et al., 2016).

The implications for the sphere of mood and psychological well-being may thus become clear. In support of these speculations, growing evidence explored the effects of creativity on mood (Akbari Chermahini & Hommel, 2012; Liknaitzky, 2018) showing positive effects of DT on emotion. According to Zuo and colleagues' study (2021), who analyzed the impact of a DT training on anxiety, depression and stress (through the DASS scale, Lovibond & Lovibond, 1995) on healthy individuals, an anxiety decrease emerged; contrary to their expectations, instead, DT training exerted no effect on depression and stress, demonstrating that such relations need to be further investigated.

Over the years, creativity has been shown to represent a window of communication and expression of well-being in the elderly, improving problem-solving ability, self-esteem, coping skills, life satisfaction (Flood & Phillips, 2007), as well as communication and connections among neurons (Cohen, 2001) and general physiological conditions (Lane, 2005). However, the beneficial role of DT and CR in sustaining older subjects' psychological well-being (PWB) has been scarcely

investigated so far. The trajectories of PWB during the lifespan are complex and often nonlinear, influenced by several cognitive and social factors, whose identification is therefore pivotal for successful aging literature (Kim et al., 2021). The construct itself conceives multiple aspects, as postulated by Carol Ryff (1995). Some of them tend to decrease during the last decades of life, such as personal growth and purpose in life (Fusi et al., 2022), while others generally remain stable (i.e., environmental mastery) or even improve, like positive relations (Ruini et al., 2003). In addition, according to the “*Strength and Vulnerability Integration Model*” (SAVI) (Charles, 2010), older adults seem to perceive higher PWB because of their accumulated life experience, which allows them to develop powerful cognitive and behavioral control strategies. Researchers hypothesized the existence of an emotion–cognition interaction mechanism involving both emotional processing and emotional regulation, together with cognitive control mechanisms and strategies, that may explain these effects on perceived PWB (Scheibe, 2010; 2018). It becomes evident the possible rising link between these cognitive-emotional control mechanisms and CR and DT, both involving higher cognitive functioning as explained in previous paragraphs. In a recent study by Fusi et al. (2024), this complex relation has been explored: researchers wondered (i) whether DT abilities could predict CR, (ii) CR would be positively related to PWB and (iii) DT and PWB had a positive relationship between each other. Results regarding the first hypothesis supported the literature, confirming the link between DT and CR (Palmiero et al., 2016; Colombo et al., 2018); moreover, it emerged that the visual component of DT had a strong relation with CR, evidencing that not only verbal but also figural DT skills can have a positive effect on cognition, even though these abilities are more sensitive to age decline (Colautti et al., 2023). In support of the second hypothesis, the study proved that higher CR predicts higher levels of PWB, even if the link between CR indexes seems to change according to the PWB subcomponent considered (according to the multicomponent nature of the construct, Ryff 1995). In the end, an indirect positive effect of DT on PWB through the mediation of CR emerged, especially on the perceived good emotional competence sphere. These findings confirm the pivotal roles of DT and an active life and lifestyle in building greater CR, helping older adults not only to maintain efficient cognitive functioning but also to perceive higher PWB (Fusi et al., 2024).

## **2.4. Study 1. CReativity in Everyday life Challenges: the potential role of Divergent Thinking on Cognitive and Psychological Well-Being of Older Adults**

### **2.4.1. Introduction and aim of the study**

According to the literature overview just introduced, researchers have developed a renewed interest in the creative process over the years, in particular on DT abilities and on the cognitive processes that underlie it, and on its impact on the cognitive and psychological sphere during the lifespan. Starting from the construct of DT developed by Guilford (1957), it is defined as the ability to find more than one correct solution to an open-ended problem or situation and represents a way of thinking which requires the exploration of a variety of directions, possibilities and novel associations between conceptual spaces (Acar & Runco, 2014, 2015).

Thanks to the development of cognitive psychology and neuroscience research over the years, experimental paradigms based on neuroimaging gave us an overview of brain areas and neuronal networks involved in DT abilities: the role of crystallized components of intelligence to draw on for the development of new ideas, like episodic and semantic memory, was explored (Abraham & Bubic, 2015; Beaty et al., 2020), as well as the contribution of attentional skills (Zabelina, 2018; Benedek & Fink, 2019) and fluid-processing components. Between them executive functions (EFs), in particular updating, switching and inhibiting abilities (Benedek et al., 2014c; Beaty & Schacter, 2018) aimed at facilitating semantic associations, inhibiting automatic thinking and changing the attentional focus flexibly (Palmiero et al., 2022). Moreover, the interplay between different brain networks emerged during DT tasks, such as the Default Mode Network (DMN), the Executive Network (EN) and the Salience Network (SN) (Beaty et al., 2015; 2016; Zabelina & Andrews-Hanna, 2016).

However, despite literature in the field is far from being homogeneous, its relationship with CR has been highlighted by recent evidence (Palmiero et al., 2016; Colombo et al., 2018; Colautti et al., 2023; Fusi et al., 2024), considering DT as a proxy indicator of CR.

Exercising divergent and creative thinking has been taken into consideration as a way to promote mental health and active aging by fostering creative cognition in daily life (Cropley, 1990), contributing to build a greater CR. As a result of this proven relationship and assuming that CR can be continuously modified by life experiences (Liberati et al., 2012), DT has been proposed as a possible target for cognitive stimulation interventions (Palmiero et al., 2012, 2019). This may have important implications both to maintain efficient cognitive functioning and to perceive higher PWB (Fusi et al., 2024). According to the literature overviewed in the previous paragraph, in fact, DT

abilities and higher CR has been positively associated with PWB in the lifespan, that is a multidimensional construct as defined by Carol Ryff (1995) whose trajectories during the lifespan are complex and still to be understood (Kim et al., 2021). DT abilities have also been linked to the mood sphere, showing a positive impact especially on anxiety (Zuo et al., 2021); but its impact on other dimensions such as stress and depression need further investigation.

Following this line, the aim of the study is to investigate the possible role of creativity in promoting active aging through a new training that stimulates DT skills. In particular, we want to explore the effects of a training based on DT abilities (the adapted form of CREC, by Colautti et al., 2018) on the cognitive functioning and on PWB and mood state of a healthy older adult sample. We expect a positive impact of DT training as emerged in the literature overviewed. In addition, we want to better understand the role of CR in such a relationship, expecting that people with greater CR will have better performances on both cognitive and psychological levels, and that CR may have an impact on any increases.

#### **2.4.2. Material and methods**

##### *Participants*

The study involved a total of 43 participants. From the total sample, 29 were healthy older adults (age range=58-87, Mage=68.24, SDage=5.95; Medu=14.14; SDedu=3.58) who underwent the training program based on divergent thinking (Experimental Group); 72.4% females. 14 were healthy control subjects (age range=59-77, Mage=65.07, SDage=5.27; Medu=12.86; SDedu=3.66) who filled out only t0 and t1 assessments (43% females).

No differences between groups emerged for demographic data (i.e. age and educational level), global cognitive functioning (MMSE) and the total score of cognitive reserve (CRIq\_Tot), as we can see from Table 3 in the “Data analysis” section.

All participants included in the sample had to meet the following inclusion criteria: age  $\geq 60$  years old (to be considered older adults according to the World Health Organization, [https://www.who.int/health-topics/ageing#tab=tab\\_1](https://www.who.int/health-topics/ageing#tab=tab_1)); the absence of global cognitive impairments as defined by Mini-Mental State Examination (MMSE; Measso et al., 1993)  $\geq 24$ ; no history of neurologic impairments or neurosurgical interventions; and the absence of psychiatric disease or history of alcohol or drug addiction.

## *Procedure*

Data collection was performed online from January 2022 to June 2024. All participants took part in the study on a voluntary basis. No incentive was provided.

It is an experimental study including two time-points: the baseline (t0) and a follow up (t1) after 5 weeks; they correspond to the assessment before and after the training program respectively. For the assessment, individual online sessions were scheduled, lasting about 60-90 minutes. The training program consisted of the online administration of an adaptation form of CREC (*CReativity in Everyday life Challenges*; Colautti et al., 2018) twice a week, for a total of 10 sessions lasting 60 minutes each. Sessions were divided in small groups of 3 participants with one or two operators conducting the exercises.

All participants underwent an initial online assessment of their global cognitive functioning (itel MMSE; Aiello et al., 2022) and of their cognitive reserve (CRI-q; Nucci et al., 2012). Then they filled out a neuropsychological battery and questionnaires assessing their psychological well-being and mood state (anxiety, stress and depression). The entire assessment was administered only at the baseline (t0), while during the follow up (t1) participants underwent only the neuropsychological battery and psychological well-being and mood state measures, in order to examine if there were improvements compared to the baseline.

The study was conducted according to the Declaration of Helsinki (WMA, 2013) and was approved by the Institutional Ethical Committee of the University of Bergamo and by the one of the Catholic University of the Sacred Heart in Milan. All the participants signed informed consent forms.

### *CReativity in Everyday life Challenges: CREC*

The training used in the present study is an adapted version of CREC, developed by Colautti and colleagues (2018). It has been developed in order to stimulate the three main mental operations of creative thinking proposed by the ACR model (Antonietti et al., 2011): widening, connecting and reorganizing. Exercises are aimed at finding innovative and effective strategies and solutions to solve problems. They are structured exercises of different nature and complexity with progressive adherence to daily life situations. In particular, it is composed of three exercises:

- 1) Visuo-spatial abilities: in this first exercise, subjects are provided with some different figures that they have to combine in different ways. They progressively have to adapt to some rules that examiners give them (i.e., to merge only some figures and keep others

- separate or to adapt the figure to a specific category). It helps people to develop their praxic constructive abilities as well as their cognitive flexibility;
- 2) Paradoxical scenarios: subjects are provided with a brief scenario which can only take place by considering some necessary conditions. They have to find the possible correct solutions without breaking those conditions. It allows people to develop their mental flexibility, inhibition skills and association processes.
  - 3) News/movies/real situation: examiners showed participants a piece of a news, a piece of a movie or a description of a real situation that can present critical or problematic issues. Subjects have to provide as many solutions as possible comparing the answers with each other. This last exercise promotes the ability to think divergently to a more than one solution and thanks to the comparison it allows a changing point of view incrementing cognitive flexibility.

### *Materials*

#### Cognitive Reserve and Global Cognitive Functioning

1. *Cognitive Reserve Index questionnaire* (CRI-q; Nucci et al., 2012) is a 20-item questionnaire designed to evaluate the amount of CR acquired during a person's lifetime. It is composed of three sections that correspond to the sources of CR: the individual's education (CRIq school; CRIq\_S), occupation experiences (CRIq work; CRIq\_W), and activities carried out during leisure time (CRIq leisure activities; CRIq\_LA). The items aim to investigate the type and frequency of activities carried out from the age of 18 up to the present. In particular, they consider the individual's engagement in weekly, monthly, and annual activities. Three different scores are provided to quantify cognitive reserve related, respectively, to school, work, and leisure activities. These three subscores are summed to obtain the total score; scores < 70 correspond to very low levels of CR, those >130 correspond to very high levels, and those between 85 and 129 correspond to medium levels of CR.
2. *Itel Mini-Mental State Examination* (MMSE; Aiello et al., 2022) is a screening test which evaluates general cognition and it's the telephone-version of Mini Mental State Examination (Measso et al., 1993). It is composed of 22 items investigating seven cognitive domains (temporal and spatial orientation, words registration, attention and calculation, words recall, language, and repetition). It has a maximum total score of 22 that undergoes a conversion procedure in order to convert the total score on a 30-points score. Thanks to this procedure it

can be treated like the original version, where a cut-off score of above 24/30 indicates a normal global cognitive functioning.

## Cognitive measures

The neuropsychological battery consisted of an online adaptation of some neuropsychological tests used in the clinic assessment. They were administered through *INQUISIT-Millisecond* software.

1. *Digit Symbol Substitution Test* (Thorndike, 1919) is a measure aimed to assess processing speed. Participants are presented with a 2 (row) x 9 (columns) matrix. The first row contains a sequence of digits; the second row contains boxes to be filled with digit-matching symbols. The task asks subjects to translate symbols into digits with the help of a provided key within a 2 min time frame using keys on the keyboard. Once a participant selects the current digit, the digits/symbols move to the left and a new symbol box is added to the right. Output values considered include:

- *CorrectCount* = total count of correct responses;
- *ErrorCount* = total count of erroneous responses;
- *SecondsPerCorrect* = average number of seconds per correct response.

2. *Digit Span – Forward & Backward* (Lumley & Calhoon 1934) is a measure aimed to assess verbal short-term memory and working memory respectively. In the *Forward task*, participants see digit sequences and have to recall them in the order presented by selecting the digits from a circle of digits with the mouse. Depending on performance, participants move up a level or down a level. Assessment is over after 14 trials. In the *Backward task*, participants see digit sequences and have to recall them in the reversed order.

Output values considered in both tasks are:

- *TE\_ML* = Two-error maximum length, the traditional measure of a participant's digit span (forward and backward). It is the last digit span a participant gets correct before making two consecutive errors;
- *TE\_IT* = Two-error total trials, the number of trials before the *TE\_ML* value is reached (measure of consistency).

3. *Trail Making Test – A & B* (Reitan, 1955) is a measure aimed to assess divided attention, executive functioning, motor coordination and spatial processing. Participants are asked to move the mouse in specific, predetermined sequences from nodes to nodes.

Output values considered include:

- *Trail1Errors, Trail2Errors* = counts the errors made on Trail1 and on Trail2;
- *Trail1Time, Trail2Time* = time (in ms) spent on Trail1 and on Trail 2;
- *Trail2minusTrail1* = the difference in time between performance on Trail2 and Trail1.

4. *Go/No-go Task* (Fillmore et al., 2006) is a measure aimed to assess reaction time and response inhibition. Participants are asked to press the spacebar when they see a green rectangle (=go) but refrain from pressing the spacebar when they see a blue rectangle (=nogo). The blue and green rectangles can be vertical or horizontal.

Output values considered include:

- *Meanrt* = overall mean rt (in ms) for target = go (for hits = correct responses only);
- *Errorrate* = overall error rate (omission + commission errors);
- *Omissionrate* = error rate in go-trials (participant missed to press Spacebar);
- *Commission* = error rate in nogo trials (participants hit the Spacebar).

#### Psychological measures

1. *Depression Anxiety Stress Scale* (DASS; Bottesi et al., 2015) is a 4-point Likert scale ranging between 0 and 3. It is composed of 21 total items investigating symptoms concerning three subdimensions: depression (DASS\_D), anxiety (DASS\_A), and stress (DASS\_S). The subject must respond referring to the frequency with which each symptom occurred in the last week. A total score is provided by summing all responses, representing the general levels of distress.
2. *BEN-SSC* (BEN-essere e Invecchiamento; De Beni et al., 2008) is a 4-point Likert scale ranging between 1 and 4. It is composed of 37 total items assessing psychological well-being specifically in the older adult population. All items are self-descriptive and formulated to assess positive attitudes and beliefs rather than negative ones. The questionnaire is grounded on the multidimensional concept of psychological well-being proposed by Carol Ryff (Ryff & Keyes, 1995). In addition to the original domains of the Ryff model, BEN-

SSC also includes the concept of self-efficacy. In particular, after Italian validation and a factorial analysis, BEN-SSC considers the following subscales: personal satisfaction (BEN\_PS), coping strategies (BEN\_CS), and emotion regulation skills (BEN\_CE, i.e., emotional competence). A total score is provided by summing all items' responses; higher scores represent greater levels of psychological well-being.

### 2.4.3. Data analysis

Data analyses were performed using *Jamovi* software (version 2.3). Normality was checked for all the variables with Shapiro-Wilk test and the observation of skewness and asymmetry indexes were performed; a check for outliers was run.

Descriptives (mean, standard deviation and minimum and maximum) of all measures collected at t0 and t1 in both experimental and control groups are reported below (Tables 1 and 2).

#### Experimental Group (N=29)

|              | T0     |       |       |        | T1     |       |       |        |
|--------------|--------|-------|-------|--------|--------|-------|-------|--------|
|              | Mean   | SD    | Min   | Max    | Mean   | SD    | Min   | Max    |
| MMSE         | 27.30  | 1.69  | 23.60 | 30.00  | /      | /     | /     | /      |
| CRIq_Tot     | 124.55 | 16.65 | 82.00 | 155.00 | /      | /     | /     | /      |
| Depr         | 3.57   | 2.79  | 0.00  | 10.00  | 2.76   | 2.49  | 0.00  | 8.00   |
| Anxiety      | 2.43   | 2.08  | 0.00  | 7.00   | 1.52   | 1.90  | 0.00  | 7.00   |
| Stress       | 5.68   | 3.55  | 0.00  | 14.00  | 4.03   | 2.56  | 0.00  | 10.00  |
| DASS_TOT     | 11.68  | 6.61  | 0.00  | 22.00  | 8.31   | 5.83  | 0.00  | 21.00  |
| BEN_SP       | 32.96  | 3.83  | 26.00 | 41.00  | 33.41  | 4.24  | 24.00 | 39.00  |
| BEN_SC       | 26.11  | 2.95  | 21.00 | 34.00  | 26.72  | 3.85  | 19.00 | 36.00  |
| BEN_CE       | 29.82  | 4.03  | 23.00 | 40.00  | 31.00  | 3.85  | 23.00 | 39.00  |
| BEN_TOT      | 110.71 | 10.14 | 91.00 | 140.00 | 113.03 | 12.79 | 82.00 | 135.00 |
| Forward_ML   | 6.34   | 1.56  | 4.00  | 11.00  | 6.17   | 1.58  | 4.00  | 12.00  |
| Forward_TT   | 6.31   | 1.95  | 3.00  | 11.00  | 6.07   | 1.85  | 2.00  | 12.00  |
| Backward_ML  | 5.03   | 1.45  | 2.00  | 9.00   | 5.52   | 1.82  | 2.00  | 12.00  |
| Backward_TT  | 5.41   | 1.68  | 1.00  | 9.00   | 5.83   | 1.79  | 3.00  | 12.00  |
| TrailIErrors | 1.66   | 1.82  | 0.00  | 7.00   | 1.34   | 1.37  | 0.00  | 5.00   |
| TrailITime   | 70.64  | 31.70 | 42.08 | 206.48 | 64.03  | 23.16 | 26.02 | 149.75 |

|               |        |        |        |        |        |       |        |        |
|---------------|--------|--------|--------|--------|--------|-------|--------|--------|
| Trail2Errors  | 3.79   | 4.89   | 0.00   | 23.00  | 1.93   | 2.14  | 0.00   | 7.00   |
| Trail2Time    | 111.23 | 70.00  | 52.17  | 321.61 | 91.66  | 67.79 | 50.36  | 420.65 |
| Trail2-Trail1 | 40.59  | 59.30  | -12.59 | 239.82 | 27.62  | 60.98 | -19.77 | 334.8  |
| CorrectCount  | 27.31  | 13.92  | 2.00   | 59.00  | 31.41  | 14.74 | 3.00   | 67.00  |
| ErrorCount    | 6.48   | 7.04   | 0.00   | 31.00  | 6.24   | 6.90  | 0.00   | 25.00  |
| SecxCorrect   | 7.62   | 10.84  | 2.03   | 60.00  | 6.03   | 7.33  | 1.79   | 40.00  |
| Errorrate     | 0.07   | 0.25   | 0.00   | 1.00   | 0.07   | 0.22  | 0.00   | 0.99   |
| Omissionrate  | 0.08   | 0.26   | 0.00   | 1.00   | 0.11   | 0.31  | 0.00   | 1.00   |
| Commission    | 0.07   | 0.25   | 0.00   | 1.00   | 0.04   | 0.18  | 0.00   | 0.99   |
| Mean_rt       | 422.06 | 100.28 | 283.75 | 667.26 | 411.29 | 64.62 | 320.46 | 615.20 |

*Table 1: Descriptives of all measures – cognitive and psychological measures (Experimental Group)*

**Control Group (N=14)**

|              | <b>T0</b>   |           |            |            | <b>T1</b>   |           |            |            |
|--------------|-------------|-----------|------------|------------|-------------|-----------|------------|------------|
|              | <b>Mean</b> | <b>SD</b> | <b>Min</b> | <b>Max</b> | <b>Mean</b> | <b>SD</b> | <b>Min</b> | <b>Max</b> |
| MMSE         | 28.30       | 2.06      | 25.36      | 30.00      | /           | /         | /          | /          |
| CRiQ_Tot     | 128.79      | 13.90     | 98.00      | 152.00     | /           | /         | /          | /          |
| Depr         | 2.07        | 2.70      | 0.00       | 8.00       | 2.54        | 2.99      | 0.00       | 8.00       |
| Anxiety      | 0.71        | 0.99      | 0.00       | 3.00       | 0.62        | 0.96      | 0.00       | 3.00       |
| Stress       | 3.29        | 2.70      | 0.00       | 9.00       | 3.08        | 2.33      | 0.00       | 7.00       |
| DASS_TOT     | 5.36        | 5.46      | 0.00       | 20.00      | 6.23        | 5.51      | 0.00       | 15.00      |
| BEN_SP       | 35.57       | 6.31      | 27.00      | 44.00      | 34.92       | 7.12      | 23.00      | 43.00      |
| BEN_SC       | 28.50       | 4.24      | 22.00      | 35.00      | 28.08       | 3.90      | 20.00      | 33.00      |
| BEN_CE       | 32.14       | 5.04      | 24.00      | 39.00      | 32.15       | 4.20      | 23.00      | 39.00      |
| BEN_TOT      | 119.57      | 15.63     | 98.00      | 143.00     | 117.77      | 16.05     | 94.00      | 139.00     |
| Forward_ML   | 6.14        | 0.77      | 5.00       | 8.00       | 6.93        | 1.14      | 6.00       | 10.00      |
| Forward_TT   | 4.57        | 1.45      | 3.00       | 8.00       | 5.43        | 1.99      | 4.00       | 11.00      |
| Backward_ML  | 5.14        | 1.51      | 3.00       | 8.00       | 5.79        | 1.63      | 3.00       | 9.00       |
| Backward_TT  | 4.86        | 2.14      | 2.00       | 9.00       | 5.29        | 2.13      | 2.00       | 10.00      |
| Trail1Errors | 2.07        | 3.32      | 0.00       | 13.00      | 0.79        | 0.80      | 0.00       | 2.00       |
| Trail1Time   | 68.71       | 32,81     | 42,48      | 160,184    | 61.87       | 20.80     | 39.85      | 114.10     |
| Trail2Errors | 2.07        | 1.69      | 0.00       | 6.00       | 0.93        | 1.33      | 0.00       | 4.00       |
| Trail2Time   | 85.00       | 27.69     | 52.53      | 165.24     | 70.51       | 20.03     | 48.10      | 116.92     |

|               |        |       |        |        |        |       |        |        |
|---------------|--------|-------|--------|--------|--------|-------|--------|--------|
| Trail2-Trail1 | 16.58  | 35.27 | -89.60 | 57.83  | 8.64   | 11.68 | -11.21 | 26.93  |
| CorrectCount  | 29.64  | 12.64 | 5.00   | 46.00  | 31.29  | 9.27  | 13.00  | 44.00  |
| ErrorCount    | 9.07   | 22.15 | 0.00   | 85.00  | 3.57   | 2.62  | 0.00   | 8.00   |
| SecxCorrect   | 6.20   | 6.31  | 2.61   | 24.00  | 4.27   | 1.73  | 2.73   | 9.23   |
| Errorrate     | 0.01   | 0.01  | 0.00   | 0.04   | 0.01   | 0.00  | 0.00   | 0.01   |
| Omissionrate  | 0.01   | 0.02  | 0.00   | 0.07   | 0.01   | 0.01  | 0.00   | 0.02   |
| Commission    | 0.00   | 0.01  | 0.00   | 0.02   | 0.00   | 0.00  | 0.00   | 0.01   |
| Mean_rt       | 398.42 | 53.02 | 332.43 | 549.28 | 394.19 | 38.65 | 316.47 | 459.63 |

Table 2: Descriptives of all measures – cognitive and psychological measures (Control Group).

Independent t-tests were performed to ensure that the two groups did not differ in important demographic data (age and years of education), in global cognitive functioning and global cognitive reserve measure; no significant differences were found for age, years of education, as well as for the global cognitive functioning (MMSE) and total cognitive reserve score (CRIq\_Tot; see Table 3).

|                  | <b>Experimental Group (N=29)</b> | <b>Control Group (N=14)</b> | <b>t (41)</b> | <b>p</b> |
|------------------|----------------------------------|-----------------------------|---------------|----------|
| <b>Age</b>       | $\mu$ 68.24 $\pm$ SD 5.95        | $\mu$ 65.07 $\pm$ SD 5.27   | 131.00        | 0.063    |
| <b>Education</b> | $\mu$ 14.14 $\pm$ SD 3.58        | $\mu$ 12.86 $\pm$ SD 3.66   | 158.00        | 0.243    |
| <b>MMSE</b>      | $\mu$ 27.30 $\pm$ DS 1.69        | $\mu$ 28.30 $\pm$ DS 2.06   | 162.00        | 0.276    |
| <b>CRIq_Tot</b>  | $\mu$ 124.55 $\pm$ DS 16.65      | $\mu$ 128.79 $\pm$ DS 13.90 | 171.00        | 0.414    |

Table 3: Independent sample t-tests of some demographic variables (age and education), cognitive reserve and global cognitive functioning, indicating no differences between the Experimental and Control groups.

To assess for significant differences in cognitive and psychological variables between performances at t0 and t1 in both groups, different paired sample t-tests were performed; for psychological variables Student t test was used while for cognitive measures, as some of them didn't respect skewness and asymmetry criteria, Wilcoxon ranks were calculated.

Afterwards, a series of correlations were tested in order to explore if CR was in any way associated with the improvements of the experimental sample (n=29) emerging from DT training. To better quantify improvements, we computed delta variables composed of the differences between performances at t1 and t0 of the psychological and cognitive measures. To this aim, we performed parametric correlations between CR indexes and delta variables. Before computing delta, we transformed variables that were not normally distributed into new variables through the Log10 function.

Finally, a linear regression analysis was performed starting from significant correlations, in order to understand the possible impact of CR on those improvements.

#### 2.4.4. Results

As expected from our hypothesis, there were significant differences in some of the psychological measures explored between t0 to t1 (anxiety and stress subscales and the total score of DASS, as well as the subscale related to emotional competence of BEN-SSC) only in the experimental group (Table 4). In particular, we found that anxiety levels at t1 were significantly lower ( $t(27)=3.25$ ,  $p=.003$ ) than the baseline; the same emerged for stress, which was significantly lower ( $t(27)=2.93$ ,  $p=.007$ ) after the training compared to the baseline, and for the total score of DASS scale ( $t(27)=2.95$ ,  $p=.007$ ). For the BEN-SSC scale, instead, we found a significant increase ( $t(27)=-2.11$ ,  $p=.045$ ) only on the “emotional competence” subscale (BEN\_CE) comparing the baseline to the end of the training. The same significant differences didn’t emerge in the control group.

|                |             |             | Control Group |          | Experimental Group |              |
|----------------|-------------|-------------|---------------|----------|--------------------|--------------|
|                |             |             | <i>t</i> (12) | <i>p</i> | <i>t</i> (27)      | <i>p</i>     |
| <b>DASS</b>    | Depr_T0     | Depr_T1     | -0.49         | 0.631    | 1.54               | 0.136        |
|                | Anxiety_T0  | Anxiety_T1  | 0.52          | 0.613    | <b>3.25</b>        | <b>0.003</b> |
|                | Stress_T0   | Stress_T1   | 0.33          | 0.746    | <b>2.93</b>        | <b>0.007</b> |
|                | DASS_TOT_T0 | DASS_TOT_T1 | -0.64         | 0.535    | <b>2.95</b>        | <b>0.007</b> |
| <b>BEN-SSC</b> | BEN_PS_T0   | BEN_SP_T1   | 0.64          | 0.532    | -0.74              | 0.465        |
|                | BEN_CS_T0   | BEN_SC_T1   | 0.46          | 0.651    | -1.40              | 0.174        |
|                | BEN_CE_T0   | BEN_CE_T1   | -0.53         | 0.608    | <b>-2.11</b>       | <b>0.045</b> |

BEN\_TOT\_T0                      BEN\_TOT\_T1                      0.48      0.640      -1.40      0.174

Table 4: Between group differences in psychological measures (DASS and BEN with their subscales). Significant values are in bold.

With respect to the cognitive sphere, partial results emerged. As expected from our hypothesis, some cognitive abilities improved after the DT training only in the experimental group. As it is shown in Table 5, we found significant differences ( $W=84.00$ ,  $p=0.021$ ) in “CorrectCount” value of the Digit Symbol Substitution Test. On the contrary, we found significant differences in “Trail2Errors” ( $W=224.50$ ,  $p=.034$ ) and in “Trail2Time” ( $W=332.00$ ,  $p=.012$ ) values of the Trail Making Test, which also emerged in the control group (Errors\_  $W=47.40$ ,  $p=.045$ ; Time\_  $W=88.00$ ,  $p=.025$ ). We didn’t find any other significant difference between cognitive measures.

|                     |                 |                 | Control Group |              | Experimental Group |              |
|---------------------|-----------------|-----------------|---------------|--------------|--------------------|--------------|
|                     |                 |                 | <i>W</i>      | <i>p</i>     | <i>W</i>           | <i>p</i>     |
| <b>Digit Symbol</b> | CorectCount_T0  | CorrectCount_t1 | 31.50         | 0.334        | <b>84.00</b>       | <b>0.021</b> |
|                     | ErrorCount_T0   | ErrorCount_T1   | 27.00         | 1.000        | 178.50             | 0.807        |
|                     | Sec.perCorr_T0  | Sec.perCorr_T1  | 66.00         | 0.162        | 251.00             | 0.057        |
| <b>TMT</b>          | Trail1Errors_T0 | Trail1Errors_T1 | 34.00         | 0.187        | 156.00             | 0.334        |
|                     | Trail1Time_T0   | Trail1Time_T1   | 51.00         | 0.952        | 285.00             | 0.149        |
|                     | Trail2Errors_T0 | Trail2Errors_T1 | <b>47.50</b>  | <b>0.045</b> | <b>224.50</b>      | <b>0.034</b> |
|                     | Trail2Time_T0   | Trail2Time_T1   | <b>88.00</b>  | <b>0.025</b> | <b>332.00</b>      | <b>0.012</b> |
|                     | Trail2minus1_T0 | Trail2minus1_T1 | 72.00         | 0.241        | 279.00             | 0.190        |

Table 5: Between group differences in cognitive measures with their subscales (Digit Symbol Substitution Test and Trail Making Test and their values). Significant values are in bold.

Results about correlation analysis reflected partially our hypothesis. Performing a series of parametric correlations between CR indexes and the psychological measures increased after the DT training, we didn’t find any significant correlation.

With respect to the cognitive sphere, we found negative correlations between CRIq total score ( $r=-0.38$ ,  $p=.045$ ), CRIq\_Leisure ( $r=-0.41$ ,  $p=.027$ ) and CRIq\_Work ( $r=-0.38$ ,  $p=.040$ ) and “Delta\_Trail2\_Time” of the Trail Making Test (Table 6).

|                   |          | CRIq_Leisure | CRIq_School | CRIq_Work    | CRIq_Tot     |
|-------------------|----------|--------------|-------------|--------------|--------------|
| Delta_Trail2_Time | <i>r</i> | <b>-0.41</b> | -0.03       | <b>-0.38</b> | <b>-0.38</b> |
|                   | <i>p</i> | <b>0.027</b> | 0.864       | <b>0.040</b> | <b>0.045</b> |

Table 6: parametric correlations between CRIq (and its subscales) and “Delta\_Trial2\_Time” of the Trail Making Test. Significant values are in bold.

In line with our expectations, linear regression analysis confirmed a significant impact of CR on the improvements emerging from the DT training in “Delta\_Trail2\_Time” of the Trail Making Test ( $R^2=14\%$ ,  $p=.045$ ) in the experimental group (Table 7).

| Model | R    | R <sup>2</sup> | Overall Model Test |     |     |              |
|-------|------|----------------|--------------------|-----|-----|--------------|
|       |      |                | F                  | df1 | df2 | p            |
| 1     | 0.38 | 0.14           | 4.42               | 1   | 27  | <b>0.045</b> |

Table 7: Linear regression analysis considering CRIq total score as the independent variable and “Delta\_Trail2\_Time” of the Trail Making Test used as dependent variables.

#### 2.4.5. Discussion

The present study aimed to preliminary explore the impact of a training based on DT abilities (adapted version of CREC, by Colautti et al., 2018), both on the cognitive functioning and on the

well-being sphere of a healthy older adults sample, compared with a control group of individuals who have not been given any treatment.

Results showed an effective positive impact of the DT training on the mood state and on PWB related to emotional competences. These results are in line with the literature previously discussed. Starting from the mood state, results highlighted a decrease in anxiety and stress levels after the DT training, as well as an increase in the general mood state that didn't emerge in individuals who didn't undergo any treatment. A partial explanation of such results derives from the evidence provided by Akbari Chermahini & Hommel (2012), who claimed that DT's positive effect on emotion may be partially explained by the role of dopamine. According to them, working on DT abilities might boost dopamine level which consequently triggers positive emotions (Akbari Chermahini & Hommel, 2012). According to the model proposed by Jauk (2019), in fact, interindividual differences in creative cognition and behavior seemed to arise from the variation in the dopaminergic system. Brain areas with significant dopaminergic innervation include the striatum, substantia nigra and hypothalamus; specifically, dopamine levels from the subcortical striatum are involved in functions such as flexible updating of goal representations and the shifting of task strategies, as well as habit learning and reward processing (Cools & D'Esposito, 2011; Zabelina et al., 2016). These are crucial factors in experiencing positive emotions; as Antonietti & Colombo discussed with the development of the WCR model (2013; 2016), creative cognition contains a range of abilities including accessing and applying alternative strategies, keeping an open mind, establishing new and unusual relationships and changing the perspective when it is needed. Such skills may allow individuals to maintain strong cognitive abilities and efficient performances that guarantee a certain autonomy and effectiveness in everyday life. Secondly, according to Zuo and colleagues (2021), the positive role of DT on emotions, especially on anxiety, could also be due to the associative processes that DT stimulates: as anxiety may manifest in front of uncertainty (Nolen-Hoeksema, 2000), association processes enable people to predict and minimize such uncertainty, thus decreasing their anxiety. As Mednick postulated in 1962, in fact, associative processes play a crucial role in creative thinking. He claimed that creativity results by some *remote associations*, which allow individuals to connect ideas that are distant from each other and combine different concepts to build new ones. The WCR model (Antonietti & Colombo, 2013; 2016) also reminds us that one of the three components of creative cognition is *Connecting*, referring to the ability to form reciprocal relationships between different elements, recognize analogies between seemingly unrelated things, combine ideas in creative ways and integrate diverse components into a cohesive whole.

Moving forward in the highlighted results, we also found positive effects of DT on stress, which is in contrast with some literature (Morgan & Harris, 2015; Duan et al., 2020; Zuo et al., 2021), suggesting the need for further investigation in this field. The same goes for depression: we didn't find any effect. On one hand, it is partially in line with the above mentioned literature (Morgan & Harris, 2015; Duan et al., 2020; Zuo et al., 2021) that didn't find any impact on the latter variable; on the other, it goes in contrast with Liknaitzky and colleagues (2018), who showed correlations between depression and lack of DT abilities, leading to hypothesize that working on DT abilities would positively act on depression levels. However, we ought to remember that we referred to studies which explored healthy samples who didn't suffer from any psychopathology: experimental designs carried out on clinical samples (i.e., depressive or anxiety disorders) may help the research to find more consistent and homogeneous results.

In addition, the above mentioned results are in line with the literature supporting a greater PWB in the elderly population (Charles, 2010; Scheibe, 2010; 2018), especially relating to emotional competence abilities (Fusi et al., 2024). As older adults built a greater accumulated life experience, allowing them to develop powerful cognitive and behavioral control strategies, the existence of an emotion–cognition interaction mechanism hypothesized by the scientific literature (Scheibe, 2010; 2018) could be the key to such results. This mechanism involves both emotional processing and emotional regulation, together with cognitive control mechanisms and strategies. The development of such mechanism thanks to life experiences that bring a certain cognitive effort, may allow individuals to perceive a better control on their emotions and on their behavioral strategies, and so in their environment and in their social relationship, guaranteeing them a better PWB perceived. As recent evidence shows, DT abilities involved in creative cognition, contributing to an active life in building greater CR, help older adults not only to maintain efficient cognitive functioning but also to perceive higher PWB (Fusi et al., 2024).

The relation between DT abilities and CR is complex and far from being clearly understood. As we saw in this chapter, DT has been linked to CR by consistent literature in the last decade (Palmiero et al., 2016; Colombo et al., 2018; Colautti et al., 2023; Fusi et al., 2024), considered as a potential CR indicator. In this study, no impact of CR was found: it means that CR would not have a predictive role on the effects that DT training has on PWB and on mood state. These results are partially in line with some recent evidence (Fusi et al., 2024) that tried to explore the intricate relationships between the three constructs (DT, CR and PWB) finding that, in the aging population, higher DT abilities predict higher scores of CR – confirming that DT can be considered a resource and a protective factor during the aging process (Palmiero et al., 2016; Colombo et al., 2018) - which, in turn, predict higher levels of PWB (but only in some of its subcomponents, like emotional

competence). This means that having higher DT potential, and so building CR, exerts a positive effect (through CR) on some components of PWB, suggesting that people with higher DT tend to be involved in more complex jobs and to have heterogeneous interests in their free time during life, influencing their well-being.

However, paying attention to some methodological factors should be useful to bring to more efficient results in future studies. Firstly, the study design: considering the dynamic nature of CR, with a longitudinal design it would be possible to monitor subjects' well-being over time and check if beneficial effects of the DT training on individuals' psychological sphere will improve. Secondly, sessions of DT training repeated over time would be required to make the effects deeper and generalizable; this could be crucial to transpose changes in daily life, thus perceiving a greater well-being over time.

In relation to the cognitive sphere, consistent results emerged in the present study. Processing speed abilities, divided attention, motor coordination and spatial processing showed an improvement after the training based on DT abilities. Such skills, in fact, fall within the broader executive functioning, defined as the set of basic cognitive processes that control both thought and action, and proven to be linked with creativity (Benedek et al., 2014c). Our results reaffirm the involvement of EFs on DT abilities, intervening in facilitating semantic associations, inhibiting automatic thinking and changing the attentional focus flexibly (Palmiero et al., 2022). However, the relation between DT and EFs is far from being clear and uniform, as the contribution of EFs would depend on the extent to which different cognitive mechanisms are used by individuals (Palmiero et al., 2022).

Finally, considering the role of CR in such relationships, interesting results emerged showing a significant positive impact of CR on divided attention, motor coordination and spatial processing. This is in line with numerous studies that associated CR proxies with EFs (Álvares-Pereira et al., 2022; Oosterman et al., 2021; MacPherson et al., 2017;) indicating that high CR levels are linked to better EFs (Frau et al., 2024). As we said in the first chapter, in fact, greater CR has been associated with an increased ability to select the best strategy for performing a task (Stern, 2012). However, such considerations don't disregard the fact that lower EF levels in individuals with low CR may reflect lower lifelong intellectual functioning, as opposed to CR providing a protective effect against declining EF (Frau et al., 2024).

Some limitations in the present study should be considered. The first potential limitation may arise from the conceptualization and measurement of CR. In the current study, CR was measured through one of the most used tools in the literature (CRIq by Nucci et al., 2012) that considers three of the most common proxies used for older adults (years of education, work and leisure activities). As it

has been reviewed in the first chapter, a lot of CR proxies have been considered over the years and an homogeneous methodology has not been achieved. As recently highlighted by Frau and colleagues (2024), in order to better quantify CR, an integration of CR static proxies (such as education and IQ) and dynamic ones (e.i., leisure activities and social support) can be considered, reflecting a specific timeframe in the first case and a multi-dimensional view in the second one. Studies that consider static proxies may not completely represent the dynamic nature of CR that changes over time (Malek-Ahmadi et al., 2017); in the same way, considering only the dynamic ones risks to provide a limited vision, given the importance of education in CR literature (Mondini et al., 2022). So, a more comprehensive measurement of CR should be used to clearly understand CR in its complexity, including both static and dynamic proxies.

Another potential limitation may be related to the number of participants; the little sample size (n=43) may have affected the generalization and applicability of the results. Greater clarity on the role of DT abilities and CR on cognitive and PWB in the life-span would have been reached by recruiting more healthy older adults. In line with this limitation, we ought to consider the imbalance between the control (n=14) and the experimental group (n=29). It would have been advisable to achieve a similar sample size between the two groups to have results with a higher validity.

Lastly, a further consideration can be made regarding the methodological approach: subjects involved in the study were administered an online test battery which required the use of a computer, a tool that elderly people may not be accustomed to, slowing down or making some performances more complex. Cognitive tools that evaluate processing speed, for example, need to measure response times as accurately as possible; although a computer is a convenient and easy tool, since it allows for remote assessments, it risks limiting precise and totally representative results of the individuals' performance. In future studies, it would be recommended to carry out in-person assessments in order to limit any systematic error.

#### **2.4.6. Conclusions and practical implications**

The present study found that an intervention based on DT abilities, administered weekly and in small groups for more than 2 months, have positive effects on the mood state, on PWB and on the cognitive functioning of older adults. In particular, working on DT abilities has proven to have an impact on anxiety, stress and on a greater perception of one's emotional skills, highlighting a possible emotion-cognition interplay. Moreover, DT abilities resulted in better cognitive performances relating to executive processes such as speed abilities, divided attention, motor

coordination and spatial processing, reaffirming EFs involvement in creative thinking. Relating to CR, any impact on the sphere of well-being has emerged, confirming the complex relationship between these two multidimensional constructs, while a predictive role of CR on cognitive improvements after the DT training has been found (still within executive skills), confirming the association of CR proxies with executive functioning.

Future longitudinal research would be fundamental to fully provide a more comprehensive understanding of the complex and multifaceted concept of cognitive reserve. Thanks to the results provided by this study and the existing literature, the practical implications should lead to an increase of cognitive stimulation protocols aimed at supporting active aging that also rely on creative cognition, maybe on DT abilities, becoming a pivotal protective factor against cognitive decline and to promote better psychological well-being. Paying particular attention to the role that DT interventions can have on building greater CR, allow to intervene not only on the cognitive sphere, but also on psychological well-being along the aging process.



## CHAPTER 3: COGNITIVE RESERVE AND WELL-BEING IN CARDIOVASCULAR DISEASES

### 3.1. Cardiovascular diseases: a brief context

Spini, Bernardi & Oris (2017) defined vulnerability as an intrinsically dynamic process that involves the range of the available resources and the compensatory actions undertaken along individuals' lives. In this perspective, vulnerability becomes manifest as a consequence of a latent vulnerability, consisting of a period of fragility that may affect the balance of the available resources, being often associated with the increasing exposure to risk situations and stress factors. In addition, it may become manifest when the individual faces a critical event such as disease.

The diseases of the 21st century are essentially chronic degenerative ones, generally affecting the adult and elderly population (Belfiore, 2019). Chronic pathology is defined by the World Health Organization as "*the set of health problems that require continuous treatment over a period of time ranging from years to decades*". Among chronic diseases, cardiovascular diseases (CVDs) play an important role, as they represent the main cause of mortality in the elderly population. In recent decades, the average life expectancy of Western countries has progressively increased, leading to an aging of the general population: in Italy, 22.6% of the population is over 65 years old, while only 13.4% is under 15 years old (Belfiore, 2019).

According to the data from the Superior Institute of Health, CVDs are responsible for 44% of all deaths in our country. In particular, ischemic heart disease is the leading cause of death in Italy and it is responsible for 9.9% of all deaths, while cerebrovascular accidents are in third place (with 13%) after tumors (ISS, 10/31/2022). Furthermore, it is estimated that the prevalence of CVDs is progressively increasing in the various age groups (Belfiore, 2019).

In recent years, researchers have highlighted that cardiovascular disorders may be associated with both psychological (Ladwig et al., 2022) and cognitive (Ihle et al., 2018) impairments which, in turn, lead to numerous effects both at the behavioral level, such as lower therapeutic adherence, and at the physiological one, such as worsening of the clinical condition (Ho et al., 2009). The combination of these aspects inevitably has an impact on their health status. A more-in-depth look at these factors is provided in the next paragraphs.

### **3.2. The problem of poor Adherence to pharmacological treatment and factors associated**

Poor adherence, which represents one of the main behavioral effects of psychological and cognitive impairments associated with CVDs, has a crucial impact on the quality of life (QoL) of patients (Ponzani & De Riu, 2018).

With the term *adherence* we refer to an active participation, almost an alliance between doctor and patient in order to obtain the best possible clinical outcome. It therefore presupposes an informed, motivated and conscious choice on the part of the patient (Burra & Germani, 2021). Generally, the patient is considered compliant with treatment if he/she takes more than 80% of the prescribed drug (Rudd, 1995).

Suffering from a chronic disease has been shown to have a certain impact on adherence behavior (Ho et al., 2009). Furthermore, it has been shown that adherence persistence is particularly slow in subjects with chronic diseases: adherence to medical care seems to be higher in patients with an acute condition compared to those with a chronic condition (Fabbri & Sartini, 2010).

According to the World Health Organization, the main causes of non-adherence to medical prescriptions involve: (i) aspects related to the patients (i.e., advanced age, presence of cognitive, visual or hearing deficits or psychological disorders such as depression), (ii) to the clinical condition (suffering from a chronic pathology and/or the presence of multiple comorbidities), (iii) to the therapy (high frequency of administrations or high number of drugs prescribed), (iv) to the socio-economic system in which the patient is involved and (v) to the health system itself (Colivicchi et al., 2010). Among the causes that play a particularly relevant role, there are those related to the patient's clinical condition: scientific evidence showed that the impairment of cognitive functions can substantially compromise adherence behaviors in CVDs (i.e., heart failure, Alonso et al., 2012; and hypertension, Chudiak et al., 2018). For this reason, a deep look on the importance of cognitive functioning and thus on the potential increase of cognitive reserve in the cardiovascular field has given in this chapter.

#### **3.2.1. Cognitive functioning and Cognitive Reserve**

As already mentioned, one of the main causes of poor adherence involves aspects related to the patients' clinical condition, in particular their cognitive functioning (Alonso et al., 2012; Chudiak et al., 2018). In this context, an important element to take into consideration is CR; acting as a protective factor in the processes of healthy and pathological aging, it can be considered an important key factor to indirectly act on therapeutic adherence behaviors.

As we saw in the first chapter, the concept of CR is complex and multidimensional and allows to understand how individual differences lead some people to better cope with the consequences of brain damages than others (Colombo et al., 2018). Moreover, Stern (2009) emphasized that the concept of CR is relevant not only in cases of subjects affected by dementia or other neurological conditions linked more or less consistently to age, but also for normal aging. Thus, according to the defined concepts of vulnerability (Spini et al., 2009) and CR (Stern, 2002; 2009) provided, some individuals would be more vulnerable than others, consequently they should have more difficulty in dealing with treatment situations. On the contrary, less vulnerable individuals who have accumulated a greater reserve in multiple domains throughout their life, should be more skilled in dealing with treatment situations (Ihle et al., 2018).

### 3.2.2. The role of the physical component: steps toward Motor Reserve

In recent years, a growing branch of the literature is addressing the impact of the physical component on the health status of patients affected by CVDs, both at a psychological and cognitive level.

The association between physical activity and cardiovascular health, however, is not new in the CVDs panorama: it has been treated focusing on the impact that treatments based on physical activity could have on a manifest cardiovascular event. It is crucial, instead, to consider a preventive approach on health, that tries to better understand the role of physical activity performed consistently throughout life on the development and progression of CVDs, paying attention to the trend of those factors associated with patients' global clinical condition (as reported in the previous paragraphs). This may represent an initial step to the development of the recent construct of Motor Reserve (MR), underlying the capacity exhibited by some patients to maintain motor functionality in the face of a certain level of disease (Giustiniani & Quarantone, 2024), showing a possible role on cognitive and psychological status of patients affected by CVDs; it will be better reviewed and discussed in paragraph 3.3.

Literature provides evidence (Jin et al., 2023) supporting physical activity's role in promoting vascular and circulatory health, also increasing CR (Qiu & Fratiglioni, 2018); older adults have been found to delay cognitive decline by increasing their physical activity (Benedict et al., 2013; Wolf et al., 2020). In accordance, already in the previous decade, evidence about clinical sample affected by neurodegenerative diseases (such as dementia) has highlighted that individuals who consistently perform greater cognitive but also physical activity throughout their lives, have a lower chance on incurring cognitive decline (Valenzuela et al., 2008).

Following this line, a recent work by Blumen and colleagues (2024) considered physical activity as an effective indicator of CR on older healthy adults, showing that both cognitive and physical CR proxies are associated with cognitive decline. In their study, physical activity was computed considering the number of blocks walked per day and the weekly physical activity days.

Physical activity has also been associated with greater mental health. Literature showed that physical activity can be conceived as a means to selfhood maintenance when a pathological condition already emerged, suggesting that, apart from maintaining body functions, it can be a way to sustain well-being and selfhood, improving both physical and cognitive functions, activities of daily living and decreasing dependency from the environment (Cedervall et al., 2015).

Further implications of MR on well-being and individuals' QoL have been shown in a recent work (Giannì et al., 2024); they will be discussed in the next section (paragraph 3.3).

### 3.2.3. Illness perception

In the field of CVDs, talking about adherence to therapy is a sensitive topic as several factors come into play and have an impact on such behavior: between them, we find the *illness perception*. With this term, we consider the cognitive and emotional representations that a person develops about the disease he/she suffers from. Perception of illness is fundamental in determining the patient's approach to the disease and to the adherence behavior (Akut et al., 2022).

Leventhal and colleagues (1984) developed the *Self Regulatory Model* to describe the process by which individuals respond to the perception of something that is threatening to their health. According to the model, the individual would first form a representation of the disease or perceived threat, then implement behaviors to cope with it and finally evaluate the effectiveness of these behaviors. Therefore, the model incorporates a sort of continuous feedback loop, in which the results of the evaluation are reported into the representation of the disease, which in turn leads to the adoption of certain responses.

During the last decades, it has been shed light on the association between perception of illness as it has been defined (Leventhal et al., 1984) and the adherence to treatment (Weinman et al., 2000). It emerges that increasing the perception of illness in CVDs ensures patients a faster adaptation to healthier lifestyles, and so to the achievement of higher levels of physical, mental and social well-being (Akut et al., 2022).

#### 2.3.4. Self-Care

Facing vulnerable situations such as suffering from a chronic illness requires daily and consistent healthcare management (Ausili et al., 2014). Consequently, the major health threat and the primary driver of healthcare costs, researchers and healthcare providers are focusing on interventions that can prevent or control exacerbations. In this context, the importance of self-care is increasingly recognized, representing the primary means of caring for a chronic condition (Riegel et al., 2018).

In the *Middle Range Theory of Self-Care of Chronic Illness* developed by Riegel and colleagues (2012), self-care is defined as a process of maintaining health through health promoting practices and managing illness. In this theoretical model, three concepts are specified: *Self-care maintenance*, which refers to behaviors implemented to maintain physical and emotional stability (i.e., smoking cessation, eating healthy food), as well as to prevent an exacerbation of the clinical condition (i.e., taking medications as prescribed); *Self-care monitoring* refers to the process of observing oneself for changes in signs and symptoms (i.e., body listening) to early detect a health change; *Self-care management* is the response to signs and symptoms when occur (Riegel et al., 2017).

Self-care is thus a complex structure and a wide variety of factors may influence the decisions that individuals make about engaging in self-care (i.e., emotions or mood states, Smith et al., 2016a; Xu et al., 2018; disease-related distress, Pandit et al., 2014; personality traits, Skinner et al., 2014; social, Fivecoat et al., 2018; or interpersonal factors and clinical factors).

Advances in the literature have yielded valuable insights into how effective self-care monitoring and management are influenced by knowledge, attention, expectations and identity (Whitaker et al., 2015). Moreover, self-care behaviors that are consistent with individual goals are more likely to develop into habits and be maintained over time (Grunseit et al., 2019).

Issues such as the influence of culture on self-care behavioral choices and the difficulty performing self-care with multiple chronic conditions are still little covered issues by the literature (Riegel et al., 2019b). It emerges that an exploration of factors such as CR and MR and their relationship with the implementation of self-care behaviors could be an interesting issue, as they allow individuals to build, as we have seen previously, a wide range of skills and resources. It may be hypothesized that greater CR and MR could increase self-care behaviors, acting on the patients' global health sphere.

Taken together, those results allow us to focus on two main aspects. Firstly, it is necessary to clarify the gaps in literature and to better understand what we know about the possible impact of cognitive and physical factors on CDVs, deepening the implications for patients' mental health and QoL (as it will be reviewed with the state-of-the-art review in paragraph 3.3). Secondly, it would be interesting to explore if greater CR and MR could lead to higher adherence to treatment, acting on patients' health status; it would be necessary to also consider those factors that are more associated with a

poor adherence to treatment, such as the cognitive functioning, the perception of illness and the implementation of self-care behaviors and thus fill further gaps in the literature (as it will be argued with the experimental study in paragraph 3.4). It would bring consistent implications on prevention and on clinical practice in the field of CVDs.

### **3.3. Study 2. The role of Cognitive and Motor Reserve on QoL in Cardiovascular Patients: a state-of-the-art review**

#### **3.3.1. Introduction**

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels which include conditions such as coronary heart disease, congenital heart disease or acute events like heart attacks and strokes. CVDs represent the leading cause of mortality worldwide, with an estimated 17.9 million deaths from CVD in 2021 (WHO, 2021). Patients affected by CVDs have implications both on their physical and emotional sphere; they experience physical symptoms such as fatigue, dyspnea or chest pain that automatically impact their emotional and social well-being, bringing a significant impairment in their quality of life (QoL) (Morys et al., 2016). QoL is defined as “*a broad-ranging concept affected in a complex way by the person’s physical health, psychological state, level of independence, social relationships and their relationship to salient features of their environment*” by the World Health Organization (WHO, 2021); another dimension closely linked to QoL but focused on health, which is widely considered in the field of CVDs, is health-related quality of life (HRQoL), defined as the individual’s functioning in life concerning his or her perceived well-being in physical, mental, and social domains of health (Hays et al., 2010).

Currently, a great deal of effort is being made to understand how the burden of CVDs can be reduced; in fact, as the population ages, the global CVD burden is continuing to increase, especially among older adults due to their older age, multiple comorbidities and frailty (Aidoud et al., 2023). It seems that a partial solution lies in including CVDs management interventions at the primary care level, making interventions more usable and accessible for everyone (WHO, 2021). However, it represents only a partial solution as it acts when the pathological condition is already established; it would be useful to act, in a complementary way, at a preventive level, by an intervention on the involved risk factors (e.g., unhealthy diet, tobacco, harmful alcohol use and physical inactivity) (WHO, 2021). Moreover, at an interventional level, current strategies for the management of patients with CVDs are intended to reduce mortality and prolong survival, while treatments should be also focused on improving patients’ QoL (Morys et al., 2016): cardiac rehabilitation programs focusing on lifestyle modification, psychological interventions and education seem to enhance patients’ QoL (Shepherd & Alison, 2022).

Starting from these promises, the review aims to highlight the possible role of two constructs, cognitive (CR) and motor reserve (MR), which correspond respectively to the individual amount of cognitive and physical activities accumulated during the lifespan, on CVDs patients’ perceived QoL. We hypothesize that these two concepts would be fundamental to (i) operate preventively,

constituting a protection and buffer effect to deal with the pathology and (ii) influence patients' QoL when the pathology is full-blown, with a specific focus on the older population.

Insights into these two constructs will be discussed and an overview of “if and how” CR and MR have been associated with QoL will be provided, first in a more general literature and then in CVD patients.

### **3.3.2. Cognitive Reserve and its relation with Quality of Life**

Most of the CR literature concentrates a large part of the studies on the effects on cognitive functioning, showing what different levels of CR entail in the cognitive sphere. Thus, CR has been investigated primarily in dementia (Stern, 2012), acquired brain injury (Basagni et al., 2023) and stroke (Contador et al., 2022) and then the concept was extended to healthy aging and a broad range of neurological and psychiatric conditions. Its protective role in global cognitive functioning has been widely proven, both in healthy aging (Stern, 2002; Opdebeeck et al., 2016; Cabeza et al., 2018) and in a range of neurological conditions such as Alzheimer's disease (Stern, 2006), Parkinson's disease (Pernecky et al., 2008) or multiple sclerosis (Stein et al., 2023).

The relationship between CR and the psychological framework is less explored. Recent findings, in line with previous literature, showed a positive influence of CR on perceived psychological well-being in healthy older adults (Fusi et al., 2024), thereby indicating that people with more years of work accumulated, who held jobs requiring more cognitive and behavioral flexibility and involved in diversified free time activities, perceive better coping strategies and higher emotional competences. Another recent work by Porricelli and colleagues (Porricelli et al., 2024) explored the relationship between CR and mental health in healthy adults and showed that higher levels of CR corresponded to a greater mental health, considering measures of anxiety, depression and stress. However, more knowledge in the field is required, especially regarding the effects of CR on QoL. From a speculative point of view, it is possible that people with greater levels of CR, who are supposed to be able to better cope with various disorders, could also experience a greater QoL. According to Lara and colleagues (Lara et al., 2017), who measured CR in a sample of older healthy adults considering the three main indicators previously highlighted (education, work and leisure-time activities), higher CR is associated with higher QoL. Furthermore, considering the health-related aspect of QoL and in line with previous findings, a more recent work by Ihle and colleagues (Ihle et al., 2022) considered the association between CR, cognitive functioning and health-related quality of life (HRQoL) levels on a sample of healthy older adults. They reported that better cognitive functioning together with higher CR (operationalized by education and cognitive

level required at work) is fundamental to sustaining perceived good QoL, particularly for the mental component related to the health status.

There are only a few studies that have focused on CR and QoL in clinical samples, and they focused on heterogeneous pathologies such as psychiatric disorders (Anaya et al., 2015), multiple sclerosis (Schwartz et al., 2013) and other medical conditions (Gomez-Beldarrain et al., 2015). Contrasting results emerged from these studies: Anaya and colleagues (2015) found that higher CR was positively associated only with the physical component of QoL and negatively with the mental component, indicating that psychiatric patients with bipolarism who have higher CR levels perceive better physical health but they show a worse subjective perception of their mental health than patients with lower CR. Otherwise, Schwartz and colleagues (2013) and Gomez-Beldarrain and colleagues (2015), who analyzed respectively patients with multiple sclerosis and with chronic migraine, found positive associations between CR and both components of QoL (physical and mental QoL). These contrasting results have arisen due to the heterogeneous samples analyzed and due to the use of different tools to measure QoL and CR. The majority of the studies on clinical samples and on healthy elderly people usually measure QoL by dividing it into two sub components, mental and physical QoL; one of the most used tool in this field is SF-36 (Ware & Sherbourne, 1992) or its short version, the SF-12. Others used comprehensive tools such as WHOQOL-AGE (Caballero et al., 2013), which is specific for the older adult population (Lara et al., 2017). Again, other studies (i.e., Ihle et al., 2022) focused on a specific construct that is very close to QoL, which is HRQoL, reflecting an individual's functioning in life concerning his perceived well-being in physical, mental and social domains of health (Hays et al., 2010).

Another reason that brings contrasting results can be found in the use of different tools and methods to operationalize CR. Considering only the studies mentioned, we can see that none of them used the same tool and the same proxies: some used CR Questionnaire (Ihle et al., 2022), which considers a lot of proxies of CR together (level of education, parents' level of education, training courses, occupation, musical training, languages, reading activities and intellectual games; Rami et al., 2011); others used more than one tool (i.e. CR Questionnaire and CRI-q) to collect more indicators at a time (Schwartz et al., 2013; Gomez-Beldarrain et al., 2015) and others used only single proxies or the union of more indicators without a specific instrument (i.e. educational level, occupational attainment, Ihle et al., 2022; and premorbid IQ, Anaya et al., 2015).

When taking these considerations together, it becomes really difficult to compare studies where constructs are not homogeneous.

It is also necessary to consider that the relationship between CR and QoL is often mediated by other health-related factors such as depression, cognitive functioning, disability Lara et al., 2017, health-

related behaviors (Schwartz et al., 2013) and coping strategies (Schwartz et al., 2016). Indeed, it has been shown that CR seems to influence those problematic health behaviors such as smoking and obesity, which may affect both the severity and the course of the disease, acting across a broad spectrum on patients' QoL (Schwartz et al., 2013). Furthermore, greater CR levels might allow individuals to use effective coping strategies to handle potentially stressful situations, for example those derived from their functional limitations (Schwartz et al., 2016). Thus, it is useful to keep in mind that finding a direct relationship between these two constructs is challenging, especially considering the amount of factors that can mediate this relation and that these factors can vary depending on the clinical sample examined.

### **3.3.3. Cognitive Reserve and Quality of Life: a focus on patients with Cardiovascular Diseases**

The problem relating to the operationalization of CR makes it difficult to analyze this construct, especially if we want to explore and relate it to huge and complex medical conditions like CVDs.

There is very little literature available regarding CR on this cohort of patients; this is because most of the research focuses on alterations in the cognitive domain resulting from a cardiovascular event or a chronic condition and less on how a starting cognitive level or reserve can affect patients' well-being and QoL. Moreover, as we have seen in the last Paragraph, QoL is investigated in different ways or it is often overcome by HRQoL, especially in clinical samples. The last, but not least, point concerns the influence of those health-related factors that mediate the relationship between CR and QoL, making it challenging to reach homogeneous considerations.

Over the years, some attempts have been made to associate some proxies of CR with QoL in the field of CVDs. Most studies considered specific cardiac pathologies individually, while really few evidence considered the general cardiovascular framework.

Level of education as a predictor of QoL was the indicator mostly considered in the field of CVDs. For example, it has been analyzed considering samples of patients with heart failure (HF) (Riedinger et al., 2000; Barbareschi et al., 2011). Results showed that low education levels were associated with a worse QoL; moreover, from a longitudinal point of view, they found better QoL for highly educated patients in both physical and functional domains.

From a wider point of view, other findings confirmed the role of higher educational levels in cardiac patients' QoL and they also considered occupational status (Rahnavard et al., 2006; Yousefi et al., 2011). However, findings about this last proxy are contrasting; other empirical evidence, indeed, showed no relationship between occupation and QoL for example in patients with myocardial infarction (MI) (Hasanpour-Dehkordi et al., 2007). It means that further clarification on the role of occupational status in CVDs is still needed.

Moreover, it would be necessary to increase studies in the field to clarify predictors of QoL in this cohort of patients. A proposal going in this direction could be trying to quantify CR and put it in relation with QoL, considering homogeneous samples and methodologies. It would be a turning point for the knowledge in the field, representing the starting point to plan clinical interventions based on CR, which is modifiable during the lifespan, and hypothetically directly acting to promote patients' QoL.

However, according to this aim, we ought to consider factors that influence the relationship between CR and QoL in cardiovascular patients, in particular the role of cognitive functioning and health-related behaviors. In fact, from a physiological point of view, modified cardiovascular conditions can induce changes in cerebral perfusion, which is one of the determinants of cognitive deterioration (Picano et al., 2014). Attention, working memory, executive function and psychomotor speed seem to be mostly affected by cardiovascular events. Moreover, a growing line of evidence shows the importance of the cardiovascular system for the pathogenesis of dementia (De la Torre, 2004; Stone et al., 2015; Levin et al., 2020). According to this evidence, the cognitive decline that arises from some form of dementia is caused by a clinically silent bleeding of small cerebral vessels; such a hemorrhage seems to be induced by a long exposure to the stress of the pulse. With age, in fact, the arterial tree stiffens, and the intensity of the pulse grows. Therefore, it emerges that the pulse becomes more intense and destructive with age, thus causing vascular breakdown, a progressive loss of neurons and, consequently, cognitive decline (Stone et al., 2015). The alteration of the cognitive domain represents, in turn, an important factor that can limit patients' ability to follow correct health-related behaviors (i.e., following their dietary or medication regimes), further reducing their QoL (Bennet et al., 2005). Following this line, in a recent review by Zaben and Khalil (2019) conducted on patients with acute coronary syndrome (ACS), they highlighted the importance of self-behaviors, together with health literacy, for patients' QoL. So, according to this evidence, a good general executive functioning is crucial for the relationship between the cognitive domain and QoL and, as it will be shortly discussed, also considering the motor reserve (MR). Furthermore, in a lifespan perspective, executive functioning is often the first domain to be impaired with aging, contributing to cognitive impairment, loss of autonomy and reduction in QoL (Verhaeghen & Cerella, 2002; Verhaeghen, 2003).

#### **3.3.4. Motor Reserve: construct definition**

The MR is a relatively recent concept in the literature and even if it has not been fully addressed yet, it refers to the flexible and dynamic construct that potentially increases over time and compensates for age-related motor and cognitive loss (Pucci et al., 2024).

It represents another form of reserve, emerging from studies on clinical samples, in particular from patients affected by neurodegenerative disorders such as Parkinson's disease (PD). In this field, in fact, MR has been preliminary defined as an active process explaining the discrepancy between the severity of symptoms exhibited by patients with PD and their levels of brain degeneration (Youn et al., 2023). It seems that a higher MR is associated with a greater ability to cope with the pathological motor skill decline, both in a pathological condition and in healthy late adulthood (Bastos & Barbosa, 2022). It seems that the amount of motor deficits may differ among patients depending on levels of dopamine depletion (Youn et al., 2023): in some PD patients, motor symptoms appear only after the loss of a certain amount of dopaminergic neurons, suggesting that compensatory processes may take place. Just like CR, as we saw, this mechanism allows patients to reach normal performances in the face of the disease burden (Habets et al., 2021).

To better clarify what we intend with MR, it is necessary to highlight that physical activity's beneficial effects derive from the activity carried out regularly over time (Pucci et al., 2024); without consistency and frequency it wouldn't be possible to build a strong reserve and it would correspond only to a sporadic physical exercise leading to insufficient physiological changes (Simonsson et al., 2023).

Starting from studies about patients with PD, also in the field of the motor domain some proxies seem to contribute to the enhancement of MR, including dominant side-laterality (Ham et al., 2015), educational attainment (Sunwoo et al., 2016) and premorbid exercise engagement (Sunwoo et al., 2017); such proxies seem to allow patients to better cope with PD-related pathological deficits. Over the years, more evidence tried to gradually separate the concept of MR from PD and to understand its functioning from a more general point of view. In a recent work by Pucci and colleagues (2024), they explored the potential effect of MR on the cognitive functioning of a sample of healthy individuals over 50 years and tried to operationalize MR in a specific way. They considered the amount of physical activity (PA) and physical exercise (PE) carried out by individuals, defining PA as the result of unstructured daily activities in various contexts such as work, housekeeping, walking and leisure (Cabeza et al., 2018; Bherer et al., 2013) and PE as all movements produced by skeletal muscles resulting in energy expenditure including structural physical activities (Caspersen et al., 1985). According to this evidence, an active lifestyle and engagement in structured PA help to keep the body healthy but also to guarantee an effect on the brain, cognition and mood (Pucci et al., 2024).

In line with that and considering that a large part of the population is nowadays low-active or sedentary and is engaged in levels of physical activity that are insufficient for health gain (Camisuli et al., 2023), guidelines support the importance for older adults to engage in exercise

training to promote both physical and cognitive health (Nelson et al., 2007). Recommendations suggest that a program of regular exercise including cardiorespiratory, resistance, flexibility and neuromotor training can improve physical fitness and is essential for health status vitality in most adults (Rivera-Torres et al., 2019). Moreover, according to the World Health Organization (WHO, 2010), it seems that adults aged 65 and older should perform at least 150 minutes per week of moderate-intensity activity or 75 minutes of vigorous-intensity activity. Thus, regular physical activity of moderate intensity has been recognized as a significant beneficial factor for health, both reducing the risk of developing CVDs (i.e., heart disease, stroke, hypertension, type 2 diabetes etc.), psychiatric symptoms such as depression and anxiety (Grande et al., 2019; Cunningham et al., 2020), and also sustaining older adults' cognitive functioning (Nelson et al., 2007).

The relationship between physical exercise and cognition is complex, physiological changes have been proposed to precede changes in cognition (Jonasson et al., 2017), and this is why a longer intervention is needed to observe a significant change in global cognition.

Physical activity is important because it seems to slow down the process of age-related neuronal and volumetric loss and reduce both lesions in the white matter and myelin loss, promoting better oxygenation and blood supply to the brain (Goenarjo et al., 2020). Moreover, it maintains the neural network through neuroplasticity, brain perfusion and neurogenesis; so, people with good physical fitness can tolerate a greater neuropathological burden without suffering cognitive impairment (Wallace et al., 2019). Recent evidence has highlighted its beneficial effects especially on some cognitive abilities (i.e., executive functions, learning, memory and language) in the older population (Zhang et al., 2018). Executive functions, which are supported by lifestyles including physical activity, play a key role in the elderly's mental health, as higher levels of cognitive processes are fundamental in targeting goals, effortful behavior and environment adaptation (Corbo & Casagrande, 2022; Fusi et al., 2022). Nowadays, in fact, physical activity programs are well-established strategies for improving working memory, cognitive flexibility and inhibitory control in cognitively healthy older adults (Xiong et al., 2021).

If we try to compare the two types of reserve analyzed, it is interesting to assume that the factors that contribute to increasing MR might also increase CR; however, factors that determine high CR (i.e., education, work, cognitively stimulating leisure activities) do not necessarily lead to an increase in MR (Pucci et al., 2024). This leads to the conclusion that they are two different and independent types of reserve, both contributing to good cognitive functioning differently.

### **3.3.5. Motor Reserve and Quality of Life**

Engaging in regular physical activity, beyond the delay of age-related physiological and cognitive decline and the reduction of risk of developing common diseases, seems to also improve the

subjective QoL (Cunningham et al., 2020; Falck et al., 2019; Edholm et al., 2019). These findings are supported by other evidence, postulating that MR promotes better general cognitive functioning and QoL (Siciliano et al., 2022). Any type of physical activity implies, in fact, the connection between individuals and their own body with the environment, involving numerous and coordinated actions, all requiring cognitive functioning (i.e., the perception and cognitive estimation of distance, size, shape and weight of objects and spaces, modulating the motor response and calibrating the action within the surrounding space) (Pucci et al., 2024). So, maintaining an active lifestyle in older age in terms of cognitively stimulating activities and regular physical activity across the lifespan is advantageous from multiple points of view. According to the World Health Organization, physical activity is recognized as relevant for supporting “healthy aging” in different ways, in particular as a key enabler of social participation, personal autonomy and greater psychological well-being and QoL (WHO, 2019).

Along with QoL, research has shown that engagement in structured physical activity protocols can improve some aspects of psychological well-being in the elderly, such as mood (Harris et al., 2006; Warburton et al., 2006), self-perception (Fox et al., 2007), depression (Loprinzi, 2013), emotional well-being and decreased anxiety (Rivera-Torres et al., 2019). According to these findings, the literature remains sparse, with most studies conducted to investigate the impact of structured programs of exercise on mental well-being. A growing number of studies, in fact, focused on exercise training even in cohorts of patients with hemodialysis (Myers et al., 2021; Filipic et al., 2021) and with multiple sclerosis (Fidao et al., 2023), showing that regular physical activity improves mental and physical QoL. In contrast, very little is known about the influence of daily physical activity accumulated over time. That’s why it is necessary to consider the nascent concept of MR in the field of mental well-being and QoL, especially in clinical samples that experience an impairment of QoL like patients affected by CVDs.

### **3.3.6. Conclusion**

According to the literature overviewed, CR and MR are two predictors of better cognitive functioning. Preserving good cognitive functioning is crucial to support daily activities and to maintain autonomy and QoL, especially in older adults who often present multiple comorbidities. Studies that have tried to link CR and MR with QoL in healthy adults and heterogeneous clinical samples have demonstrated a great deal of difficulties and methodological limitations, which have brought contrasting results.

The field of CVDs, a group of disorders representing the leading cause of mortality worldwide, is even more involved due to the variety of physical symptoms that influence patient’s QoL. There are few and inconsistent studies about the link between CR, MR and QoL in this cohort of patients:

some studies have individually considered one or two CR proxies (i.e., education or occupation), or they have considered only a single pathologic condition that is included in CVDs. Regarding MR, most of the evidence is focused on the effects that physical activity programs have on patient QoL; thus, the influence of daily physical activity accumulating over time from a preventative point of view has been neglected. According to such considerations, it has emerged that there is further evidence focused on relating CR and MR in CVDs. As defined in the literature reviewed, the attention on CVD patients' QoL can be useful for implementing knowledge in the field and to bring benefits in clinical practice, mainly in terms of primary and secondary, but also tertiary, prevention interventions. Indeed, considering that CR and MR can always be expanded and potentiated, preventive interventions to enhance the two types of reserve can be extremely useful in supporting CVD patients' cognitive and psychological resources. They could be useful for providing patients with more resources to act preventively on the risk factors of CVDs and for overcoming their occurrence, but also by acting retrospectively to improve their chances of responding positively and flexibly to the difficulties encountered during the disease. These resources might, therefore, potentially have significant beneficial effects on patient perception of QoL, thus also contributing to other health-related dimensions such as the ability to regulate their emotions or adherence to therapies. Future studies are needed to better clarify the relationship between these variables.

### **3.4. Study 3. The role of Cognitive and Motor Reserve on Well-Being and Adherence to treatment in Cardiovascular Diseases: preliminary results of a longitudinal study**

#### **3.4.1. Introduction and aim of the study**

According to data from the Superior Institute of Health, CVDs are responsible for 44% of all deaths in our country (ISS, 10/31/2022). It is estimated that the prevalence of CVDs is progressively increasing in the various age groups (Belfiore, 2019).

In recent years, researchers have highlighted that cardiovascular disorders are associated with psychological (Ladwig et al., 2022) and cognitive (Ihle et al., 2018) impairments which, in turn, lead to numerous effects both at the behavioral level, such as lower therapeutic adherence, and physiological one, such as worsening of the clinical condition (Ho et al., 2009). The combination of these aspects inevitably has an impact on their general health status.

Poor adherence to treatment represents one of the most impacting behavioral effects, since poor adherence behavior has a crucial influence on patients' QoL (Ponzani & De Riu, 2018). Considering that the impairment of cognitive functions can substantially compromise adherence behaviors in CVDs (Alosco et al., 2012; Chudiak et al., 2018), an important element to take into consideration is the CR. Acting as a protective factor in the processes of healthy and pathological aging (as we saw in the first chapter), CR can be considered an important key factor to indirectly act on therapeutic adherence behaviors.

Following this line, as physical activity is being even more considered in increasing the stock of individual's available resources, recent literature conceives it as an effective indicator of CR (Blumen et al., 2024). More and more literature is focusing on considering a physical reserve warehouse, independently from CR but closely interrelated. "Motor Reserve" (MR) has thus been defined as the flexible and dynamic construct that potentially increases over time and compensates for age-related motor and cognitive loss (Pucci et al., 2024).

Another aspect which is fundamental to consider and monitor in the field of CVDs is the perception of illness, which refers to the disease's cognitive and emotional representations that a person develops (Leventhal et al., 1984). During the last decades, it has been shed light on the association between this concept and adherence to treatment (Weinman et al., 2000), suggesting that increasing the perception of illness in CVDs ensures patients a faster adaptation to healthier lifestyles and so to the achievement of higher levels of physical, mental and social well-being (Akut et al., 2022).

Moreover, also the sphere of Self-care deserves consideration in this field. The *Middle Range Theory of Self-Care of Chronic Illness* (Riegel et al., 2012) defines self-care as "a process of

maintaining health through health promoting practices and managing illness". Facing vulnerable situations such as suffering from a chronic illness, in fact, requires daily and consistent healthcare management (Ausili et al., 2014). The importance of self-care is increasingly recognized, representing the primary means of caring for a chronic condition (Riegel et al., 2018). However, even if self-care has been shown to be influenced by a lot of factors (Smith et al., 2016a; Xu et al., 2018; Pandit et al., 2014; Skinner et al., 2014; Fivecoat et al., 2018), including knowledge, attention, expectations and identity (Whitaker et al., 2015), several issues are still little covered by the literature (i.e., the influence of culture and the presence of multiple comorbidities on self-care behavioral choices; Riegel et al., 2019b). For these reasons, an exploration of factors such as CR and MR could be an interesting issue, as they allow individuals to build a wide range of skills and resources, acting consequently on various other factor such as those mentioned (e.g., perception of illness or self-care behaviors). It may be hypothesized that greater CR and MR could increase self-care behaviors, acting on the patients' global health sphere.

In a period characterized by the growth of health psychology, intervening on well-being has become a central aim. In line with the latter background, it is necessary to identify those factors that help to preserve an individual's well-being considering any condition that may limit the state of health (Ihle et al., 2018). In reference to the *Selective Optimization with Compensation* model (SOC, Baltes & Baltes, 1990), well-being depends on how the individual adapts to the growing limits related to health and on how they evaluate the consequences of such limits in daily life. In accordance, McKee-Ryan and colleagues (2005) differentiate the physical aspects of well-being from the psychological ones. Well-being is thus a multidimensional and dynamic construct as postulated by Carol Ryff (1995) who, focusing on the psychological sphere, considered PWB as the positive evaluations of oneself and one's life, the sense of continuous growth and development of oneself as a person, the belief that life has a purpose and meaning, the possession of good relationships with other people, the ability to manage one's life and what is around in an effective way, as well as a sense of self-determination.

In light of this, according to evidence supporting the protective role of CR (Colombo et al., 2018) and MR (Pucci et al., 2024) on individuals' cognitive functioning and on PWB (Ihle et al., 2018), this work aims to investigate whether these two constructs may be associated with greater adherence behaviors and with better physical and psychological well-being on CVD patients over time, paying a particular attention to the PWB's dimensions identified by Carol Ryff (1995). Secondly, we would better understand whether CR and MR may have a relationship also with those factors influencing the adherence to treatment (i.e., perception of illness and self-care behaviors).

We expect that CR and MR could be associated with greater perception of illness and self-care behaviors, acting consequently on the adherence behavior and leading to a better general health status, perceiving higher physical and PWB.

### 3.4.2. Material and methods

#### *Participants*

The study involved a total of 53 participants (age range=23-88, Mage=65.47, SDage=11.49; Medu=11.19, SDedu=4.45; 20.8% females) suffering from a cardiovascular disease. The majority of the sample (N=48, 91%) suffered from a chronic cardiovascular condition, while a small portion of the sample had an isolated event (further details about CVDs category is provided in Table 8).

They all were screened for inclusion criteria which included: age > 18 years old; the absence of global cognitive impairments as defined by Montreal Cognitive Assessment (MoCA; Santangelo et al., 2015) > 17.54; no history of neurologic impairments or neurosurgical interventions; the absence of psychiatric disorders; the admission to the Cardiology Unit for a cardiovascular acute event or a chronic cardiovascular condition; having a drug prescription for cardiovascular diseases.

Additional socio-demographic data are reported in Table 8.

| <b>Marital Status</b> | <b>Frequency</b> | <b>Total %</b> |
|-----------------------|------------------|----------------|
| married               | 39               | 73.6 %         |
| divorced/separated    | 6                | 11.3 %         |
| widow/widower         | 3                | 5.7 %          |
| single                | 5                | 9.4 %          |
| <b>Who lives with</b> |                  |                |
| with partner          | 32               | 60.4 %         |
| alone with sons       | 1                | 1.9 %          |
| with mom and dad      | 1                | 1.9 %          |
| partner and sons      | 11               | 20.8 %         |
| alone                 | 8                | 15.1 %         |
| <b>Religion</b>       |                  |                |
| agnostic              | 3                | 5.70%          |
| atheist               | 1                | 1.90%          |
| catholic              | 49               | 92.50%         |
| <b>Smokers</b>        |                  |                |
| yes                   | 12               | 22.60%         |
| no                    | 41               | 77.40%         |
| <b>CVD</b>            |                  |                |
| Chronic               | 48               | 91%            |

|                     |    |     |
|---------------------|----|-----|
| Acute               | 5  | 9%  |
| <b>CVD category</b> |    |     |
| Arrhythmia          | 11 | 21% |
| CHD                 | 31 | 58% |
| Cardiomyopathy      | 6  | 11% |
| PFO                 | 1  | 2%  |
| Valve               | 4  | 8%  |

Table 8: Sample demographic data. Abbreviations: CHD=coronary heart disease; PFO=patent foramen ovale.

### Procedure

Participants were recruited at the Cardiology Unit of the Clinic Humanitas Gavazzeni in Bergamo (Italy). Data collection started in December 2023 and it still ongoing.

It is a longitudinal study including three time-points: the baseline (t0) which corresponds to the recruitment at the Cardiology Unit and two follow-ups collected after 6 (t1) and after 12 months (t2) from the baseline. However, in this study only the first follow up will be considered. The entire sample read and provided the informed consent.

All participants underwent an initial assessment of their cognitive and motor reserve through the use of two specific tools, Cognitive Reserve Index questionnaire (CRI-q; Nucci et al., 2012) and Motor Reserve Index questionnaire (MRI-q; Pucci et al., 2024), respectively. Then they filled out questionnaires assessing adherence to treatment (MARS-5; Chan et al., 2020), psychological well-being (PWB; Ryff & Singer, 1996), the general health status (FS-12; Ware et al., 1995), the perception of illness (Brief-IPQ; Broadbent et al., 2006) and self-care (SCI; Luciani et al., 2022), self-efficacy related to self-care (SCSES; Yu et al., 2021) measures. The entire assessment was administered individually and in a single session only at the baseline (t0) and it lasted about 60 minutes; after 6 months from the enrollment (t1), patients filled out all measures previously cited except for the cognitive and motor reserve. MoCA was administered again in order to monitor patients' cognitive functioning after a cardiovascular acute event or a cardiovascular chronic condition over time. In current analysis, only a few patients included in the entire sample carried out follow up (t1) measures (N=19); that's because data collection is still ongoing, so follow up (t1) measures about the entire sample aren't completed.

The research protocol and procedure were approved by the Clinic ethical committee and were conducted following the Declaration of Helsinki (WMA, 2013). All participants signed informed consent forms.

## Materials

Predictors measured only at the baseline:

1. *Cognitive Reserve Index questionnaire* (CRI-q; Nucci et al., 2012) is a 20-item questionnaire designed to evaluate the amount of CR acquired during a person's lifetime. It is composed of three sections that correspond to the sources of CR: the individual's education (CRIq school; CRIq\_S), occupation experiences (CRIq work; CRIq\_W), and activities carried out during leisure time (CRIq leisure activities; CRIq\_LA). The items aim to investigate the type and frequency of activities carried out from the age of 18 up to the present. In particular, they consider the individual's engagement in weekly, monthly, and annual activities. Three different scores are provided to quantify cognitive reserve related, respectively, to school, work, and leisure activities. These three subscores are summed to obtain the total score (CRIq\_Tot); scores < 70 correspond to very low levels of CR, those >130 correspond to very high levels, and those between 85 and 129 correspond to medium levels of CR.
2. *Motor Reserve Index questionnaire* (MRI-q; Pucci et al., 2024) is a 17-item questionnaire designed to evaluate both incidental and structured physical activity carried out across the lifespan. It is composed of six sections that correspond to the sources of MR: housework activities (MRIq Housework Activities; MRIq\_HA), walking (MRIq Waling; MRIq\_W), leisure activities (MRIq Leisure Activities; MRIq\_LA), physical exercise (MRIq Physical Exercise; MRIq\_PE), care activity (MRIq Care Activity; MRIq\_CA), workplace activities (MRIq Workplace Activities; MRIq\_WA). Each section assigns a score based on frequency and years of practice, from the age of 18 up to the present. The score of each item is calculated in hundredths proportionally to the maximum possible raw scores. The overall score goes from 0 to 100, representing the average of the mean score of each single section (MRIq\_Tot %).

Global cognitive functioning:

1. *Montreal Cognitive Assessment* (MoCA; Santangelo et al., 2015) is a screening test which evaluates general cognition. It is composed of 12 sub-tasks that investigate different cognitive functions such as attention, executive functions, memory, language, abstraction, calculation, orientation and visuo-constructional abilities. It has a maximum total score of 30 and a cut-off score of above 17.54 indicates a normal global cognitive functioning.

#### Main outcomes:

1. *Medication Adherence Report Scale* (MARS-5; Chan et al., 2020) comprises 5 items describing non-adherent behaviors. Patients are asked to evaluate how often they adopt each behavior with a 5 point scale, ranging from “always” to “never” (1-5 points). The total score ranges from 5 to 25, indicating lowest adherence and maximal adherence respectively.
1. *Psychological Well-Being* (PWB short version - 18 item; Ryff & Keyes, 1995) is based on Ryff’s multidimensional model of PWB, evaluating the personal perception of well-being relative to 6 dimensions: autonomy (PWB\_A), environmental mastery (PWB\_EM), personal growth (PWB\_PG), positive relations with others (PWB\_PR), purpose in life (PWB\_PL), and self-acceptance (PWB\_SA). It is a questionnaire composed of 18 items, 3 for each dimension, with a score ranging between 1 (strongly disagree) and 6 (strongly agree). A total score is reached by adding all six constructs, with high single scores reflecting an overall positive PWB.
2. *Health Survey* (SF-12; Ware et al., 1996) is a 12-items questionnaire consisting of 2 components: a physical component score (SF\_PCS) and a mental component score (SF\_MCS). Higher scores on the two subscales indicate greater levels of functioning and a more favorable health status, thus being indicative of a better QoL.

#### Other psychological measures:

1. *Brief Illness Perception Questionnaire Brief-IPQ*, (Brief-IPQ; Broadbent et al., 2006) is a 9-items questionnaire assessing cognitive perceptions of disease. Each question evaluates one dimension of illness perception by giving a score from 0 to 10, with lower scores indicating being least affected and higher scores being highly affected, thus having a more catastrophic perception of the disease. The total score ranges between 0 and 80.
2. *Self-Care Inventory* (SCI; Luciani et al., 2022) is a 20-item self-report instrument based on the Middle Range Theory of Self-Care of Chronic Illness (Riegel et al., 2012), with three separate scales measuring Self-Care Maintenance (SC\_MN), Self-Care Monitoring (SC\_MO), and Self-Care Management (SC\_MG). The first scale includes eight items while the second and the third include six items. All items are rated on a 5-point ordinal response scale ranging from 1 to 5; two items in the Self-Care Management scale include a 0 option. Each of the three scales is scored separately and standardized 0–100 with higher scores indicating better self-care.
3. The *Self-Care Self-Efficacy Scale* (SCSES; Yu et al., 2021) was used together with SCI; even if it isn’t a part of self-care, it is reported in literature it’s a factor that strongly

influences self-care. It is based on the most updated version of Middle Range Theory of Self-care of Chronic Illness (Riegel et al., 2019) and was proposed as a single-domain scale to measure self-efficacy in self-care maintenance, self-care monitoring and self-care management. It is composed of 10 items rated on a 5-point ordinal response scale ranging from 1 to 5; the total score is standardized mathematically to range from 0–100. A higher score indicates higher self-efficacy.

### **3.4.3. Data analysis**

Data analyses were performed using *Jamovi* software (version 2.3). Normality was checked for all the variables with Shapiro-Wilk test and the observation of skewness and asymmetry indexes were performed.

In order to better explore the relationships between CR, MR and all the above mentioned variables considered in the study, we firstly performed a series of two-tailed parametric correlations between CR and MR and the main outcomes at the baseline (i.e., adherence to treatment, the general health status and PWB with its subscales) and then between CR and MR and those factors influencing the adherence to treatment (i.e., perception of illness and self-care behaviors) at the baseline.

Secondly, we considered only the part of the sample (N=19) who carried out the follow up measures (t1). Considering this portion of the sample, we performed paired sample non-parametric t-tests, Wilcoxon ranks (due to the little sample), to explore differences between t0 and t1 in relation to the main outcomes (adherence, health status and PWB), as well as to the related factors (illness perception and self-care). Mean scores and standard deviations of each measure, both at t0 and t1, are provided.

Finally, considering significant results from paired sample t-tests and improvements in the mean scores of some of the measures collected at t1, we performed a linear regression analysis to better understand the possible impact of CR and MR on such progresses over time. To quantify improvements, we computed delta variables composed of the differences between performances at t1 and t0 of the variables considered.

### **3.4.4. Results**

Descriptive statistics regarding cognitive and motor reserve (Cri-q; Mri-q, including total scores and all the subscales) and general cognition (MoCA) are reported in Table 9. Descriptive statistics of the

other measures included in the study (including total scores and all the subscales) carried out at the baseline are reported in Table 10.

|                   | <b>Mean</b> | <b>Standard Deviation</b> | <b>Minimum</b> | <b>Maximum</b> |
|-------------------|-------------|---------------------------|----------------|----------------|
| <b>CRIq_Tot</b>   | 111.45      | 20.06                     | 75.00          | 162.00         |
| <b>CRIq_S</b>     | 104.47      | 16.13                     | 83.00          | 145.00         |
| <b>CRIq_W</b>     | 108.87      | 18.45                     | 84.00          | 151.00         |
| <b>CRIq_LA</b>    | 112.43      | 21.06                     | 64.00          | 179.00         |
| <b>MRIq_Tot %</b> | 23.47       | 11.02                     | 7.00           | 54.00          |
| <b>MRIq_HA</b>    | 29.60       | 28.40                     | 0.00           | 102.00         |
| <b>MRIq_W</b>     | 34.49       | 18.29                     | 0.00           | 78.00          |
| <b>MRIq_LA</b>    | 17.55       | 16.59                     | 0.00           | 62.00          |
| <b>MRIq_PE</b>    | 14.45       | 17.82                     | 0.00           | 74.00          |
| <b>MRIq_CA</b>    | 19.09       | 13.42                     | 0.00           | 60.00          |
| <b>MRIq_WA</b>    | 26.47       | 17.06                     | 4.00           | 78.00          |
| <b>MoCA</b>       | 24.98       | 3.20                      | 18.00          | 30.00          |

*Table 9: Descriptive statistics of cognitive (CRIq) and motor reserve (MRIq) with their subscales and of the global cognitive functioning (MoCA) at the baseline (N=53).*

|                    | <b>Mean</b> | <b>Standard Deviation</b> | <b>Minimum</b> | <b>Maximum</b> |
|--------------------|-------------|---------------------------|----------------|----------------|
| <b>MARS-5</b>      | 23.17       | 2.60                      | 14.00          | 25.00          |
| <b>SF_PCS</b>      | 42.76       | 9.40                      | 20.71          | 56.06          |
| <b>SF_MCS</b>      | 46.79       | 11.59                     | 21.34          | 66.64          |
| <b>PWB_A</b>       | 14.29       | 3.45                      | 8.00           | 18.00          |
| <b>PWB_EM</b>      | 12.13       | 3.47                      | 0.00           | 18.00          |
| <b>PWB_PG</b>      | 13.33       | 3.72                      | 0.00           | 18.00          |
| <b>PWB_PR</b>      | 13.88       | 3.64                      | 0.00           | 18.00          |
| <b>PWB_PL</b>      | 11.54       | 3.98                      | 0.00           | 18.00          |
| <b>PWB_SA</b>      | 12.62       | 3.71                      | 0.00           | 18.00          |
| <b>PWB_Tot</b>     | 77.79       | 15.47                     | 18.00          | 106.00         |
| <b>SelfCare_MN</b> | 69.81       | 14.49                     | 43.75          | 96.88          |

|                    |       |       |       |        |
|--------------------|-------|-------|-------|--------|
| <b>SelfCare_MO</b> | 61.85 | 20.16 | 20.00 | 96.00  |
| <b>SelfCare_MG</b> | 56.00 | 17.29 | 20.00 | 96.00  |
| <b>SelfCare_SE</b> | 71.92 | 18.78 | 12.50 | 100.00 |
| <b>Brief-IPQ</b>   | 53.64 | 13.24 | 23.00 | 76.00  |

*Table 10: Descriptive statistics of adherence to treatment, health status, psychological well-being, self-care and perception of illness at the baseline (N=53).*

Contrary to our expectations, exploring the relationships between CR, MR and all measures considered in the study, we didn't find any correlation between CR and MR (nor in the total scores nor in their subscales) and adherence behaviors (MARS-5). Any correlation emerged also between the two constructs and the general health status (SF-12, including the physical and mental component scores). In accordance with our hypothesis, instead, we found significant positive correlations between the “*Purpose in life*” component of PWB, CRIq total score ( $r=0.31, p=.023$ ) and some of CRIq indices: work (CRIq\_W;  $r=0.36, p=.009$ ) and leisure activities (CRIq\_LA;  $r=0.28, p=.045$ ). Significant positive correlations emerged also between the “*Self-acceptance*” component of PWB and two MRIq indices: walking (MRIq\_W,  $r=0.32, p=.022$ ) and workplace activities (MRIq\_WA,  $r=0.28, p=.046$ ). In addition, contrary to our expectation, a significant negative correlation emerged between PWB\_SA and the index of CR related to years of education (CRIq\_S;  $r=-0.27, p=.049$ ) (Table 11).

|                |          | CRIq_Tot     | CRIq_S       | CRIq_W       | CRIq_LA      | MRIq_% | MRIq_HA | MRIq_W       | MRIq_LA | MRIq_PE | MRIq_CA | MRIq_WA      |
|----------------|----------|--------------|--------------|--------------|--------------|--------|---------|--------------|---------|---------|---------|--------------|
| <b>MARS-5</b>  | <i>r</i> | -0.2         | -0.19        | -0.26        | -0.08        | 0.17   | 0.12    | 0.1          | 0.17    | 0.08    | 0.08    | 0.09         |
|                | <i>p</i> | 0.154        | 0.175        | 0.064        | 0.588        | 0.223  | 0.408   | 0.499        | 0.227   | 0.59    | 0.588   | 0.543        |
| <b>SF_PCS</b>  | <i>r</i> | 0.09         | 0.08         | 0.1          | 0.06         | -0.1   | -0.01   | -0.04        | -0.09   | -0.25   | 0.01    | 0.04         |
|                | <i>p</i> | 0.532        | 0.565        | 0.483        | 0.688        | 0.492  | 0.953   | 0.78         | 0.534   | 0.076   | 0.946   | 0.802        |
| <b>SF_MCS</b>  | <i>r</i> | 0.21         | 0.19         | 0.15         | 0.21         | 0      | -0.08   | 0.04         | 0.03    | 0.07    | -0.02   | 0.02         |
|                | <i>p</i> | 0.13         | 0.18         | 0.303        | 0.129        | 0.975  | 0.558   | 0.793        | 0.835   | 0.633   | 0.878   | 0.901        |
| <b>PWB_PL</b>  | <i>r</i> | <b>0.31</b>  | 0.15         | <b>0.36</b>  | <b>0.28</b>  | 0.09   | -0.01   | 0.06         | 0.02    | -0.01   | 0.16    | 0.14         |
|                | <i>p</i> | <b>0.023</b> | 0.294        | <b>0.009</b> | <b>0.045</b> | 0.547  | 0.966   | 0.679        | 0.89    | 0.942   | 0.245   | 0.316        |
| <b>PWB_SA</b>  | <i>r</i> | -0.01        | <b>-0.27</b> | 0            | 0.19         | 0.25   | 0.05    | <b>0.32</b>  | 0       | 0.22    | 0.07    | <b>0.28</b>  |
|                | <i>p</i> | 0.948        | <b>0.049</b> | 0.997        | 0.177        | 0.07   | 0.748   | <b>0.022</b> | 0.992   | 0.121   | 0.602   | <b>0.046</b> |
| <b>PWB_A</b>   | <i>r</i> | -0.05        | -0.15        | -0.07        | 0.07         | 0.09   | 0.06    | 0.12         | 0.03    | 0.07    | 0.01    | -0.04        |
|                | <i>p</i> | 0.71         | 0.303        | 0.599        | 0.623        | 0.534  | 0.681   | 0.389        | 0.813   | 0.598   | 0.96    | 0.77         |
| <b>PWB_EM</b>  | <i>r</i> | 0.22         | 0.14         | 0.13         | 0.25         | 0.02   | -0.17   | 0.1          | -0.14   | 0.25    | -0.09   | 0.18         |
|                | <i>p</i> | 0.125        | 0.308        | 0.342        | 0.068        | 0.893  | 0.234   | 0.473        | 0.306   | 0.072   | 0.524   | 0.197        |
| <b>PWB_PG</b>  | <i>r</i> | 0.08         | -0.11        | 0.17         | 0.12         | 0.03   | -0.02   | 0.04         | -0.23   | 0.23    | -0.08   | 0.17         |
|                | <i>p</i> | 0.565        | 0.421        | 0.219        | 0.399        | 0.828  | 0.898   | 0.765        | 0.105   | 0.101   | 0.581   | 0.232        |
| <b>PWB_PR</b>  | <i>r</i> | 0.17         | 0.06         | 0.12         | 0.22         | 0      | 0.02    | 0.06         | 0.02    | -0.13   | 0.1     | -0.08        |
|                | <i>p</i> | 0.224        | 0.658        | 0.411        | 0.116        | 0.989  | 0.872   | 0.673        | 0.865   | 0.346   | 0.466   | 0.551        |
| <b>PWB_Tot</b> | <i>r</i> | 0.18         | -0.04        | 0.17         | 0.27         | 0.11   | -0.01   | 0.17         | -0.07   | 0.15    | 0.05    | 0.16         |
|                | <i>p</i> | 0.213        | 0.776        | 0.215        | 0.052        | 0.422  | 0.92    | 0.24         | 0.629   | 0.299   | 0.741   | 0.271        |

Table 11: two-tailed correlations between CRIq, MRIq, MARS-5, SF-12 with its two subscales (PCS=physical component score; MCS=mental component score) and PWB with its subscales (PL=purpose in life; SA=self-acceptance; A=autonomy; EM=environmental mastery; PG=personal growth; PR=positive relations with others) at the baseline (N=53). Significant values are in bold.

In accordance with our expectations, we found positive correlations between CRIq total score and two of the Self-Care subscales: “*Self-care maintenance*” ( $r=0.30$ ,  $p=.005$ ) and “*Self-care monitoring*” ( $r=0.45$ ,  $p<.001$ ). Moreover, these two Self-Care subscales are positively correlated with two indexes of CR: CRIq work (with SC\_MN,  $r=0.30$ ,  $p=.029$ ; with SC\_MO,  $r=0.52$ ,  $p<0.001$ ) and CRIq leisure activities (with SC\_MN,  $r=0.36$ ,  $p=.008$ ; with SC\_MO,  $r=0.32$ ,  $p=0.019$ ). No correlations emerged between self-care behaviors and motor reserve. Any correlation was found between CR, MR and perception of illness, contrary to our hypothesis (Table 12).

|                    |          | CRIq _Tot       | CRIq_S | CRIq_W          | CRIq_LA      | MRIq_% | MRIq_HA | MRIq_W | MRIq_LA | MRIq_PE | MRIq_CA | MRIq_WA |
|--------------------|----------|-----------------|--------|-----------------|--------------|--------|---------|--------|---------|---------|---------|---------|
| <b>SelfCare_MN</b> | <i>r</i> | <b>0.38</b>     | 0.25   | <b>0.3</b>      | <b>0.36</b>  | 0.13   | 0.02    | 0.24   | 0.09    | -0.02   | 0.15    | 0.01    |
|                    | <i>p</i> | <b>0.005</b>    | 0.069  | <b>0.029</b>    | <b>0.008</b> | 0.34   | 0.894   | 0.089  | 0.536   | 0.914   | 0.298   | 0.933   |
| <b>SelfCare_MO</b> | <i>r</i> | <b>0.45</b>     | 0.26   | <b>0.52</b>     | <b>0.32</b>  | 0.01   | -0.11   | 0.13   | 0.11    | -0.11   | 0.21    | -0.08   |
|                    | <i>p</i> | <b>&lt;.001</b> | 0.068  | <b>&lt;.001</b> | <b>0.019</b> | 0.928  | 0.427   | 0.359  | 0.428   | 0.431   | 0.144   | 0.557   |
| <b>SelfCare_MG</b> | <i>r</i> | 0.2             | 0.22   | 0.22            | 0.08         | -0.03  | -0.01   | 0.03   | 0.15    | -0.2    | 0.11    | -0.17   |
|                    | <i>p</i> | 0.143           | 0.118  | 0.109           | 0.549        | 0.823  | 0.961   | 0.825  | 0.298   | 0.149   | 0.225   | <.001   |
| <b>SelfCare_SE</b> | <i>r</i> | 0               | 0.03   | -0.01           | -0.01        | 0.05   | -0.11   | 0.15   | 0.09    | -0.07   | 0.14    | 0.07    |
|                    | <i>p</i> | 0.973           | 0.845  | 0.951           | 0.944        | 0.703  | 0.453   | 0.301  | 0.503   | 0.611   | 0.323   | 0.632   |
| <b>Brief-IPQ</b>   | <i>r</i> | 0.08            | 0.05   | 0.15            | -0.01        | -0.15  | -0.21   | -0.13  | 0.17    | -0.09   | 0.1     | -0.25   |
|                    | <i>p</i> | 0.568           | 0.743  | 0.27            | 0.965        | 0.283  | 0.138   | 0.338  | 0.231   | 0.513   | 0.482   | 0.071   |

Table 12: two-tailed correlations between CRIq, MRIq, Self-Care subscales (MN=maintenance; MO=monitoring; MG=management) and Self-Care Self-Efficacy at the baseline (N=53). Significant values are in bold.

From the paired sample non parametric t-tests, we didn't find any significant differences between the two time points, except for the subscale of “*Self-care\_Monitoring*” ( $W=40.00$ ,  $p=.049$ ; Table 13). In particular, considering mean scores, we can appreciate their improvement during the follow up in almost all variables considered (Table 14), even if not significantly (except for “*Self-care\_Monitoring*”).

|                    |                       | <i>W</i>     | <i>p</i>     |
|--------------------|-----------------------|--------------|--------------|
| <b>MARS-5</b>      | <b>T1_MARS-5</b>      | 31.50        | 0.339        |
| <b>SF_PCS</b>      | <b>T1_SF_PCS</b>      | 105.00       | 0.709        |
| <b>SF_MCS</b>      | <b>T1_SF_MCS</b>      | 113.00       | 0.490        |
| <b>PWB_A</b>       | <b>T1_PWB_A</b>       | 43.50        | 0.592        |
| <b>PWB_EM</b>      | <b>T1_PWB_EM</b>      | 55.50        | 0.874        |
| <b>PWB_PG</b>      | <b>T1_PWB_PG</b>      | 61.50        | 0.491        |
| <b>PWB_PR</b>      | <b>T1_PWB_PR</b>      | 48.00        | 0.182        |
| <b>PWB_PL</b>      | <b>T1_PWB_PL</b>      | 66.00        | 0.938        |
| <b>PWB_SA</b>      | <b>T1_PWB_SA</b>      | 72.00        | 0.849        |
| <b>PWB_Tot</b>     | <b>T1_PWB_Tot</b>     | 64.00        | 0.360        |
| <b>SelfCare_MN</b> | <b>T1_SelfCare_MN</b> | 29.50        | 0.157        |
| <b>SelfCare_MO</b> | <b>T1_SelfCare_MO</b> | <b>40.00</b> | <b>0.049</b> |
| <b>SelfCare_MG</b> | <b>T1_SelfCare_MG</b> | 42.50        | 0.112        |
| <b>SelfCare_SE</b> | <b>T1_SelfCare_SE</b> | 82.50        | 0.913        |
| <b>B-IPQ</b>       | <b>T1_B-IPQ</b>       | 64.00        | 0.219        |

Table 13: Paired sample non parametric t-tests of the main outcomes (MARS-5, SF-12 and PWB), self-care and perception of illness at  $t_0$  and  $t_1$  of the follow-up sample ( $N=19$ ). Significant values are in bold.

|                  | <i>N</i> | <i>Mean</i> | <i>Standard Deviation</i> |
|------------------|----------|-------------|---------------------------|
| <b>MARS-5</b>    | 19       | 22.58       | 2.78                      |
| <b>T1_MARS-5</b> | 19       | 23.05       | 2.70                      |
| <b>SF_PCS</b>    | 19       | 42.97       | 8.86                      |
| <b>T1_SF-PCS</b> | 19       | 42.60       | 10.91                     |
| <b>SF_MCS</b>    | 19       | 51.13       | 9.86                      |
| <b>T1_SF-MCS</b> | 19       | 50.45       | 9.68                      |

|                        |    |       |       |
|------------------------|----|-------|-------|
| <b>PWB_A</b>           | 19 | 14.00 | 3.40  |
| <b>T1_PWB-A</b>        | 19 | 14.42 | 3.34  |
| <b>PWB_EM</b>          | 19 | 13.16 | 2.91  |
| <b>T1_PWB-EM</b>       | 19 | 12.84 | 2.95  |
| <b>PWB_PG</b>          | 19 | 13.00 | 4.10  |
| <b>T1_PWB-PG</b>       | 19 | 13.47 | 3.39  |
| <b>PWB_PR</b>          | 19 | 13.58 | 3.66  |
| <b>T1_PWB-PR</b>       | 19 | 14.53 | 2.48  |
| <b>PWB_PL</b>          | 19 | 12.05 | 3.32  |
| <b>T1_PWB-PL</b>       | 19 | 12.11 | 3.20  |
| <b>PWB_SA</b>          | 19 | 12.58 | 3.39  |
| <b>T1_PWB-SA</b>       | 19 | 12.74 | 3.14  |
| <b>PWB_Tot</b>         | 19 | 78.37 | 14.07 |
| <b>T1_PWB-Tot</b>      | 19 | 80.11 | 11.98 |
| <b>SelfCare_MN</b>     | 19 | 70.73 | 14.70 |
| <b>T1_Self-Care_MN</b> | 19 | 74.67 | 12.75 |
| <b>SelfCare_MO</b>     | 18 | 62.22 | 19.27 |
| <b>T1_Self-Care_MO</b> | 18 | 69.11 | 18.85 |
| <b>SelfCare_MG</b>     | 19 | 53.05 | 15.48 |
| <b>T1_Self-Care_MG</b> | 19 | 61.05 | 17.33 |
| <b>SelfCare_SE</b>     | 19 | 70.39 | 16.86 |
| <b>T1_Self-Care_SE</b> | 19 | 71.18 | 16.49 |
| <b>B-IPQ</b>           | 19 | 47.95 | 12.84 |
| <b>T1_B-IPQ</b>        | 19 | 49.42 | 11.39 |

*Table 14: Descriptive statistics of all measures at t0 and t1 of the follow-up sample (N=19).*

Contrary to our expectations, linear regression analysis didn't show a significant impact of CR on the improvements highlighted. However, in line with our hypothesis, we found a significant impact of MR on "Self-care\_Maintenance" ( $R^2=76\%$ ,  $p=.010$ ) (Table 15).

**Overall Model Test**

| Model | R    | R <sup>2</sup> | Adjusted R <sup>2</sup> | F    | df1 | df2 | p            |
|-------|------|----------------|-------------------------|------|-----|-----|--------------|
| 1     | 0.87 | 0.76           | 0.60                    | 4.89 | 7   | 11  | <b>0.010</b> |

| Predictor | Estimate | SE   | t     | p            | Stand. Estimate |
|-----------|----------|------|-------|--------------|-----------------|
| Intercept | -18.48   | 7.99 | -2.31 | 0.041        |                 |
| MRIq_HA   | 2.42     | 0.68 | 3.57  | <b>0.004</b> | 5.31            |
| MRIq_W    | 3.37     | 0.86 | 3.92  | <b>0.002</b> | 4.00            |
| MRIq_LA   | 3.24     | 0.74 | 4.40  | <b>0.001</b> | 2.86            |
| MRIq_PE   | 2.73     | 0.64 | 4.28  | <b>0.001</b> | 4.01            |
| MRIq_CA   | 2.89     | 0.74 | 3.91  | <b>0.002</b> | 3.35            |
| MRIq_WA   | 2.43     | 0.72 | 3.38  | <b>0.006</b> | 3.83            |

*Table 15: Linear regression analysis considering MR as the independent variable and “Self-Care\_Maintenance” used as the dependent variable.*

### 3.4.5. Discussion

The present study firstly aimed to explore the relationship between CR, MR, adherence behaviors and physical and PWB in patients affected by CVDs.

Thanks to the highlighted results, it emerged that higher total CR is associated with greater purpose in life, which is one of the six dimensions of PWB reported by Ryff (1995). The same dimension is also positively associated with two indices of CR, i.e. work and leisure activities. According to these results, people who have worked for several years and who carried out cognitively demanding jobs, as well as being engaged in multiple activities in their free time, develop greater goals in life and a certain sense of directedness, feel there is meaning to present and past life, hold beliefs that give life purpose and own aims and objectives for living (Ryff, 1995). This could be explained considering the amount of cognitive skills the latter processes require: having goals in life requires the ability to self-analyze and to evaluate oneself in order to develop aims and objectives that are

consistent with one's abilities and possibilities. Similarly, being involved in demanding work activities and leisure activities which are different from each other, require and allow one to develop multiple skills to be adapted to the environmental demands. On the contrary, the other CR indicator, years of education, was not significantly associated with the same PWB's dimension. However, in contrast to our expectations, it is negatively associated with the dimension related to self-acceptance, indicating that people with a high level of education also feel dissatisfied with themselves, disappointed with what has occurred in past life and troubled about certain personal qualities (Ryff, 1995). These results could be justified considering that people who devote themselves more to study, may also represent the more perfectionist ones. Perfectionism, in fact, represents a personality trait characterized by a relentless pursuit for high standards of performance, tendencies to measure one's self-worth solely on achievement and overly critical self-evaluations (Flett & Hewitt, 2002; Stoeber, 2018), leading people to feel constantly in competition with themselves and never satisfied with themselves. However, as this goes beyond the scope of the present study, it won't be further discussed.

Relating to MR, instead, two indices have shown to be positively associated with the self-acceptance dimension of PWB: walking and workplace activities. It follows our hypotheses, confirming that a greater amount of physical activity in multiple life contexts contribute to build a motor reserve over the years (Pucci et al., 2024), which may influence individuals' PWB in some of its dimensions. Contrary to our expectations, we didn't find any significant association between CR, MR, general health status (including physical well-being) and adherence to treatment. It may be partially explained considering that these are preliminary results and that both sampling and follow-ups collection are being carried out. These are data collected after six months and it couldn't be enough time to see significant changes in the way that patients adhere to the treatment and therefore to a different perception of general health. It is possible that significant results may rise after more time and with a greater number of subjects involved.

Secondly, our work aimed to explore and try to understand the relationship that CR and MR may have with perception of illness and with self-care behaviors, two crucial factors involved in the treatment adherence (Weinman et al., 2000; Akut et al., 2022). Contrary to our hypothesis, we didn't find any significant correlation between CR, MR and illness perception. The lack of studies that directly link CR, MR and perception of illness makes it difficult to justify these results. According to the *Self Regulatory Model* provided by Leventhal and colleagues (1984), the concept requires multiple cognitive processes that start with forming mental representations of the disease up to evaluate the effectiveness of behaviors implemented to cope with it, as well as providing continuous feedback between representations and evaluation processes. This should be linked to

great cognitive faculties. The absence of significant results may thus be due to the small number of participants included in the study, as well as to the multidimensional nature of CR and MR. As we previously discussed in the second chapter, CR measurement still doesn't allow literature to consider the concept in full, as different proxies are quantified between studies; regarding MR, instead, it is a relatively new concept and its proxies are being analyzed. This limits the construction and quantification of the two concepts which, however, due to their multidimensional and dynamic nature, are perhaps impossible to “objectify”.

However, in line with our expectations, the study showed significant associations between total CR, work and leisure activities and the Self-care dimensions of *maintenance* and *monitoring*. According to these results, people with higher CR (in particular those with many years of work behind them and involved in cognitively stimulating jobs and leisure activities) implement more behaviors focused on maintaining physical and emotional stability and on preventing an exacerbation of the clinical condition, as well as observing oneself more for changes in signs and symptoms, so as to early detect a health change (Riegel et al., 2017). As we already discussed for illness perception, also the faculty of maintaining and monitoring one's state of health require certain cognitive abilities; they are certainly developed through the life course by involving in cognitively stimulating situations, such as work demands and challenging leisure activities.

Finally, considering the comparison of all measures between baseline and the follow up after six months, we only found a significant difference in the self-care *monitoring*. According to this result, it emerged that people affected by CVDs tended to monitor themselves and observe for changes in signs and symptoms more over time. In addition, even if other measures didn't reach the significance, we can qualitatively appreciate improvements in almost all measures over time after six months. Undoubtedly it is necessary to continue collecting follows up to see how these measures vary over time and to explore if CR, MR or both have an impact or a potential predictive role on any change. Starting from the improvement in self-care *monitoring*, contrary to our expectation, regression analysis showed that neither CR nor MR predicted such improvements. However, we found that MR with all its indexes significantly predicted improvements in *self-maintenance* behaviors. According to Riegel and colleagues (2012; 2017), *self-maintenance* refers to behaviors implemented to maintain physical and emotional stability and translates into concrete behaviors and the adoption of healthy lifestyle (i.e., smoking cessation, eating healthy food, taking medications as prescribed and so on). It is quite clear the link between this trend and a greater MR: people who have done more physical exercise and led a more active lifestyle in different contexts (as we can see from the MR indicators collected with MRIq by Pucci and colleagues, 2024), has also preliminary implemented a series of attitudes focused on preserving a good health. In case of a

full-blown disease or event considered in the present study, those are the same persons who act to prevent an exacerbation of the clinical condition (Riegel et al., 2017).

Some limitations in the present study should be considered. The first potential limitation includes the number of drops out during the study due to patients' impossibility to complete all measures required or their unavailability; it took to consider about half of the initial sample for the follow-up measures (t1). To overcome this limitation, the enrolment procedure in the clinical contexts could be adjusted collecting the follow-up measures in conjunction with cardiology follow-up visits. However, to be able to follow this procedure, it would be necessary to consider homogeneous pathologies to have check-visits within the same timeframes. Following this line, the second potential limitation derives from the consideration of different CVDs in this study: the 58% of the sample suffered from coronary heart disease, the 21% of arrhythmia, the 11% of cardiomyopathy, the 8% of valve dysfunctions and only 2% of patent foramen ovale. It would be recommended to consider cardiovascular disorders which have a greater impact on the country's mortality first, such as ischemic heart disease (that is part of the coronary heart diseases), responsible for 9.9% of all deaths in Italy (ISS, 10/31/2022). Focusing on homogeneous pathologies will help to bring to more consistent results and so developing specific guidelines for each pathology.

Another potential limitation has to do with the conceptualization and measure of CR and MR. As we discussed in the previous chapter regarding CR and as we already discussed also for MR, they are two concepts whose multidimensional and dynamic nature make it difficult to objectify, limiting consensus results among researchers.

A further potential limitation could be related to the number of participants; the little sample size (n=53) may have affected the generalization and applicability of the results, as we preliminary discussed for the study 1.

Lastly, given the longitudinal nature of the study, considering a unique follow up after six months may have been limiting; it might be a short time which is not enough to see real changes over time, both in terms of well-being (cognitive and psychological) and in terms of practical behaviors in everyday life (self-care behaviors). However, the study is still ongoing and along with the increase of the number of participants, the collection of another follow up after 12 months will help to achieve more consistent results.

### 3.4.6. Conclusions and practical implications

The present study found an effective relation between CR, MR, PWB (only for some of its dimensions provided by Ryff, 1995) and self-care behaviors. In particular, global CR, work and leisure activities were positively correlated with purpose in life, highlighting that people who have worked for several years, who carried out cognitively demanding jobs and have engaged in multiple activities in their free time developed an amount of cognitive skills that allow to build greater goals in life, a greater sense of directedness and own aims and objectives for living. The same indexes have also been positively correlated with self-care maintenance and monitoring, indicating the implementation of behaviors focused on maintaining physical and emotional stability and observing oneself to detect any health change. CR index related to education, instead, was negatively associated with self-acceptance (another dimension of PWB), indicating a possible more marked perfectionist trait in those people who devote themselves more to study.

Regarding MR, the study showed that only two indicators were positively associated with self-acceptance; in particular, those who walk more and who are engaged in workplace activities requiring more energy expenditure seem to accept themselves more. Contrary to our expectations, any significant association between CR, MR, general health status, adherence to treatment and perception of illness have emerged.

Considering longitudinal results, self-care monitoring is the only variable significantly predicted by MR, indicating that carrying out physical exercise and leading a more active lifestyle in different contexts bring people to maintain their physical and emotional stability, implementing self-care behaviors to early detect a health change.

Future longitudinal research would be fundamental to continue providing consistent results about the role of CR and MR on adherence to treatment and on the well-being sphere of patients suffering from CVDs, as well as to better understand how perception of illness and self-care behaviors act in this scenario. A crucial first step could be to consider homogeneous samples: cardiovascular disorders with a greater impact on the country's mortality (e.g., ischemic heart disease) are worthy of further study, helping the health context to reach consistent results and developing specific guidelines for each pathology. It is crucial to consider a preventive approach on health that tries to better understand the role of our "cognitive and physical luggage" on the development and progression of CVDs, being both (CR and MR) two dynamic constructs that are potentially modifiable throughout the entire life span. Consistent knowledge on these two dynamic constructs should be fundamental to bring benefits in clinical practice, mainly in terms of primary and secondary, but also tertiary, prevention interventions. Lastly, in the panorama of heart diseases,

gaining a greater understanding of factors that may impact variables such as adherence to drug therapy and self-care behaviors, could be a huge help to the health context in the management of chronic patients.

## **General conclusions and practical implications**

The overall aim of the present dissertation was to explore, first, the relationships between CR, cognitive and psychological well-being in healthy older adults, with a particular focus on a specific CR index, which is divergent thinking; secondly, to explore the relationships between CR, MR, adherence to treatment and the general health status of clinical samples affected by CVDs.

As reported in the first chapter, CR is a multidimensional and dynamic construct referring to the brain's ability to use alternate paradigms to solve problems when the standard approach is no longer available (Stern, 2012), denoting a cumulative improvement in neural resources resulting from the interaction of innate differences and environmental factors (Cabeza et al., 2018). It emerged that individuals are able to optimize their performances through differential recruitment of brain networks and cognitive strategies, demonstrating that two individuals can differ in the way they react to a brain injury or a neurodegenerative disease such as dementia (Chicherio et al., 2012).

Traditionally, attempts to operationalize CR have been made through the measurement of different proxies; nowadays, the most used are education, work and leisure activities (Nucci et al., 2012), even if homogeneity is far from being achieved and experimental designs considering static proxies (i.e., education and IQ) and dynamic ones (i.e., leisure activities and social support) need to be integrated in CR literature. Despite this important limitation, literature agrees on the protective role that CR plays both on the cognitive (Cabeza et al., 2018) and psychological (Ihle et al. 2017; 2020) sphere.

However, in the course of time, a lot of proxies have been considered; one of them is DT, considered a measure of the individuals' creative potential (Runco & Acar, 2012). The association between DT and cognitive functioning has been highly explored and continues to be considered attractive especially due to DT tasks' ease of administration, representing approximately 51% of creativity assessments in neuroscience research (Benedek et al., 2019).

In line with these considerations and with the literature overviewed in the second chapter, results from the first experimental study conducted in this work are quite consistent. Interventions on DT abilities have brought positive effects on the mood state, on PWB and on the cognitive functioning of the healthy sample. In particular, DT abilities have proven to have an impact on anxiety, stress and on a greater perception of one's emotional skills, highlighting a possible emotion-cognition interplay that would be useful to deepen in future studies. Moreover, DT abilities resulted in better cognitive performances, in particular regarding those executive processes implied in DT abilities (such as attentional abilities and processing speed). However, CR didn't show any impact on the

sphere of well-being, while a predictive role of CR on cognitive improvements after the DT training has been found.

These results respond partially to our first general aim, confirming the association between DT abilities (in particular between executive skills) and a greater CR. However, the association between CR and both cognitive and psychological sphere is far from being clearly understood, especially concerning PWB which includes different dimensions (as postulated by Ryff, 1995), thus being differently influenced by CR. It would be worthwhile to conduct studies in the future that will focus on the impact of CR on such PWB dimensions, in particular to better clarify which proxies of CR can contribute a better PWB perception (and in which dimension) in the ageing perspective.

Undoubtedly, this study brings important practical implications, sharing light on the importance of continuing to improve CR during the lifespan, working on its proxies such as DT, representing a possible cost-effective method to prevent or delay symptoms of mild cognitive disorder or dementia. It may consequently act in a preventive way to further protect our brain from a physiological cognitive decline or any brain damage. However, further investigation is needed in the multidimensional field of PWB during the life-span.

The second general aim of the present work wanted to better explore literature about CR and PWB, and consequently the QoL, of patients affected by CVDs. Moreover, an attention to the recent construct of MR deserves to be reported in this field.

Since CVDs are responsible for 44% of all deaths in our country (ischemic heart disease is the leading cause of death in Italy, being responsible for 9.9% of all deaths) and given their potential consequences both on psychological (Ladwig et al., 2022) and cognitive (Ihle et al., 2018) levels, an in-deepen study and attention to the multiple effects they can bring to patients' QoL and PWB is needed. From the state-of-the-art review reported in the third chapter (Giannì et al., 2024), it emerged that in the literature there are few and inconsistent studies about the link between CR, MR and QoL in this cohort of patients; moreover, in the study considered, there is quite heterogeneity in quantifying CR, as in some of them only individual CR proxies are considered (i.e., education or occupation), while different proxies' combinations have been conceived in others. Regarding MR, most of the evidence is focused on the effects that physical activity programs have on patients' QoL; thus, the influence of daily physical activity accumulating over time from a preventative point of view has been neglected. Further investigation in this field is needed to bring benefits in the clinical practice, mainly in terms of primary and secondary, but also tertiary, prevention interventions.

In the end, to better clarify the relationship between these variables, the last study involved in the present work, which has a longitudinal design, highlighted an effective relation between CR, MR,

PWB (only for some of its dimensions provided by Ryff, 1995) and self-care behaviors. Regarding MR, the study confirmed partially our expectations showing an association with a single dimension of PWB (self-acceptance). Any significant association between CR, MR, general health status, adherence to treatment and perception of illness have emerged, suggesting the need for further investigation including all these constructs. From the longitudinal results, which are still being collected, self-care behaviors seem to be predicted by MR, indicating that carrying out physical exercise and leading a more active lifestyle in different contexts bring people to maintain their physical and emotional stability, implementing self-care behaviors to early detect a health change. It may help clinical practise by paving the way for an update of the guidelines on CVDs, considering that the amount of physical activity carried out regularly over time and in different contexts (Pucci et al., 2024) and the amount of cognitive stimulating activities can contribute to monitor, maintain and manage a better health status.

Results emerged from the present dissertations are far from being uniform, but they try to lead the way in a field that is constantly developing and that includes constructs, some of them recent, that have a multidimensional and dynamic nature. However, considering that CR and MR can always be expanded and potentiated during the life course, preventive interventions to enhance the two types of reserve should be fundamental to bring benefits in clinical practice, supporting CVD patients' cognitive and psychological resources but also providing specific guidelines to help the health context managing the chronic patient. Providing patients with more resources during the lifetime, CR and MR could bring to some beneficial effects also on perception of a better QoL and PWB, thus contributing to other health-related dimensions such as adherence to therapies and self-care-behaviors. This shouldn't be underestimated especially if we consider the mortality that cardiovascular diseases bring to our country.



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## APPENDICES

## List of figures

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Article

## The Role of Cognition in Divergent Thinking: Implications for Successful Aging

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**Abstract:** Promoting active and successful aging has become crucial to improve quality of life in later adulthood and reduce the impact of cognitive decline. Increasing evidence suggested that the ability to think creatively (e.g., via divergent thinking), similar to cognitive reserve, could represent a beneficial factor against the negative effects of aging. However, there is still little evidence investigating the relationships between divergent thinking, cognitive functions, and cognitive reserve in late adulthood. The present study explored these relationships in a sample of 98 individuals ranging from 61 to 88 years old (mean age:  $72.44 \pm 6.35$ ). Results showed that visual, but not verbal, divergent thinking was affected by aging. Interestingly, visual divergent thinking performance was predicted by both the cognitive component of crystallized intelligence and cognitive reserve. Only the crystallized component of intelligence was found to mediate the aging effect on visual divergent thinking performance. These results suggest that in later adulthood a potential shift strategy to prior knowledge and semantic components over executive and control components of cognition could underlie a preserved ability to think divergently and, plausibly, creatively. Limitations of the study and implications for successful aging are discussed.

**Keywords:** creativity; divergent thinking; executive functions; crystallized intelligence; cognitive reserve; cognition; aging

### 1. Introduction

As life expectancy has increased, it has become crucial to sustain and promote active aging [1]. Several factors contribute to active aging, and, among them, cognitive functioning plays a pivotal role in supporting everyday life duties and preserving autonomy and personal growth [2,3]. However, there is evidence that some cognitive abilities are more susceptible than others to life changes and to the consequent physiological decline [4]. For instance, cognitive functions that pertain to the crystallized intelligence domain are mainly preserved, while cognitive mechanisms associated with fluid intelligence and supporting cognitive control—like executive functions (EFs)—usually are more susceptible to decline [1,4–8]. Cognitive decline is characterized by structural and functional changes

Article

## Can Creativity and Cognitive Reserve Predict Psychological Well-Being in Older Adults? The Role of Divergent Thinking in Healthy Aging

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**Abstract:** The maintenance of psychological well-being (PWB) in the older adult population is a pivotal goal for our rapidly aging society. PWB is a multicomponent construct that can be influenced by several factors in the lifespan. The beneficial role of divergent thinking (DT) and cognitive reserve (CR) in sustaining older subjects' PWB has been scarcely investigated so far. The present study aims to investigate the relationships between DT, CR, and PWB in a sample of 121 healthy older adults (61 females; M age: 73.39 ± 6.66 years; M education: 11.33 ± 4.81 years). The results highlight that better DT performance predicts higher CR, which mediates an indirect positive effect of DT on emotional competence, one of the PWB factors. It follows that DT and CR can be considered protective factors in aging, and their effects go beyond cognitive functioning, revealing a positive effect even on some PWB components. The practical implications regarding targeted health interventions for prevention in the older adult population to support well-being and promote healthy aging are discussed.

**Keywords:** aging; cognitive reserve; divergent thinking; well-being; emotional competence; health

### 1. Introduction

#### 1.1. Psychological Well-Being in Aging

Life expectancy has consistently grown over the years [1], and the number of older adults continues to grow worldwide [2]. Research has revealed that psychological well-being (PWB) plays a key role in older adults' health, both reducing the risk of developing chronic diseases (lung diseases, cognitive decline, cardiovascular diseases, etc.) and promoting longevity [3–7]. Therefore, international organizations have stressed the need to promote mental health and psychological well-being in all stages of life [8–10].

A few decades ago, Carol Ryff [11] defined PWB as a multidimensional construct based on the eudaimonic component, which concerns personal development and growth, as the realization of individual potential [12]. Conversely, the hedonic dimension conceives PWB as the personal pleasure linked to positive sensations and emotions [13].

Review

## A State-of-the-Art Review on the Role of Cognitive and Motor Reserve on Quality of Life: A Focus on Cardiovascular Patients in a Lifespan Perspective

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**Abstract:** Cardiovascular diseases (CVDs) reflect a huge and diversified condition that influences patient quality of life (QoL) both in the physical and mental aspects, especially in older adults who often present comorbidities and may be affected by cognitive decline. The concept of cognitive reserve (CR), which is built through life course experiences, has widely been considered a protective factor against cognitive decline, while the results of QoL in the field of CVDs are still controversial. In particular, there is a lack of evidence that explicitly explores the effects of CR on the QoL in CVD cases since studies have considered only single CR proxies (e.g., education) or specific cardiovascular conditions. Moreover, none of them have considered the motor reserve (MR), another recent concept that considers the amount of physical activity carried out during a lifespan. Its potential role in preventing age-related diseases has been observed, but more clarification is needed given the importance of the physical component in CVDs. The present state-of-the-art review aims to (i) examine how the literature conceives CR and its proxies in CVDs relating to QoL and (ii) integrate the concept of MR in this framework. Implications for clinical practice will also be discussed.

**Keywords:** cognitive reserve; motor reserve; cardiovascular diseases; quality of life; aging



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### 1. Introduction

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels that include conditions such as coronary heart disease, congenital heart disease or acute events like heart attacks and strokes. CVDs represent the leading cause of mortality worldwide, with an estimated 17.9 million deaths recorded in 2021 [1]. Patients affected by CVDs have implications both on their physical and emotional sphere; they experience physical symptoms such as fatigue, dyspnea or chest pain, which automatically impacts their emotional and social well-being, thus bringing a significant impairment in their quality of life (QoL) [2]. QoL is defined as “a broad-ranging concept affected in a complex way by the person’s physical health, psychological state, level of independence, social relationships and their relationship to salient features of their environment” by the World Health Organization [1]; another dimension closely linked to QoL but focused on health, which is widely considered in the field of CVDs, is health-related quality of life (HRQoL). This is defined as the individual’s functioning in life concerning their perceived well-being in physical, mental and social domains of health [3].

Currently, a great deal of effort is being made to understand how the burden of CVDs can be reduced; in fact, as the population ages, the global CVD burden is continuing to increase, especially among older adults due to their older age, multiple comorbidities and frailty [4]. It seems that a partial solution lies in including CVD management interventions