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Cognitive Reserve in Language
How exposure to learning experiences influences language processing and pragmatic communication in healthy aging and in neurodegenerative disorders

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Summary

Cognitive Reserve (CR) can be defined as a repository of cognitive abilities and learnings, which increase the complexity of brain networks and in turn become protective for preventing age-related changes and brain pathologies. Since human language is one of the most studied cognitive domains, the effect of CR on language can provide new perspectives on understanding how CR influences cognition. Previous studies have shown that high CR is correlated with language proficiency as measured with vocabulary size or verbal analogy. However, to date, it is not clear whether the effect of CR on language is homogenous across psycholinguistic characteristics. This project mainly aimed at investigating the CR effect on language processes (i.e., lexical access, semantic association and reading processes) and on pragmatic abilities (i.e., the ability to communicate in different contexts, through detecting and manifesting communicative intentions). Furthermore, one of the pragmatic tasks used in this project was transformed from its original paper-and-pencil version into a user-friendly computer application, for a more agile examination of pragmatic skills in clinical contexts.

This project includes five studies. Study 1 involved 65 healthy older adults whose performance was analyzed using a digital tool, which I devised, that combines three language tasks (Lexical Decision, Semantic Matching and Sentence Reading). The aim was checking the effect of CR on performance while varying lexical frequency (high vs. low) and lexical semantics (concrete vs. abstract words), and on reading times of sentences with either syntactic or semantic violations. CR predicted the overall language performance, with stronger effects on low-frequency and abstract words compared to high-frequency and concrete words. CR influenced reading times in both syntactic and semantic violations, but at different points in the time-course of sentence processing. These findings suggest that abstract words and low-frequency words can be well preserved by maintaining an active lifestyle in aging, and that high CR not only implicates higher knowledge of grammar rules but also better monitoring of these rules "on-line" during reading.

Study 2 and Study 3 are strictly connected to each other. Study 2 explored the retrieval of proper names and the sensitivity of this lexical category to the modulatory effect of CR in patients with dementia. Thirty-two elderly patients with dementia were matched to healthy controls. All participants were administered the Montreal Cognitive Assessment (MoCA) to measure their global cognitive performance, a paper-and-pencil Famous Face Naming test to assess proper name retrieval, and the Cognitive Reserve Index (CRI) questionnaire. Findings showed that naming proper names was independent from CR possibly due to their lexical nature, which lies in a poor semantic connection between proper names and their bearers. Study 3 aimed at examining the effect of CR not only on proper names, but also on names with other semantic features (logo names and common nouns). To do this, I used a new digital tool which I developed, suitable for finer analyses of behavioral outcomes. The hypothesis was that CR contributed more in retrieving common nouns and logo names, which are highly semantically interconnected, than retrieving proper names, which are pure referring expressions. Forty-six Italian healthy older adults were tested. The results showed that participants were significantly faster and more accurate in name retrieval when CR was high. As regards accuracy, the effect of CR was lower for proper names than for common nouns and logo names, which did not differ from each other. These findings suggest that high CR may help context-driven information

processing. Availability of context information seemed therefore a very interesting topic to explore in association with the possible effects of CR.
A crucial component for the efficient use of language is the “context” where a message occurs, which directly falls into the pragmatic domain. Different neurological diseases can affect the ‘pragmatic system’ at different levels, interfering with ability to communicate in varying contexts and with different interlocutors, but, to my knowledge, no study to date has investigated the pragmatic profile of patients with Parkinson’s Disease (PD) and how CR can relate to this profile. This was the issue of Study 4, which showed that CR measures were highly associated with pragmatic comprehension abilities and weakly associated with pragmatic production abilities. which were correlated with the severity of patients’ motor deficit.
Assessment of pragmatic abilities is important in clinical contexts. In the traditional neuropsychological assessments, however, pragmatic traits of a patient are typically assessed qualitatively through an informal conversation. Study 5 aimed at developing a user-friendly and agile software application by converting a structured paper-and-pencil task for pragmatic assessment. The task lasts 5 minutes. In the paper-and-pencil traditional form, the examiner has to evaluate twenty-two pragmatic discourse features, trying to simultaneously count their frequency of occurrence. Thus, in its paper-and-pencil form, the administration of this task can be very demanding for the clinician. Study 5 allowed to create a digital Interview task which optimizes time and resources of administration. To my knowledge, this is the first attempt to develop the digital version of a highly professional tool for the evaluation of several dimensions of pragmatic and paralinguistic features of discourse.

CHAPTER 1. GENERAL INTRODUCTION

1.1 The concept of 'Cognitive Reserve'

Every person has a certain level of Cognitive Reserve (CR), which refers to all the learnings acquired throughout the lifespan. The type of learnings which makes up CR has often been referred to a person's 'formal education', which is a very important component of CR, but not the only one. Acquiring competences at work, being constant in a hobby or physical activity may contribute to the whole amount of reserve. CR can thus be interpreted as a repository of cognitive abilities and learnings, which increase the complexity of the brain networks and in turn become protective in preventing age-related changes or brain pathologies. CR refers to exposure to stimulating activities able to optimize neural connectivity and to the development of cognitive strategies (and behavioral outcomes) adaptive to changes in the environment or in the brain itself. The wording *cognitive reserve* responds to the need to identify and understand the mechanisms of brain resilience. Figure 1.1 presents how CR can mediate between age-related pathology and its clinical expression, and shows that the pathology has to be more advanced before the cognitive functioning of people with higher CR is affected, thus delaying the manifestation of the disease. This graphical representation shows also that once the cognitive decline has begun it is more rapid in a person with higher CR.

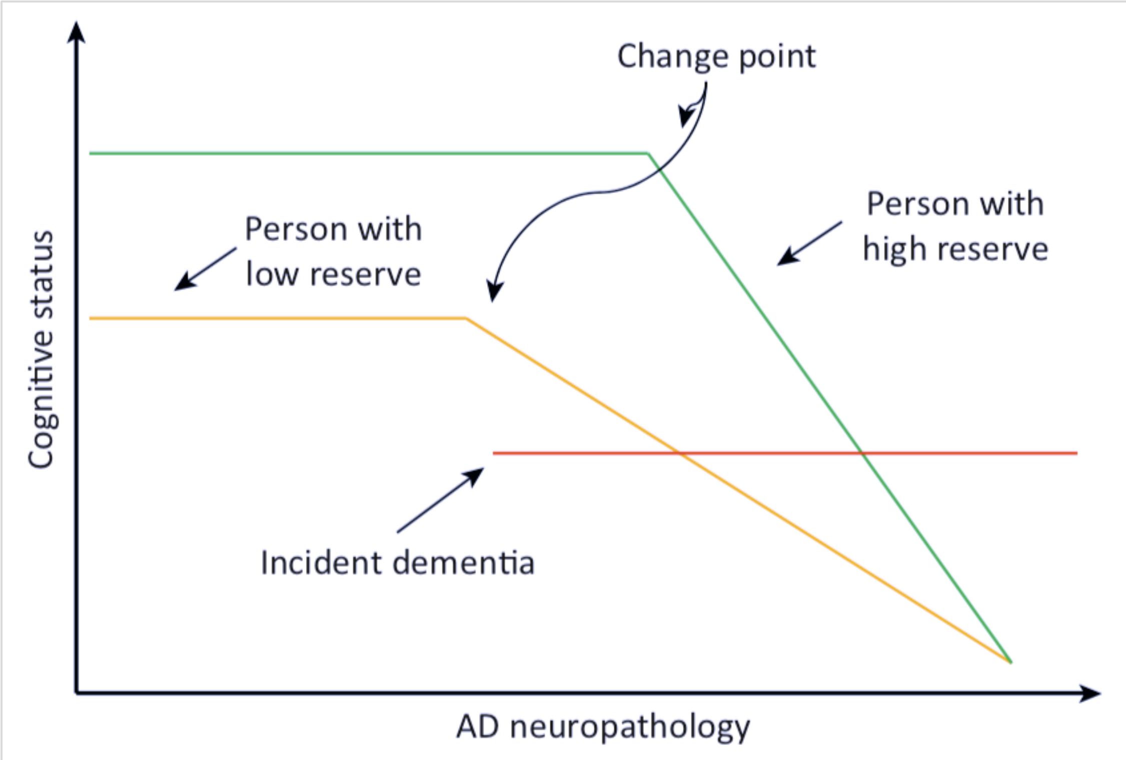

Figure 1.1 CR mediation between Alzheimer's Disease (AD) and its clinical expression (from (Barulli & Stern, 2013). Reported on the x-axis is the age-related brain pathology (Alzheimer's type Dementia, AD) which slowly increases over time. On the y-axis the cognitive functioning.

Research topics referring to CR have been of great interest for years and today a great amount of literature is available on the topic. However, the idea of a reserve that helps to flexibly adapt to brain changes took some years to be settled. Between the late 19th and the early 20th century, the most prominent theories about brain functioning came from histological studies describing the nervous pathways as being 'fixed and immutable in the adult brain' where 'everything may die, nothing may be regenerated' (see Colucci-D'Amato, Bonavita, & Porzio, 2006). A number of studies were necessary to overcome this stagnant view, and only in the late 1950s – early 1960s the belief of an 'immutable brain' was replaced by the evidence of a brain that is constantly shaped by experience. Through neurochemical and neuroanatomical experiments on rats, Rosenzweig and his colleagues showed that those that had been living for a certain time in enriched environments (i.e., interacting with other rats and with an array of tools at their disposal) showed lower cortex cholinesterase activity, higher subcortical activity, greater cerebral cortex weight, and greater total brain cholinesterase activity, compared to those who had lived in impoverished environments (i.e., deprived of activities and 'social' interactions) (see Krech, Rosenzweig, & Bennett, 1960; Rosenzweig, Krech, Bennett, & Diamond, 1962). These findings allowed to revolutionize the idea of an immutable brain, leading to scientific advances towards the concept of a 'plastic brain'. Several studies followed (on both animal and human subjects) to test the hypotheses that keeping the cognitive system active over the lifespan generates resources that are especially useful in aging.

In the 1970s, researchers have put more and more efforts on studying *how* individuals get old and *why* individuals are able to reach a very healthy aging status while others are not. In those years, the concept of 'successful aging' progressively gained relevance in research, together with concepts like 'longevity', 'life satisfaction', and 'socio-economic status' (e.g., Blazer & Houpt, 1979; Havighurst, 1973; Palmore, 1979). Researchers were seeking new preventive techniques for detecting early sings of dementia (Cooper & Bickel, 1984; Gurland, 1981), and cognitive screening adjustments were increasingly based on years of education, as an indicator of brain plasticity (Anthony, Niaz, Von Korff, & Folstein, 1982; Kittner et al., 1986).

In the late 1980s, the role of education in the screening of dementia was better delineated through a series of studies indicating that low education (similarly to age and gender), represents a risk factor *per se* for dementia as the result of a "deprivation in early life" (e.g., Katzman et al., 1989; Katzman et al., 1988; Zhang et al., 1990). Brain changes mediated by education actually consist in synaptic changes at level of neurotransmitters, interneuron modulation, re-generation of synapsis, and re-arrangement of brain connections (Jung & Herms, 2014). Scientific interest in the fact that accumulating learnings results in human brain resilience grew rapidly from Katzman and colleagues' (1988) observations and interpretations. The authors analyzed 137 older adults (mean = 85.5 years old) post-mortem and hypothesized the presence of neuronal reserve in a specific sub-group of subjects who had spared mental status but histological brain changes of the Alzheimer's type. The existence of a neural reserve was supported by the fact that the brains of these subjects was heavier, which suggested that they either had less brain atrophy than normally found in the very elderly, or that they started with more neurons and larger brains (Katzman et al., 1988).

Yaakov Stern and his colleagues (1992) observed three groups of patients with dementia with different degrees of education (i.e., less than 12 years; high school graduates, at least 12 years; and greater than high school, up to 24 years) and found high prevalence of dementia in persons with fewer years of education, putting forward the idea of education as protective factor against dementia. Their study showed advanced brain impairment in persons with higher education, as if education could hide the manifestation of the disease by delaying its onset.

Another very famous longitudinal study about resilience and age-related pathology is the "Nun Study of Aging and Alzheimer's Disease", started in 1986 by David Snowdon and his colleagues. The study was realized thanks to 678 Catholic sisters aged between 75 and 107 who were repeatedly tested in a longitudinal study, whose findings were published at the end of 1990s – early 2000s (e.g., Snowdon 1997, 2003). The authors showed that the clinical consequences of neuropathological changes partially depended on location, type and amount of lesions and that they were also strongly associated with a highly dynamic life-style. An example of that was a sister who, despite her genetic predisposition to Alzheimer's Disease and an abundance of Alzheimer's Disease lesions in the neocortex, possessed a remarkably intact global cognitive profile, preserved daily living abilities (e.g., walking, dressing, and feeding), instrumental abilities, and also a self-rate of self-care capacity considered as "excellent." (Snowdon, 2003). These findings were presented whilst the meaning of CR was gaining clarity in research, so they were interpreted along with the definition of CR as reflecting the brain capacity of resisting the expression of symptoms of AD (Stern, 2002). They also remarkably shed light on the idea that CR is not only conveyed by education, but it derives from exposure to a multitude of different life activities/experiences. Furthermore, the abovementioned study made by Snowdon showed that the sisters who gained more advantages from lifetime attitudes where the ones who not only used to have social and physical activities in adulthood but also in the later stages of life.

Later, White and colleagues (1994) demonstrated how not only education but also occupational attainments play a crucial role in the detection of dementia. Thus, they measured the degree of effort required in working activities, and grouped occupations according to the educational level required for a given job. They proposed the following classification: l = professional, technical, and clerical occupations; 2 = managers, administrators, and farm managers; 3 = housewives; 4 = craftsmen, kindred workers, farmers -owners and tenants-, and farm laborers; 5 = equipment operators, laborers -except farm-, domestics. The results of their study indicated that occupations requiring low education and low education itself were both independent predictors of cognitive decline, as controlled for age, stroke, and gender.

By this time, the idea of education as unique proxy of CR had been surpassed by the evidence that CR included activities carried out/experiences made outside formal education and occupational attainments, that is, leisure activities (Snowdon et al., 1996; Snowdon, 1997; Stern et al., 1995; Stern, Gurland, Stern, Gurland, & Tatemichi, 1994). Scarmeas and Stern conducted a study in which 1,772 healthy individuals, aged 65 years and older, were assessed through a longitudinal study with follow-ups up to 7 years. They considered as leisure activities: hobbies (e.g., knitting, or music), physical activities (e.g., walking, excursions or sports), social activities (e.g., visiting friends, being visited by relatives or friends), going to the cinema or the restaurant, reading activities (e.g., newspapers, magazines or books), watching television or listening to the radio, volunteering, playing some games, going to church, or attending religious communities). The results of their study shed light on the strongly positive impact of leisure activities on the prevention of dementia manifestation. They found a high relationship between leisure activities and education, and between leisure activities and occupation, with effects on cognitive performance over time (Scarmeas, Levy, Tang, Manly, & Stern, 2001). At that time, this was in line with only few other studies reporting the beneficial effects of being socially active on the prevention of age-related pathology (Hultsch, Hertzog, Small, & Dixon, 1999; Schaie, 1989; Snowdon et al., 2003). The interest in the role of CR has constantly grown over the years (Mortimer, Borenstein, Gosche, & Snowdon, 2005; Nikolaos Scarmeas & Stern, 2003) and has recently enhanced knowledge on the effects of CR on flexibility of high-order cognitive functions (Delgado-Losada et al., 2019; Roldán-Tapia, García, Cánovas, & León, 2012; Satz, Cole, Hardy, & Rassovsky, 2011) and brain efficiency (Lee et al., 2019).

Other life exposures other than education, working activities and leisure activities have been investigated as possible proxies of CR. Multilingualism (e.g., Perquin, Vaillant, Schuller, & Pastore, 2013) and emigration (i.e., adaptation efforts in new living environments; Mondini, Guarino, Jarema, & Mapelli, 2014) have been found to be crucial in many recent research works on CR.

In the present project, CR will be considered as a composite concept comprising a large variety of life experiences able to build cognitive resources. CR will refer to the result of education, different working activities and their demands, and varying leisure activities carried out for a minimum of five years in adulthood.

Although wide understanding of CR has been achieved in research, interpreting age-related changes and the relative brain differences is still a challenge. The concepts of neural resources and CR have been dichotomized in terms of 'brain reserve' and 'CR'. Brain reserve refers to quantitative brain characteristics explaining susceptibility to impairment, while CR refers to differences in cognitive processes depending on intellectual activities and exposure to environmental factors (see Barulli & Stern, 2013 for a review). New currents of thought, however, are attempting to overcome this distinction ("brain reserve" vs. "CR"), which nowadays has been defined somehow “artificial”, in favor of the use a simpler terminology (Cabeza et al., 2018). Cabeza and colleagues (2018) proposed to refer to: *compensation* to indicate “cognition-enhancing recruitment of neural resources in response to relatively high cognitive demand”; *maintenance* to indicate: “the preservation of neural resources which entails ongoing repair and replenishment of the brain” (in response to natural damage incurred at the cellular and molecular levels); and *reserve* to indicate “a cumulative improvement, due to genetic and/or environmental factors, of neural resources that mitigates the effects of neural decline caused by aging or age-related diseases” (see Figure 1.2; from Cabeza et al., 2018).

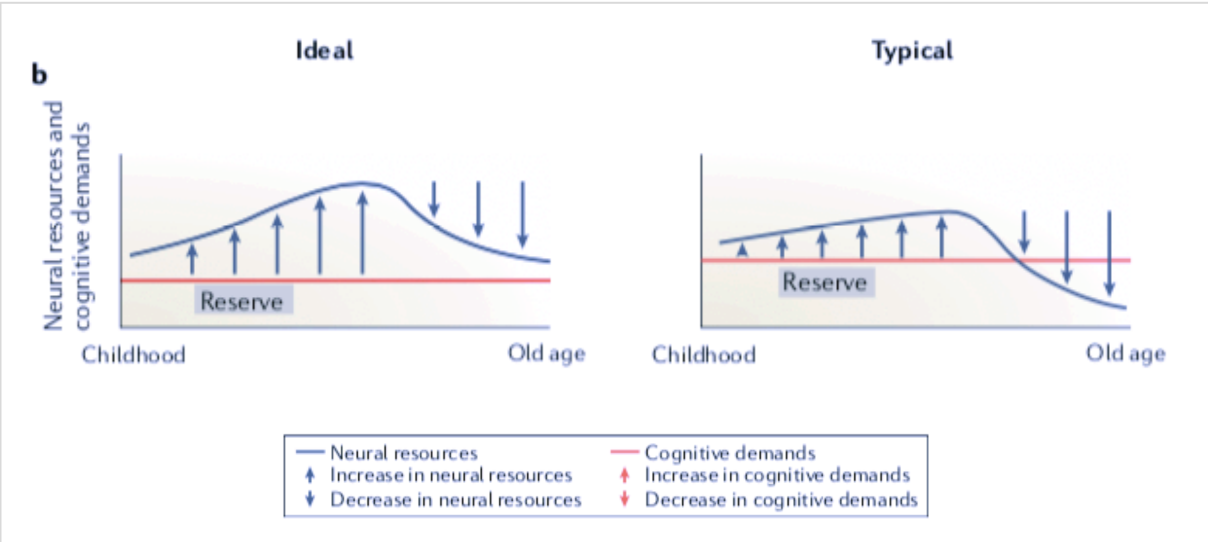

Figure 1.2. Graphical representation of the concept of reserve with cognitive demands (from Cabeza et al., 2018).

In this project, the concept of CR is understood as reflecting all learnings acquired throughout the lifespan, and its role will be explored considering healthy aging individuals, elderly individuals with dementia, and individuals with Parkinson’s Disease.

1.2. Cognitive Reserve in healthy aging and in pathological conditions

In healthy aging higher availability of cognitive resources provides more flexible and efficient use of cognitive networks (Barulli & Stern, 2013), which is reflected in an increased ability to select and use the strategies needed to perform a task. Individuals normally develop new networks across new learnings, along with the continuation of lifetime processes that sculpt the brain (Fabiani, 2012). In healthy conditions, high CR reflects high neural resources (Barulli & Stern, 2013), that is: i) networks needing to activate to a smaller degree than less efficient networks to perform the same task at comparable level of performance; ii) networks that can activate to a greater degree as task difficulty increases; and iii) flexibility in network selection (Barulli & Stern, 2013; Tucker & Stern, 2011). The role of CR in healthy aging can be measured in different ways (Barulli & Stern, 2013), such as comparing younger and older adult performance on the same cognitive tasks, or assessing older adults at different degrees of task difficulty (Darby, Brickhouse, Wolk, & Dickerson, 2017), while other studies have adopted paradigms like "Posterior-Anterior Shift in Aging" (PASA), "Compensation-related utilization of neural circuits hypothesis" (CRUNCH), or "Hemispheric Asymmetry Reduction in Older Adults" (HAROLD; Ansado et al., 2013; Barulli & Stern, 2013). In this research project, healthy elderlies' performance in cognitive tasks as a function of CR is evaluated based on different degrees of task difficulty and task characteristics.

Since CR plays a crucial role also in pathological conditions, this project also aims at analyzing its effect on a series of cognitive tasks performed in presence of neurodegeneration. In pathological aging, even primary task-related networks can be impaired, and this makes the additional use of compensatory networks necessary to accomplish the same task. This means that, in pathological aging, having high compensatory mechanisms allows to adopt alternative networks to face brain changes and preserve brain functioning (Barulli & Stern, 2013). When dementia is suspected, especially in early neuropsychological evaluations, the possible compensatory effect of CR should be always considered. In fact, having high CR can help the patient to perform even complex tasks although a neural degeneration has already started in the brain; in these cases, the symptoms of decline can be "masked" by high CR until the late stages of the disease (Mortimer et al., 2005).

The ability of the brain to re-organize its networks allows to preserve cognitive abilities in both healthy and pathological conditions, but this mechanism may occur in many different forms. What is clear to date is that cognitive flexibility in a healthy aging brain is granted by dynamic and adaptive neurofunctional mechanisms that provide "optimal engagement of age-affected resources and recourse to the most advantageous distribution of cognitive processing and resources" (Ansado et al., 2013).

Although evidence exists about the capacity of CR to predict performance in many cognitive tasks (Lojo-Seoane, Facal, Guàrdia-Olmos, Pereiro, & Juncos-Rabadán, 2018), its effect across different cognitive mechanisms is not clear-cut (Arcara et al., 2017; Lavrencic, Churches, & Keage, 2018; Šneidere et al., 2018). Being able to detect which cognitive functions are not predicted by CR is important for patients who have high reserve and perform very well in all cognitive tasks except those which are not protected by CR.

In the present project, the effect of CR is examined in healthy and pathological populations, with particular attention to language processes. It is important to note that, since the effect of CR is crucial in late adulthood and aging, the populations tested in the studies of my research project (Studies 1 to 4) were all adults and older adults. This can be considered suitable for making inferences from results of analyses where CR predicted performance. The beneficial effects of CR on language performances have been already reported in previous studies (Snowdon 1996; Thow et al., 2018), but to date, only general aspects of language have been treated, and the full understanding of the impact of CR on language mechanisms is still to be investigated. Therefore, in this project the role of CR will be analyzed across types of language tasks involving different psycholinguistic features. The issue of CR and language is important for several reasons: cognitive decline due to aging or brain pathology often impairs the ability of communicate and such impairment can affect many daily tasks. This has some relevant implications in terms of prevention, as well as in making a reliable diagnosis, in tailor-making language rehabilitation, and in better understanding how the language use is interconnected with an actively stimulating lifestyle.

In Study 1, the role of CR will be examined across psycholinguistic variables and different degrees in task difficulty. In Study 2 and in Study 3, the critical impact of CR on the ability to retrieve names across semantic word characteristics, will be investigated in clinical and healthy populations. In Study 4, the pragmatic use of language in Parkinson's Disease and its relationship with CR will be explored. Finally, Study 5 will address the digitalization of a pragmatic paper-and-pencil task into a user-friendly software application, developed by neuropsychologists and Information Technology (IT) experts. Details of assumptions and hypotheses of each single study will be considered separately in the following chapters.

CHAPTER 2. COGNITIVE RESERVE ACROSS PSYCHOLINGUISTIC FEATURES

2.1. Introduction

Psycholinguistics, or the 'psychology of language', outlines how language characteristics interplay with psychological mechanisms. Some psycholinguistic features explain why some language processes are easier to perform than others. For example, lexical frequency (i.e., the frequency of word occurrence in social environments) is an important determinant of language processing, with high-frequency words easier to process than low-frequency words (Gardner, Rothkopf, Lapan, & Lafferty, 1987; Rubenstein, Garfield, & Millikan, 1970; Rubenstein, Lewis, & Rubenstein, 1971). Another characteristic of the human language is the difference in word representation of concrete and abstract words, where concrete words are usually easier to process compared to abstract words (for a review see Paivio, 1991). This difference has been explained by the 'dual-coding theory', which posits that concrete words are processed verbally and encoded non-verbally in an image-based system (Paivio, 1991), and by the 'context-availability model', which assumes only one semantic system as responsible for concrete and abstract word processing, where concrete words are more easily put into a semantic context than abstract words (Schwanenflugel, 1991).

All in all, low-frequency and abstract words are more difficult to process than high-frequency and concrete words, because context-driven information is less available to the former than to the latter. Thus, assuming that a high CR -which is the result of a rich interplay with the environment- plays a beneficial role in cognitive performance, the hypothesis is that it could also be useful for processing low-frequency and abstract words. In Study 1, the interaction between CR and lexical frequency (high vs. low), as also between CR and lexical semantics (concrete vs. abstract) was explored through a *Lexical Decision Task* and a *Semantic Matching Task*. Lexical decision task performance is highly sensitive to the lexical frequency of words (Balota, Ferraro, & Connor, 1991; Forster & Chambers, 1973; Schwanenflugel, Harnishfeger, & Stowe, 1988) and lends itself to probing the relationship between degree of CR and lexical frequency in word access. Moreover, CR has been shown to predict cognitive performance in tasks that require semantic information processing (Darby et al., 2017), which may suggest an interconnection between CR and availability of semantic information (meaning of words). In other terms, CR could convey contextual information acquired through experience, providing higher accessibility to word knowledge. We used not only high-frequency and low-frequency words, but also abstract and concrete words. Abstract concepts have no direct sensory referents to their bearers, compared to concrete words (Balota et al., 1991; Schwanenflugel, 1991). The lexical semantic features of concrete and abstract words could be associated with different degrees of context availability so that more information is conveyed when referents are frequent or concrete, as the result of being associated either with an individual's prior world knowledge or with the contexts in which those words may occur (Schwanenflugel et al., 1988).

To sum up, the first hypothesis of Study 1 was that CR can influence the way in which language is processed, in relation to lexical frequency and lexical semantics. More specifically, the hypothesis was that performance on the *Lexical Decision Task* and on the *Semantic Matching Task* might be differentially sensitive to the effect of CR, with a possible stronger effect of CR in more demanding conditions (i.e., with low-frequency and abstract words), compared to less demanding conditions (i.e., with high-frequency and concrete words).

Lexical frequency and lexical semantics were not the only variables used in Study 1. Through a *Sentence Reading Task,* the impact of CR was also assessed by measuring reading times, based on syntactic and semantic violation processes. Although a strong positive association between CR and reading skills has been already reported (e.g., Jefferson et al., 2011), it is not clear how CR modulates different reading mechanisms. Sentences used in Study 1 were taken from De Vincenzi and colleagues (2003), but while those authors tested younger individuals and did not consider the CR impact on violation, we investigated the effect of CR on syntactic and semantic violation in a population of older adults.

In the study of De Vincenzi and colleagues (2003), different behavioral patterns emerged comparing syntactic and semantic violations in sentence reading. The authors showed that syntactic anomaly (a grammatical error with the verb) produced a reading slowdown that continued only until the following word, whereas the effect triggered by the semantic anomaly (a pragmatically implausible verb) produced a reading slowdown that lasted until the end of the sentence, as if the reader kept "continuing reading by looking for an incoming following context" that would fix the incongruence (see De Vincenzi et al., 2003). They suggested that the semantic violations were more difficult than the syntactic ones, because of the possible alternative semantic interpretations the reader expected. Assuming that a slowdown occurs when syntactic/semantic anomaly is encountered during reading, we expected that, since CR provides cognitive flexibility (Tucker and Stern 2011; Puente, Lindbergh, and Miller 2015) it could modulate reading times and facilitate the monitoring of violations in the reading course.

2.2. Study 1: Cognitive Reserve in Lexical Frequency, Lexical Semantics and in reading times of sentences with either Syntactic or Semantic Violations [1]

2.2.1. Method

Participants

Sixty-five Italian native speakers, mean age 70.98 years, with 9.7 years of education took part in this study. They were recruited from different socio-economic backgrounds; four participants were excluded due to their difficulties in understanding the instructions as they spoke only an Italian dialect and also were not motivated to participate in the experiment. All participants were volunteers; they signed an informed consent form that ensured that they understood the nature of the study. The study was approved by the Local Ethics Committee of the School of Psychology of the University of Padua and was conducted in accordance with the principles of the Declaration of Helsinki.

Procedure and Materials

A cognitive screening, a semi-structured interview and a language task were administered in a counterbalanced order. To obtain a screening of the global cognitive status, we used the Montreal Cognitive Assessment test (MoCA, Nasreddine et al., 2005). An index of Cognitive Reserve was obtained with the Cognitive Reserve Index questionnaire (CRIq,

[1] Part of results of Study 1 have been reported in the following article: Montemurro, S., Jarema., G., Mondini S., Effects of Cognitive Reserve on language processing: A study of healthy Italian older adults (submitted to *Aging, Neuropsychology and Cognition*).

Nucci, Mapelli, & Mondini, 2012), and language performance was measured by means of a three-fold computerized language task which included a *Lexical Decision Task*, a *Semantic Matching Task*, and a *Sentence Reading Task*. These three subtasks were administered in a counterbalanced order.

The MoCA test (Nasreddine et al., 2005) is a brief neuropsychological paper-and-pencil screening allowing to obtain a measure of the global cognitive status of older persons through a series of subtasks. It assesses memory, language, visuospatial skills, executive functions, and orientation in time and space; its administration lasts about 10 minutes and the maximum score is 30. We used the Italian version of the MoCA with raw scores adjusted for age and education; no participant showed any signs of dementia in this task based on Italian normative data (Conti et al., 2015)

The Cognitive Reserve Index questionnaire (Nucci, Mapelli, & Mondini, 2012) has been validated on 588 Italian individuals; it is semi-structured interview aimed at obtaining a quantitative measure of Cognitive Reserve (CRI, Cognitive Reserve Index) in terms of activities carried out throughout the lifespan. It requires 10-15 minutes to be administered and quantifies three CR components: education (CRI-Education), working activities (CRI-WorkingActivity), and leisure activities (CRI-LeisureTime). CRI-Education refers to the years of formal education achieved, and any possible course carried out during adulthood for at least 6 months. CRI-WorkingActivity refers to years of occupations carried out over the lifespan, on five levels of job areas according to the degree of intellectual involvement and personal responsibility required. CRI-LeisureTime measures the amount of social, intellectual and physical activities that a person carried out in adulthood and its frequency in terms of years (e.g., reading books, making art, volunteering, gardening, doing sports, etc.). The CRI total score corresponds to the average of the CRI-Education, the CRI-WorkingActivity and the CRI-LeisureTime and it is an estimation of the amount of CR. The

CRI total score and all three sub-scores are adjusted for age via regression-based methods to allow comparisons between groups of different ages (see Nucci et al., 2012 for further details). Table 2.1 shows demographic and neuropsychological data of participants, recruited in the North-East of Italy.

	Participants (N = 65)		
	M	*SD*	*Range*
AGE	70.98	6.42	59 - 87
EDUCATION	9.7	3.23	3 - 21
MoCA	24	2.38	17 - 29
CRI total	100	12.01	78 - 130
CRI-Education	101	10.81	83 - 141
CRI-WorkingActivity	100.2	16.32	68 - 151
CRI-LeisureTime	98	13.65	76 - 131

Table 2.1. Demographic and neuropsychological data of participants. AGE = years; EDUCATION = years of formal education; MoCA = raw scores on the MoCA test; CRI total = total Cognitive Reserve Index; CRI-Education = Cognitive Reserve Index associated with formal education; CRI-WorkingActivity = Cognitive Reserve Index associated with working activity; CRI-LeisureTime = Cognitive Reserve Index associated with leisure time activities.

The language tasks were built by means of OpenSesame, an open-source software suitable for experimental psychology testing. Administration of the language tasks lasted about 20 minutes. All the stimuli had a standard size of 60 pixels and were shown in white color on a black background. Participants were asked to respond to the tasks by pressing a key on the computer. All of them attended a training session before starting with the experimental section of the task and instructions were repeated when needed. The three performances required in the language task were: lexical decision, semantic matching and sentence reading.

- *The Lexical Decision Task* was made up of eighty words, randomly presented at the center of the screen; forty were existing Italian words, forty were non-real words. Participants pressed a green right-hand key to indicate real words and a red left-hand key to indicate non-real words. Real words were selected from an Italian corpus of 517,564 frequency estimates derived from Italian movie subtitles (i.e., SUBTLEX, (Crepaldi, Amenta, Mandera, Keuleers, & Brysbaert, 2016), which is one of the most recent sources for Italian lexical frequencies (http://crr.ugent.be/subtlex-it/). Non-words were generated through a 1:1 length matching with the real words, by means of the software Wuggy (Keuleers & Brysbaert, 2010). Real words were all singular and referred to non-living entities. They were controlled for lexical frequency, so that twenty of them were in the low-frequency range (i.e., between 70 and 2,000 frequency count), and twenty in the high-frequency range (i.e., between 11,000 and 25,000 frequency count) according to SUBTLEX-IT. Real words were also balanced across lexical semantic characteristics, so that twenty of them were concrete (i.e., referring to physical entities) and twenty were abstract. All words were balanced across length and ranged from four to nine letters. A fixation point was presented centrally for 1000 milliseconds (ms), followed by the target (i.e., a real or a non-real word); each word remained on the screen until the participant gave a response. To familiarize themselves with the task, all participants first performed a training session. Feedback was provided both at the end of the training and of the experimental sessions to encourage active engagement with the task. See APPENDIX A.1 for more details about the Lexical Decision task.

- The *Semantic Matching Task* included eighty pairs of randomly presented Italian words (i.e., forty pairs of synonyms and forty pairs of words unrelated in their meaning). All pairs were presented centrally and aligned vertically. Participants stated whether the pairs of words had the same meaning or not by pressing a right-hand green key for affirmative answers and a left-hand red key for negative answers (see example in Figure 2.1).

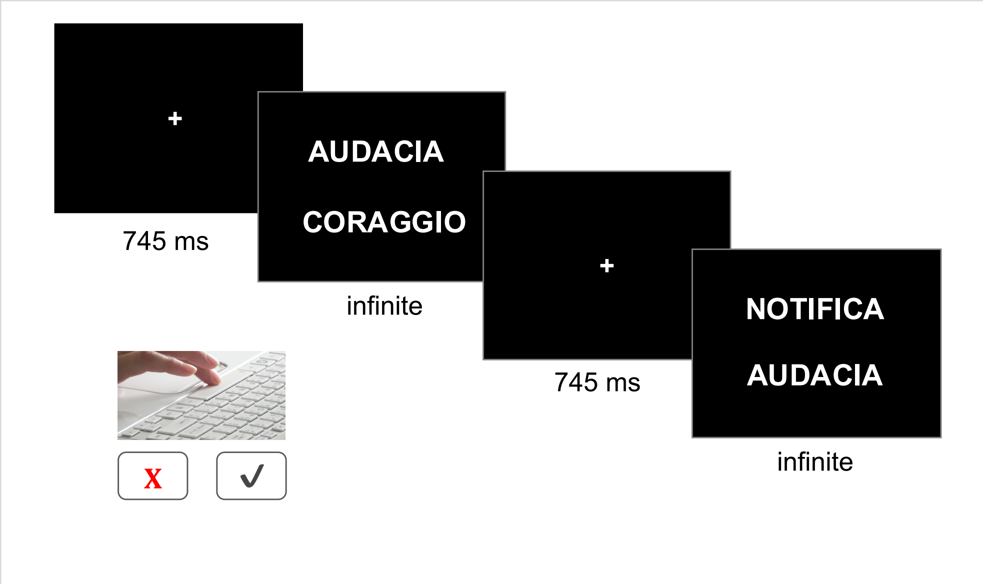

Figure 2.1. Example of stimuli of the *Semantic Matching Task*. The Italian words *AUDACIA* and *CORAGGIO* can be translated as "PLUCK" and "BRAVERY", while the Italian word *NOTIFICA* can be translated as "NOTIFICATION".

Words were balanced across verbs and nouns, high and low lexical frequency, and abstract and concrete representation. In the set of synonyms, twenty words had different lexical frequencies according to SUBTLEX (Crepaldi et al., 2016); thus, twenty were in the low-frequency range (i.e., between 70 and 2,000 frequency count) and twenty were in the high-frequency range (i.e., between 11,000 and 25,000 frequency count). Twenty stimuli in the pairs of synonyms were concrete words and twenty were abstract words. Examples of concrete words used are *scuotere* ('to shake') as a verb or *cibo* ('food') as a noun; examples of abstract words used are *credere* ('to believe') as a verb or *scelta* ('choice') as a noun; see APPENDIX A.2 for more details about the stimuli used in the Semantic Matching task.

To obtain a reliable pairing of synonyms, we used a series of Italian synonym dictionaries and MultiWordNet, which is an Italian lexical database (multiwordnet.fbk.eu/english/home; Pianta, Bentivogli, & Girardi 2002). Presentation of words was counterbalanced, so that the same word was used as the synonym or as the unrelated word, and appeared randomly either at the top or at the bottom of the screen. All words presented in this task were singular. They were four- to nine-letter long, balanced across length. A central fixation point was presented for 745 ms, followed by the pair of words, which remained on the screen until participants gave a response. The words of each pair were 32 pixels distant from the center of the screen and 64 pixels distant from each other. A training session preceded the start of the experimental session. A visual feedback, consisting in the percentage of correct responses given, was shown at the center of the screen at the end of both sessions. In both the *Lexical Decision Task* and the *Semantic Matching Task,* we did not include words that have homographs, for example: *letto* ('bed') vs. *lett*o ('read' as past participle), or *sveglia* ('alarm clock') vs. *sveglia* ('wake up' in imperative form). We did not include words that can be used as prefixes for compounding (e.g., '*auto'*, '*foto'*), nor derived nouns like *fioraio* ('florist'), or compound words like *cavatappi* ('corkscrew').

- The *Sentence Reading Task* comprised eighty Italian sentences; forty of them were well-formed and forty contained either a syntactic or a semantic violation. Sentences used in this task derived from the pool of stimuli used in De Vincenzi and colleagues (2003), who evaluated reading times of sentences with syntactic and semantic violations in young Italian readers (18-25 years old). For our study we selected sentences with both human and inanimate subjects, all in the singular form. In the syntactic violation condition, forty pairs of sentences were entered in the task, with only one version of each pair characterized by a subject-number error (the syntactic violation). In the semantic violation condition, forty pairs of sentences were entered, with only one version of each pair characterized by semantic/pragmatic ambiguity (the semantic violation). See Table 2.2 for an example.

Syntactic violation
La macchina sportiva viaggia/viaggiano sulla strada montana The sports car travels/travel along the mountain road
Semantic violation
L'autista del taxi sterza/evapora per evitare un ostacolo The driver of the taxi swerves/evaporates to avoid the unexpected obstacle

Table 2.2. Examples of sentences used in the Sentence Reading task with syntactic and semantic violations. In the examples above the first verb is correct, while the second verb is grammatically incorrect or ambiguous. Stimuli are adapted from De Vincenzi et al. (2003)'s material.

The word containing the violation (the critical word) was always a verb in the present indicative tense, either intransitive or transitive and without a direct object. It was always in the fourth position in the sentence followed by three or four words (in both syntactic and semantic conditions). Verbs were four- to nine-letter long. No word included in the sentences was longer than 12 letters. In the semantic condition, the regular verb and the semantically violated verb were matched for lexical frequency and letter length (for more details see De Vincenzi et al., 2003). Sentence presentation was counterbalanced, so that half of the participants were assigned to Group A, and half to Group B. In this way, each participant responded only to one version of the sentence (either to the violated or the non-violated form), thus avoiding biases due to familiarization with the stimuli. As shown in Figure 2.2, participants in groups A and B did not differ in age (B = 0.05, SE = 1.63, p = 0.97) and in total Cognitive Reserve Index (B = 1.56, SE = 3.02, p = 0.61).

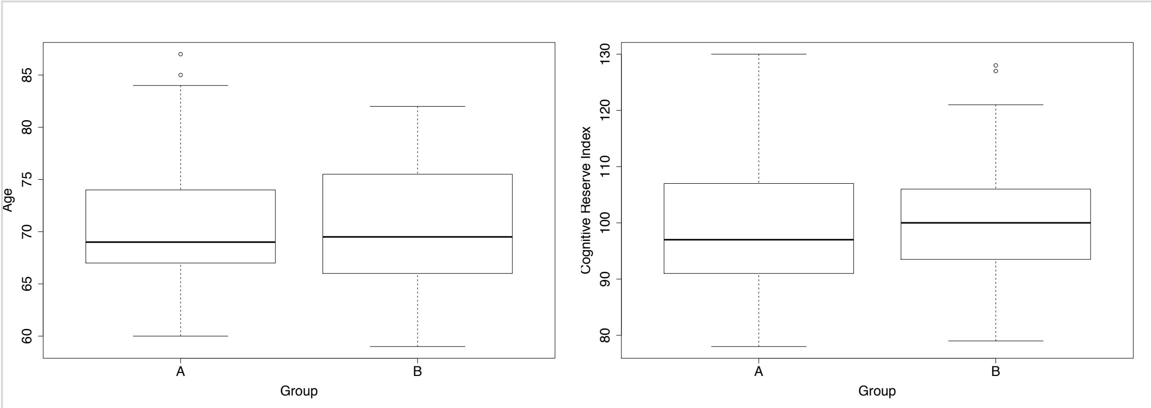

Figure 2.2. Groups of older adults performing the *Sentence Reading Task*. Comparisons between Group A and Group B, by Age and Cognitive Reserve.

The *Sentence Reading Task* was a self-paced reading task: participants controlled the presentation rate of each word by pressing a "go" key (the spacebar); see Figure 2.3 for an example. They were asked to read with maximum attention a series of sentences with the aim to understand each sentence, from the beginning to the end. Participants were suggested to read aloud.

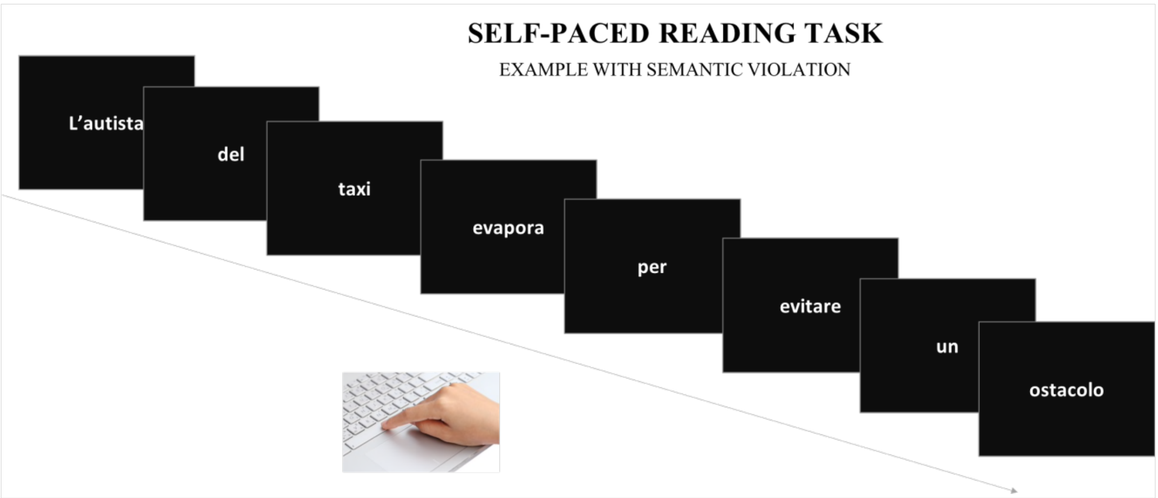

Figure 2.3. Example of semantic violation included in the self-paced reading task. Participants controlled their own reading pace by pressing the spacebar.

They were told that some sentences would be 'odd' with respect to others, that is, they could include some anomaly. To ensure that participants paid attention to the content of the sentences, they were asked to respond to twenty-seven yes/no comprehension questions that randomly appeared after some sentences, by pressing M for "yes" and Z for "no" on the keyboard. These comprehension questions were never related to the linguistic violation. Before starting with the experimental session, all participants performed a training session, which was repeated until they showed full comprehension of the task. All the sentences used are listed in APPENDIX A.3.

Statistical Analyses

Data were analyzed by means of mixed-effect models which allow to address the whole structure of data as a combination of fixed and random effects in order to obtain enhanced statistical power (Pinheiro & Bates, 2006). Mixed-effects models are suitable for analyzing psycholinguistic data (Baayen, Davidson, & Bates, 2008), since they reduce the possibility that the observed results are due to few participants or few items. Rather, they allow to work on complex data structures including both categorical and continuous predictors. In this study, Response Times and Accuracy were specifically treated with Generalized Linear Mixed-effect Models (Baayen et al., 2008; Bates, Maechler, & Bolker, 2013; Quené & van den Bergh, 2008) entering subject identity and word trial list as random effects. The dependent variable Accuracy was entered in the form of binomial data (correct/incorrect), allowing to avoid data proportion aggregation (Quené & van den Bergh, 2008).

To examine model plausibility we used the Likelihood Ratio (LR) test, whereas the Akaike's Information Criterion (AIC, Bertrand et al. 2006), and the Delta-AIC (Burnham & Anderson, 2002) were used to make comparisons among models. Models with lower AIC indicate a better model fit than models with higher AIC, and Delta-AIC quantifies the difference between models. Cook's distance (Cook & Weisberg, 1982) was measured to check for the presence of influential data and the whole dataset was considered without excluding any observations[1]. Results in the *Lexical Decision Task* and in the *Semantic Matching Task* were analyzed separately, and two different types of models were built respectively for Response Times (continuous variable) and Accuracy (binomial variable)[2]. Since the effect of CR on language processing was of primary interest, we first analyzed the effect of CRI (as a continuous variable in scaled form) on the global language performance, then we entered the psycholinguistic features (i.e., Lexical Frequency and Lexical Semantics) as predictors together with CRI. Lexical Frequency included high- and low-frequency words, whereas Lexical Semantics included concrete and abstract words. Participants' scores at the MoCA test were entered as continuous variables in post-hoc analyses. In the *Sentence Reading Task*, participants' Reading Times were our dependent variable and two analyses were performed for syntactic and semantic violations, respectively. The variable Position referred to the position of each word within the sentences: seven positions in sentences with syntactic violations and eight positions in the sentences with semantic violations. The variable Violation was another categorical factor with 2 levels (violated and non-violated).

We first analyzed Reading Times without considering the effect of CR as a predictor to see whether our findings, based on a population of older adults, replicated the findings of De Vincenzi et al. (2003), carried out on younger individuals. Then, the CRI was entered in the model with the variables Position and Violation to see the effect of CRI at different points in the sentences. All the analyses were performed by means of R Software (R Core Team, 2016 version 3.3.1) and GLMM were run by means of lme4-package (Bates et al., 2014), with an α level of 0.05 defining significance.

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[1] Invalid (null) responses were eliminated from the dataset.

[2] Results of the *Semantic Matching Task* included only the correct responses for Response Times, and both the correct and incorrect responses in binomial form for the analysis of Accuracy.

2.2.2. Results

Lexical Decision task: Response Times and Cognitive Reserve

The CRI was our measure of global Cognitive Reserve and the main predictor of interest. Response Times of participants averaged 951 ms (SD = 431) in the condition with real words and 1,443 (SD = 917) ms in the condition with non-real words. In line with the purpose of this study, the variables Lexical Frequency and Lexical Semantics were treated in multiple GLMM analyses both as unique predictor and in interaction with CR. CRI-Education was shown as the best predictor of Response Times[1]. CRI-Education predicted the overall participants' speediness in performing the *Lexical Decision Task* (B = -0.08, t = -2.17; p = 0.02)[2]. Then, Lexical Frequency and Lexical Semantics were entered in the model[3]. Responses were significantly different across the levels of Lexical Frequencies, with faster responses in the case of high-frequency words compared to low-frequency words (B = 0.16, t = 4.37; $p < 0.001$). Lexical Frequency itself was a very strong predictor of Response Times in the Lexical Decision task (Delta-AIC between the model with Lexical Frequency and the model with Lexical Frequency x CRI = 119). Considering CR and Lexical Semantics together as predictors of Response Times produced a significant improvement of the model fit ($\chi2$ (2) = 6.61, p = 0.03); see Figure 2.4. No significant differences were observed in the effect of CR across different lexical frequencies, and abstract words seemed to be more sensitive to CR, compared to concrete words. More details are shown in Table 2.4.

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[1] CRI-Education is not only based on formal education but includes all the possible courses carried out in adulthood (Stern, 2002, 2009); see the Method section for further explanations.
[2] This result refers to the response of all participants to the entire set of stimuli presented, considering the time in which participants correctly responded to real and non-real words.
[3] Considering only real words.

Lexical Decision: Accuracy and Cognitive Reserve

Participants correctly responded to 98.57% of real words and to 91.81% of non-real words. The CRI total score of participants predicted accuracy on Lexical Decision (B = 0.02, z = 2.05; p = 0.03)[1]. In parallel with the results of the Lexical Decision Response Times, a strong Lexical Frequency effect emerged, with more accurate responses to high-frequency words compared to the low-frequency ones (B = -1.59, z = -2.51; p = 0.01). Moreover, in line with the hypothesis, a significant interaction was found between CRI and Lexical Semantics, with abstract words being significantly more sensitive to the effect of CRI than concrete words (B = -0.74, z = -2.01; p = 0.04); see Figure 2.5 and Table 2.4. To check whether this effect was biased by some other factors, the MoCA scores of the participants' performance on a different series of brief cognitive tasks were entered in the model. Entering MoCA scores as a covariate of CRI and Semantic Representation produced no significant improvement in the model fit ($\chi 2$ (4) = 2.14, p = 0.71), suggesting that the interaction effect between CR and Lexical Semantics on accuracy of Lexical Decision was not better explained by differences in participants' global performance.

Semantic Matching: Response Times and Cognitive Reserve

Response Times of participants averaged 2,021 (SD = 1,142) ms in the case of related words and 2,354 (SD = 1,188) ms in the case of unrelated words. The variables Lexical Frequency and Lexical Semantics were treated in subsequent multiple GLMM analyses. Higher CRI predicted faster Response Times in detecting synonyms (B = -0.08, t = -1.98; p = 0.04). A

[1] This result refers to the responses of all participants in the *Lexical Decision Task*, considering both correct and incorrect answers to real words and non-real words. When Lexical Frequency and Lexical Semantics were included as predictors of interest in the model, only real words were considered.

significant interaction was found between CRI and Lexical Frequency, showing that when CR was in the higher range, its effect was stronger for low-frequency than for high-frequency words (*B* = -0.02, t = -2.36; *p* = 0.01). Entering CRI and Lexical Semantics as interaction terms produced a significant improvement in the model fit compared to the model with CR as the only predictor of interest ($\chi 2$ (2) = 6.73, *p* = 0.03). This suggests that participants' response speed on this task was the result of both the cognitive resources and psycholinguistic characteristics of the words (see Figure 2.4 and Table 2.4 for more details).

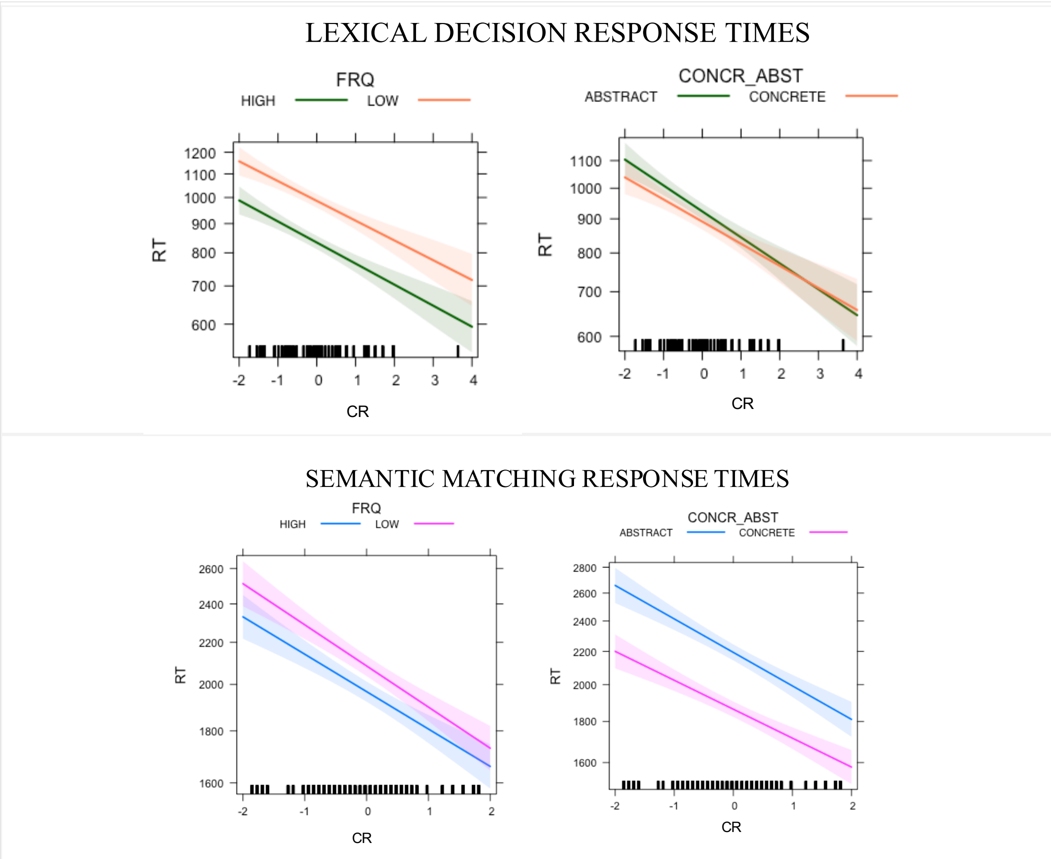

Figure 2.4. Response Time results in the *Lexical Decision Task* (top figures) and in the *Semantic Matching Task* (bottom figures), with Lexical Frequency and CR as interaction terms on the left-hand side and Lexical Semantics and CR as interaction terms on the right-hand side of the figures.

Semantic Matching: Accuracy and Cognitive Reserve

Participants accurately responded to 88.65% of related words and to the 93.31% of unrelated words. Moreover, older adults with higher CR were more accurate in distinguishing pairs of synonyms from pairs of unrelated words ($B = 0.46$, $z = 3.51$; $p < 0.001$). Synonyms including high lexical frequency words were more accurately detected compared to synonyms including low-frequency words ($B = -1.22$, $z = 2.69$; $p < 0.01$). We found a significant interaction between CRI and Lexical Frequency ($B = 0.49$, $z = 3.28$; $p < 0.01$) indicating that low-frequency words were more sensitive to the effect of CR compared to high-frequency ones (see Fig 2.5).

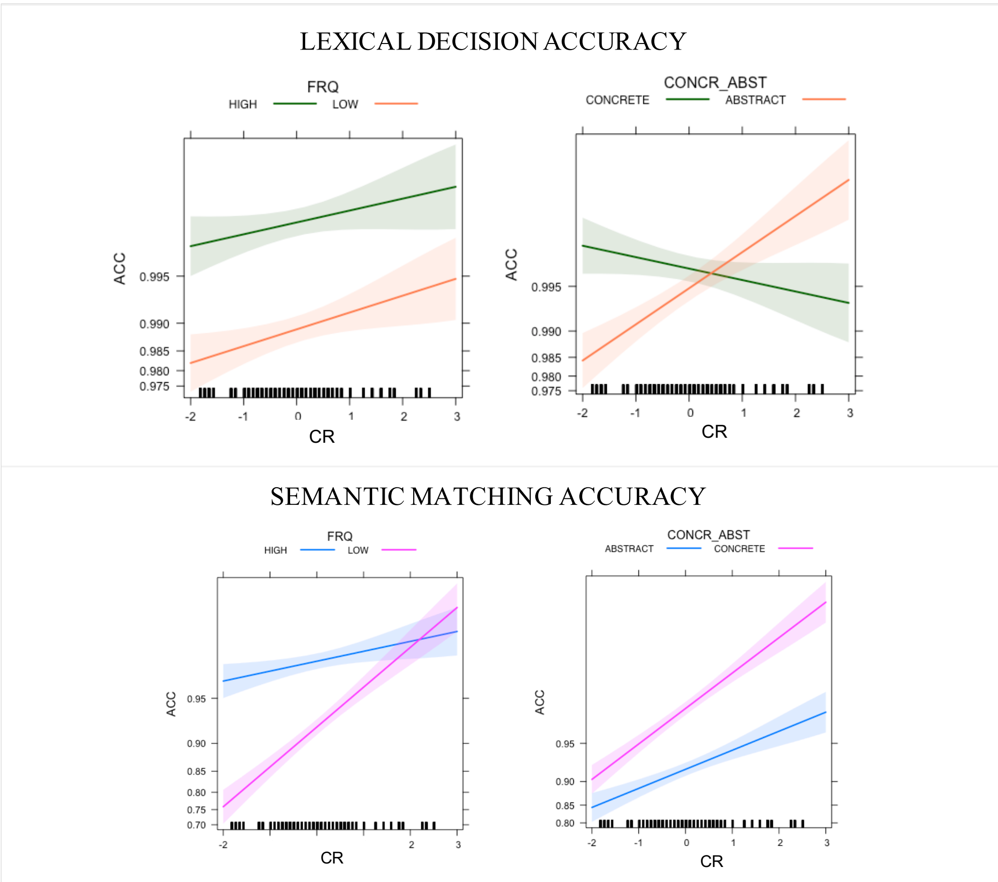

Figure 2.5. Accuracy results in the *Lexical Decision Task* (top figures) and in the *Semantic Matching Task* (bottom figures), with Lexical Frequency and CR as interaction terms on the left-hand side and Lexical Semantics and CR as interaction terms on the right-hand side of the figures.

To check whether this effect was biased by some other factors we entered the MoCA scores in our model. Entering the MoCA scores as a covariate of CRI and Lexical Frequency produced no significant improvement in the model fit ($\chi2$ (4) = 3.95, $p = 0.41$). Furthermore, Delta-AIC model comparison showed that the model with CR and Lexical Frequency as interaction terms was 5501 times more plausible than the model with Lexical Frequency considered as the only predictor of interest. Considering Lexical Semantics, our findings showed that participants were more accurate with concrete words than with abstract words ($B = 1.07$, z = 2.38; $p = 0.01$), with a significant interaction between Lexical Semantics and CRI ($B = 0.32$, z = 1.97; $p = 0.04$) (see Table 2.4 for more details).

Lexical Decision Task						
	Fixed Effects	*Beta*	*SE*	*t*	*p-value*	*AIC*
Response Times	Intercept	6.81	0.05	123.4	< 0.001**	3,4760.36
	CR	-0.08	0.03	-2.17	0.02*	3,4757.87
	FRQ = High vs. Low	0.16	0.03	4.37	<0.001**	3,4748.31
	SR = Concrete vs. Abstract	-0-03	0.05	-0.69	0.49	3,4761.91
	CR x FR	0.005	0.009	0.57	0.57	3,4747.53
	CR x SR	0.01	0.009	1.46	0.14	3,4759.28
Accuracy	-	*Beta*	*SE*	*Z*	*p-value*	*AIC*
	Intercept	4.42	0.26	16.23	< 0.001	1,683.26
	CR	0.02	0.01	2.05	0.03*	1,681.11
	FRQ = High vs. Low	-1.59	0.63	-2.59	0.01*	356.71
	SR = Concrete vs. Abstract	0.42	0.66	0.64	0.52	362.52
	CR x FR	0.07	0.47	0.15	0.87	359.07
	CR x SR	-0.74	0.36	-2.01	0.04*	360.81
Semantic Matching Task						
	Fixed Effects	*Beta*	*SE*	*t*	*p-value*	*AIC*
Response Times	Intercept	7.53	0.06	130.6	< 0.001	40,137.31
	CR	-0.08	0.04	-1.98	0.04*	40,135.54
	FRQ = High vs. Low	0.12	0.07	1.67	0.09	40,136.65
	SR = Concrete vs. Abstract	-0.18	0.07	-2.6	< 0.001**	40,133.23
	CR x FR	-0.02	0.01	-2.36	0.01*	40,131.26
	CR x SR	0.01	0.01	0.81	0.42	40,132.81
Accuracy	-	*Beta*	*SE*	*Z*	*p-value*	*AIC*
	Intercept	3.01	0.27	10.76	< 0.001	1,490.31
	CR	0.46	0.13	3.51	< 0.001**	1,481.03
	FRQ = High vs. Low	-1.22	0.45	-2.69	< 0.01**	1,485.46
	SR = Concrete vs. Abstract	1.07	0.45	2.38	0.01*	1,487.06
	CR x FR	0.49	0.15	3.28	< 0.01*	1,468.24
	CR x SR	0.32	0.16	1.97	0.04*	1,476.05

Table 2.4 Response Times and Accuracy in the *Lexical Decision Task* and the *Semantic Matching Task.* CR = Cognitive Reserve, FRQ = Lexical Frequency, SR = Semantic Representation. Note: in the *Lexical Decision Task*, the best estimator of CR was CRI-Education. The two rows in grey refer to the whole set of words presented in the *Lexical Decision task* (i.e., correct and incorrect answers to real and non-real words). Note: *p-value < 0.05; **p-value<0.01.

Sentence Reading Times and Cognitive Reserve

This was a self-paced reading task. To ensure that participants understood what they had read they were asked to respond to a total of 27 randomly presented comprehension questions. Results show that participants responded correctly to 90% of the questions, indicating that the task was performed appropriately. Participants' reading times averaged 900 (SD = 490) ms in the non-violated condition and 940 (SD = 519) ms in the violated condition (Figure 2.6).

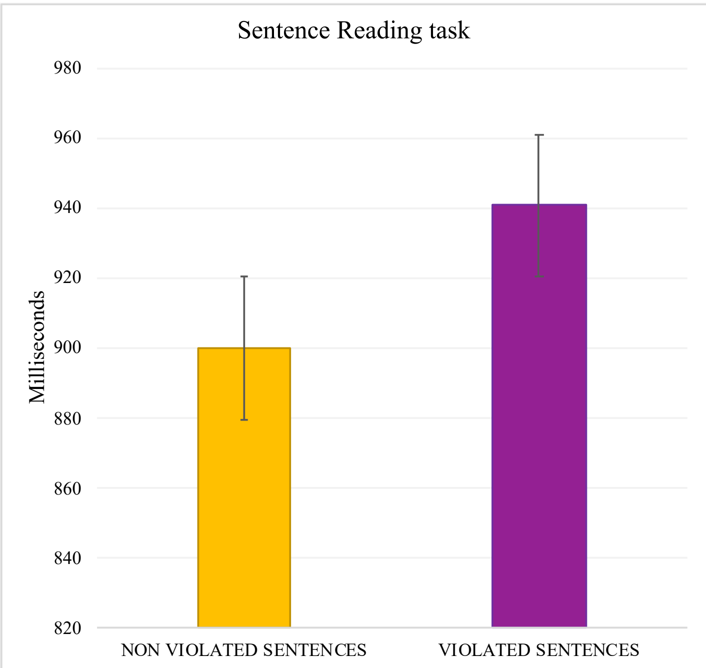

Figure 2.6. Response time differences in the Sentence Reading task. Participants read significantly faster when the sentences did not contain any grammatical or semantic violation.

In the syntactic violation condition, ungrammatical and grammatical versions of the sentences were compared. For example, *La macchina sportiva* ****viaggiano*** *sulla strada montana* ('The sports car ****travel*** along the mountain road') vs. *La macchina sportiva* ***viaggia*** *sulla strada montana* ('The sports car **travels** along the mountain road'), showing a significant slowdown of reading time in the ungrammatical condition, starting from the critical word, that is, the incorrect verb appearing in the fourth position ($B = 0.23$, $t = 10$; $p < 0.001$). As Figure 2.7 demonstrates, this slowdown persisted only until the following word in the fifth position ($B = 0.07$, $t = 3.43$; $p < 0.001$), which is a replication of the results shown for younger adults by De Vincenzi and colleagues (2003). In line with their findings, we have shown that the syntactic anomaly was immediately detected on the critical word, with the slowdown continuing until the next word (see Table 2.5 for further details).

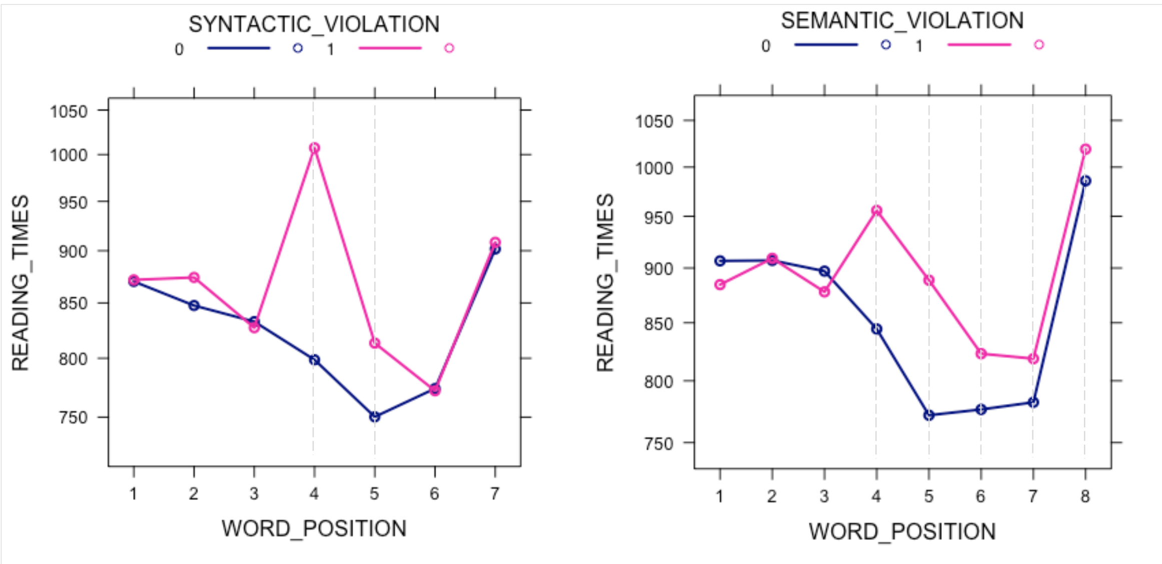

Figure 2.7. Difference between violated and non-violated sentences. Left-hand side: Syntactic Violation condition; right-hand side: Semantic Violation condition. Dotted lines = significant difference in Reading Times between violated and non-violated sentences; the violated word was always in fourth position in both the syntactic and semantic violation conditions.

SYNTACTIC VIOLATION (word position x violation)

	Fixed Effects	*Beta*	*SE*	*t*	*p-value*
Reading Times	Intercept	6.76	0.05	132.82	< 0.001
	POS2	-0.02	0.01	-1.62	0.11
	POS3	-0.04	0.01	-2.71	< 0.01*
	POS4	-0.08	0.01	-5.29	< 0.001**
	POS5	-0.14	0.01	-9.14	< 0.001**
	POS6	-0.11	0.01	-7.23	< 0.001**
	POS7	0.03	0.01	2.19	0.02*
	VIOLATION	0.01	0.01	0.11	0.91
	POS2 x VIOLATION	0.02	0.02	1.26	0.21
	POS3 x VIOLATION	-0.01	0.02	-0.37	0.71
	POS4 x VIOLATION	0.23	0.02	10.01	< 0.001**
	POS5 x VIOLATION	0.07	0.02	3.43	< 0.001**
	POS6 x VIOLATION	-0.01	0.02	-0.19	0.85
	POS7 x VIOLATION	0.01	0.02	0.24	0.81

SEMANTIC VIOLATION (word position x violation)

	Fixed Effects	*Beta*	*SE*	*t*	*p-value*
Reading Times	Intercept	6.81	0.05	130.11	< 0.001
	POS2	0.01	0.01	0.08	0.93
	POS3	-0.11	0.01	-0.64	0.52
	POS4	-0.07	0.01	-4.12	< 0.001**
	POS5	-0.16	0.01	-9.09	< 0.001**
	POS6	-0.15	0.01	-8.78	< 0.001**
	POS7	-0.14	0.01	4.73	< 0.001**
	VIOLATION	-0.02	0.01	-1.32	0.18
	POS2 x VIOLATION	0.02	0.02	1.14	0.25
	POS3 x VIOLATION	-0.01	0.02	0.12	0.91
	POS4 x VIOLATION	0.15	0.02	6.02	< 0.001**
	POS5 x VIOLATION	0.16	0.02	6.61	< 0.001**
	POS6 x VIOLATION	0.06	0.02	2.71	< 0.01*
	POS7 x VIOLATION	0.05	0.02	2.23	0.02*

Table 2.5. Results of GLMM analyses on Reading Times in the *Reading Task*. POS = word position. Note: *p-value < 0.05; **p-value<0.01.

In the semantic violation condition, Reading Times of the sentences containing an anomalous verb and Reading Times of the sentences containing a plausible verb were compared. For example, *L'autista del taxi* ****evapora*** *per evitare un ostacolo* ('The taxi driver ***evaporates** to avoid the unexpected obstacle*'*) vs. *L'autista del taxi* ***sterza*** *per evitare un ostacolo* ('The taxi driver **swerves** to avoid the unexpected obstacle*'*), showing a significant slowdown in the semantically unacceptable condition, starting at the critical word, that is, the verb in the fourth position (B = 0.15, t = 6.02; p < 0.001). This slowdown of Reading Time continued until the end of the sentence (Figure 2.7). As the focus of our study is the effect of CR on language processing, we entered CR into our model. In the Syntactic condition, analyses showed that older adults with high CR had faster reading times than older adults with low CR (B = -0.12, t = -2.82; p < 0.001). More interestingly, we found an interaction effect between CRI and the variable Violation precisely at the point of the critical word (i.e., Position 2: B = -0.01, t = -0.31, p = 0.76; Position 3: B = -0.01, t = -0.65, p = 0.51; Position 4: B = -0.08, t = -3.53, p < 0.001, Position 5: B = -0.01, t = -0.19, p = 0.85, Position 6: B = -0.02, t = -0.89, p = 0.37, Position 7: B = -0.03, t = -1.35, p = 0.17). Post-hoc analyses showed that the higher the CRI, the lesser the gap between the ungrammatical and grammatical condition (Figure 2.8). These results indicate that high CR predicted not only faster overall reading times, but also a decrease in slowdown when the grammatical incorrectness was detected. In the semantic condition, CR overall predicted participants' shorter reading times (B = -0.11, t = -2.63; p < 0.01), but no differences emerged when considering CRI across violated and non-violated conditions; see Figure 2.8.

Then the effect of CR was probed considering only the sentences in which a violation (either syntactic or semantic) occurred. In the case of a syntactic violation, the higher the CR, the faster the overall Reading time. In particular, at the point of the syntactically violated word (fourth position in the sentence) participants with low CR recorded a more marked slowdown in Reading times than participants with high CR (Figure 2.8). A similar effect at the point of the violation is not present in the case of the semantic condition (see Figure 2.8).

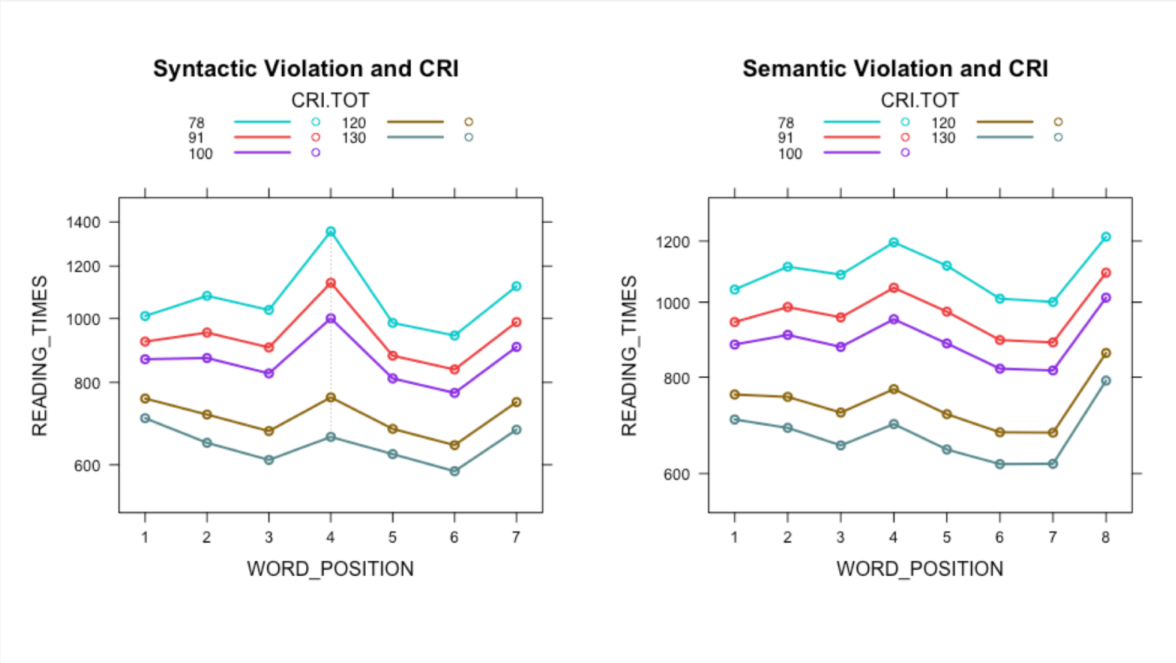

Figure 2.8. CR effect on Reading Times of Syntactic and Semantic violations. The graph on the left-hand side shows the effect of CRI on Reading Times in the syntactically violated condition; the graph on the right hand-side shows the effect of CR on Reading Times of the semantically violated condition.

2.2.3. Discussion

In this study the effect of Cognitive Reserve on language processing was measured in a group of healthy older adults. CR was assessed through the Cognitive Reserve Index questionnaire (Nucci et al., 2012), a tool for estimating the level of CR acquired through years of education, working activities, and leisure time activities. Our assessment of language was obtained through a three-fold experiment that measured Response Times and Accuracy in a *Lexical Decision Task* and in a *Semantic Matching Task*, whereas Reading Times were recorded through a *Sentence Reading Task*.

First, we showed that healthy older adults with higher CR gave faster and more accurate responses in both the *Lexical Decision Task* and the *Semantic Matching Task*. These results strengthen the idea that having a high CR provides not only general cognitive efficiency (Opdebeeck, Martyr, & Clare, 2016), but also language maintenance in terms of prompt and correct responses. Recent studies have shed light on the significant relationship between CR and language (e.g., Thow et al. 2018) but, to the best of my knowledge, this is the first study exploring in older adults the impact of CR on response time and accuracy of responses in lexical decision and semantic matching tasks.

We investigated the relationship between CR and Lexical Frequency (across low and high frequencies) and also between CR and Lexical Semantics (across abstract and concrete words), in order to determine whether CR might have differential effects on language performance depending on the specific psycholinguistic features of lexical frequency and lexical semantics. As expected, a lexical frequency effect was found in both the *Lexical Decision Task* and the *Semantic Matching Task*, with low-frequency words being generally more difficult to access compared to high-frequency ones. This result is in line with the previous literature, according to which words with low frequency of occurrence are more difficult to access than words that are encountered more frequently (Diependaele, Lemhöfer, & Brysbaert, 2013; Gardner et al., 1987; Kuchinke, Võ, Hofmann, & Jacobs, 2007; Rosenzweig & Postman, 1958). The lexical frequency effect usually explains existing regularities of language emerging from our life experiences (Ellis, 2002), which CR is made of. While in the *Lexical Decision Task*, frequency predicted performance, entering both CRI and frequency into the model did not yield any significant effect. By contrast, the *Semantic Matching Task* displayed a significant relationship between CR and lexical frequency, both in Response Times and in Accuracy. More specifically, in this task low-frequency words were more sensitive to the effect of CR, compared to high-frequency words. It might be the case that, in a single-word identification task such as the *Lexical Decision Task*, responses were more strictly influenced by the intrinsic nature of words as being frequent vs. infrequent in the environment, whereas in the *Semantic Matching Task* responses were less influenced by lexical frequency and more influenced by participants' CR.

Accuracy in the *Semantic Matching Task* primarily served as a vocabulary richness measurement, in which higher Accuracy reflected larger knowledge of alternative words for the same concept. Participants who reported some difficulties in the *Semantic Matching Task* motivated their struggles, or errors, with the fact that they possess, and use, only a small amount of words. Some tasks for measuring vocabulary size have already been used as proxies of CR, because vocabulary represents knowledge that crystalizes throughout lifetime (Barulli & Stern, 2013a; Roldán-Tapia et al., 2012; Thow et al., 2018). Our findings indicate not only that CR and vocabulary size are two closely associated concepts, but also that having a cultured vocabulary could be the result of actively participating in stimulating activities in adulthood.

We used abstract and concrete words to determine whether the effect of CR varies as a function of context availability, which refers to the capacity of concrete words to convey less ambiguous context information than abstract words, whose processing is more demanding due to the high variability in their interpretation across contexts (Hoffman, 2016). While contextual availability is a psycholinguistic variable (Balota et al., 1991; Schwanenflugel et al., 1988), CR refers to factors that enrich a person's cognition. Our Accuracy results in the *Lexical Decision task* showed a stronger effect of CR when processing abstract words as compared to concrete words, which could be linked to the fact that abstract words gain larger benefits when context-related semantic information is available (Schwanenflugel et al., 1988). To date, a number of studies are in line with the finding that abstract concepts are processed differently from concrete concepts, since the former refer to intangible entities (e.g., emotions, cognitive states, ideas), whereas the latter refer to entities that have physical attributes (e.g., places, things, or living entities), (Barsalou

& Wiemer-Hastings, 2005). The differences between concrete and abstract processes reported in previous studies (Della Rosa et al., 2014; Schwanenflugel, 1991) have been explained in terms of neural connectivity (Crutch & Warrington, 2005), in which abstract and concrete words belong to qualitatively different representational systems. In general, abstract thinking has been associated with cognitive skills in the higher-level range and, importantly, CR has been found to play a crucial role in high-level cognitive processing (Darby et al., 2017; Tucker & Stern, 2011). For example, being constantly involved in highly demanding tasks may result in the development of cognitive strategies that are useful for coping with tasks requiring mental flexibility. An unexpected result of this study was the interaction between CR and lexical semantics on Accuracy. While CR predicted performance in both the abstract and concrete condition, this effect was slightly stronger in the concrete condition, a finding that is somewhat counterintuitive as abstract words were expected to benefit more from high CR. This outcome might reflect the age-related attenuation of the concreteness effect as reported by Peters and Daum, (2008) and Rissenberg and Glanzer (1987).

In Study 1, participants underwent also a reading task in which syntactic violations (subject-verb number disagreement) and semantic violations (verb-context incongruence) were compared to their correct counterparts. Interestingly, the results of our study replicated, in an elderly population, those reported by De Vincenzi et al. (2003) for young adults. After including CR as a predictor in our analyses, we found that Reading Times were significantly longer in healthy older adults with low CR, which is in line with Miller and Stine-Morrow's (1998) study where low cognitive skills predicted longer reading times. The authors explained their results in terms of the need of allocating greater resources for planning and organizing information while reading.

Study 1 shows not only an overall benefit in reading rates as a function of CR, but also that having high CR predicts a faster resolution of syntactic violations, thus suggesting that participants with high CR detected earlier such violations and hesitate less. A similar resolution in the case of semantic violation was not found. This difference might reflect that CR is enriched by exposure to the systematic use of syntactic rules that are typical of one's native language. Such an interpretation would explain the absence of CR effects in the semantic violation condition, in which no language-specific strategy is available to the reader when the verb is pragmatically implausible. In this case, the anomalous word triggers interpretation attempts across the whole sentence, with a slowdown spread over all words following the violation.

CHAPTER 3. EFFECTS OF COGNITIVE RESERVE ON NAMING PERFORMANCE IN PATHOLOGICAL AND HEALTHY AGING

3.1. Introduction

In this chapter Study 2 and Study 3 will be presented. Study 2 evaluated the effect of CR on global cognitive performance and the ability to retrieve the specific category of proper names in patients with dementia. Proper names constitute a lexical category requiring specific processing and storage (for reviews see Brédart, 2017; Semenza, 2009). The specific attributes of proper name processing make aging particularly sensitive to this category. Older persons, in fact, often experience word retrieval difficulties, which may become noticeable when retrieving names of well-known individuals (Cohen & Burke, 1993). Given the importance of proper names in social interaction, this can be a cause for embarrassment and frustration even in healthy elderly. Moreover, failure with proper names is often one of patients' first complaints and this difficulty seems to be what elderly people refer to when they complain about "memory failure" to their physicians. To a certain extent, this phenomenon can be considered physiological (Semenza, 2006). However, a significant early impairment of proper name retrieval could be informative on the onset of dementia (Semenza, Mondini, Borgo, Pasini, & Sgaramella, 2003). Some evidence has been provided that naming can be predicted by a person's level of CR, although only common nouns have been considered so far in this respect (Allegri et al., 2010; Karrasch & Laine, 2003). The question therefore arises about whether the specific retrieval of proper names is predicted by high CR in older persons. The specific characteristics of proper names suggest that this may not be the case, as they are devoid of semantic attributes. According to philosophical tradition (see Kripke, 1970), proper names in fact are considered pure referring expressions since, unlike common nouns that indicate categories, they point to individual entities that do not imply attributes. Furthermore, it has recently been argued that also cognitive abilities like mathematics, which have poor semantics, may not be protected by CR (Arcara et al., 2017). The aim is therefore to analyze the association between CR and proper name retrieval and see whether older persons with early decline and very high CR are less prone to failures with proper names compared to older persons with low CR.

In Study 2 the effects of CR on proper name retrieval focus on a population with initial signs of dementia matched with a population of healthy older adults. Participants of Study 2 were individuals experiencing a series of cognitive failures in daily life. Therefore, on the indication of their family doctor, they underwent a full neuropsychological assessment. We used a proper name retrieval task and a screening task for assessing global cognitive performance. In this context, a test for the retrieval of common nouns was administered in the neuropsychological evaluation of Study 2. However, as this test was performed almost at ceiling even by patients, it was not entered in the statistics and only proper names were considered in the analysis (in the form of responses to a paper-and-pencil picture naming task). Assuming a differential semantic interconnection between nouns and bearers and assuming a strong relationship between CR and semantic richness, we expected a weak relationship between proper names and CR in both patients and healthy controls.

In Study 3, I developed a more sensitive computer-based task for name retrieval, not only for evaluating proper name retrieval but also for matching the proper name category with other types of names. As mentioned above, some previous studies have already shown significant age-related effects on proper name retrieval (Almond & Morrison, 2017; Rastle & Burke, 1996). Almond and Morrison (2017), for example, compared young and older adults in two experimental tests involving the retrieval of proper names: (1) a face-name association task and (2) a pure-list task. Their results showed evidence of age-related deficits in the face-name association task, which however was claimed to be not highly suitable for assessing age-related name recall deficits. In their study, however, names and faces used were neither famous nor familiar (i.e., participants were instructed to learn names associated to new faces). Instead, for assessing name retrieval of familiar faces, very famous people (e.g., political figures, famous actors, religious figures, etc.), widely known outside their specific domain of fame should be considered (e.g., Semenza et al., 2003). In fact, persons with name retrieval deficits can find it difficult to retrieve names of entities they have known for a long time[1]. Whether CR can modulate proper name retrieval is a relatively recent question (Mondini & Semenza, 2016), which we want to address considering also global cognitive conditions. Mondini an Semenza, (2016) analyzed the performance of 40 mildly cognitive impaired patients and showed that, while CR was positively correlated to better global cognitive profile as assessed by the MMSE, it did not predict name retrieval of famous people in a paper-and-pencil task (Semenza et al., 2003). The authors interpreted this finding as due to the arbitrary link between proper names and bearers. More clearly, the semantic operations necessary for naming proper names may, at some point of the retrieval process, be different from naming other categories of names. Moreover, since previous studies (Darby et al., 2017) showed that patients with Alzheimer's Disease and patients with mild cognitive impairment could benefit from CR in tasks that require executive and semantic functions, we expected that the semantic requirement might explain the weak relationship between CR and proper names. The theoretical distinction between proper names and common nouns has a long history (e.g., Koller & Searle, 1970; Kripke, 1970). These philosophers described the linguistic properties of proper names defining them as expressions which convey reference but not sense. Later, a series of experimental studies contributed to this issue (Evrard, 2002; Pelamatti, Pascotto, & Semenza, 2003; Semenza, 2006, 2009; Gorno-Tempini et al., 1998), reporting disproportionate age-related problems in lexical access to

[1] Although deficits in picture naming can be expected in later stages of aging (see Feyereisen, 1997) cases of earlier name retrieval deficits are often reported, especially for the category of proper names (Greene & Hodges, 1996; Semenza et al., 2003).

proper names compared to common nouns, especially in production (Brédart, Brennen, & Valentine, 1997). In contrast to common nouns, whose attributes are linked with each other in rich semantic interactions, the link between proper names and their bearers has been considered weak (e.g. Burke, MacKay, Worthley, & Wade, 1991; Semenza, 2009; Semenza & Zettin, 1988). Proper names possess particular linguistic features as do brand names (Gontijo, Rayman, Zhang, & Zaidel, 2002), which can also be very familiar due to people's exposure to commercial and advertising communication. Logo names are arbitrarily assigned to products, companies or associations and sometimes acquire popularity. They do not designate unique entities and can be conceptually categorized, similarly to common nouns (Gontijo et al., 2002). Both proper names and some logo names can be considered, at the level of retrieval, pure referential expressions since they are arbitrarily attributed to their bearers. However, while proper names are related to individual episodic experience with the bearer (i.e., episodic facts), logo names are generally more related to repeated and shared knowledge (i.e., semantic facts), which makes logo names very similar to widely used names in our social environment. Logo names, in fact, can be conceptually categorized (Gontijo et al., 2002); saying "Mercedes" while looking at its logo, may recall not only car-specific features, but also various models of the same car, which may have different engine powers, different colors, etc.

Study 3 examined (in terms of Latency and Accuracy) the effect of CR through a computer-based tool and by including more categories of names to see whether the effect of CR on proper names varied compared to name categories with varying semantic features. In this study we expected that CR would show a differential influence in retrieving names with different degrees of semantic name-bearer interconnection. We used Proper Names, Logo Names and Common Nouns as we assumed that the higher the semantic interconnection between target and bearer, the higher the influence of CR on the task. Logo Names and Common Nouns are related to the repeated and shared knowledge of their bearers, and this would make them more responsive to CR than Proper Names, which are instead weakly connected with their bearers.

To sum up, Study 2 used a traditional paper-and-pencil task to analyze the effect of CR on proper name retrieval and on global cognitive performance (MoCA scores) in persons with clinical signs of dementia matched with healthy controls. In Study 3, instead, the effect of CR was assessed not only on proper names, but also name categories with different semantic characteristics, by using a digital tool which can be suitable for the analysis of behavioral outcomes like response times and accuracy. Participants of Study 3 were older persons without dementia.

3.2. Study 2. Cognitive Reserve in pathological aging: the special case of Proper Names[1]

3.2.1. Method

Participants

The experimental sample was made of 32 participants (18 male and 14 female) who had received a medical diagnosis of probable major or mild neurocognitive disorder due to Alzheimer's Disease. They were aged 59–86 years (mean 75; SD = 6.5) with formal education of 3–22 years (mean 9; SD = 4.6). They reported a series of cognitive failures in daily life and,

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[1] Part of results of Study 2 have been reported in the following article: Montemurro, S., Mondini, S., Nucci, M., & Semenza, C. (2018). Proper name retrieval in cognitive decline. *The Mental Lexicon*, 13(2), 215-229.

on the indication of their family doctor, had undergone full neuropsychological assessment. A qualitative neuropsychological interview preceded the psychometric evaluation, allowing to obtain qualitative information about the person based on their medical history (e.g., diabetes), psychological history (e.g., loss of a family member) and cognitive history (e.g., education, occupation and other activities). The final diagnosis derived from all medical and all neuropsychological tests, the clinical interview and the medical history of each participant. The control group comprised thirty-two older individuals living independently, with no previous psychiatric history or brain impairment, who reported no difficulty in everyday life. Inclusion criteria were the absence of cognitive impairments (MoCA above the cut-off according to Conti et al., (2015); this cut-off depends on age and formal education and thus may vary among participants). This group consisted of 17 females and 15 males aged 66–92 (mean 77; SD = 6.5), with formal education of 3–18 years (mean 7; SD = 3.2). Table 3.1 shows means (M), standard deviations (SD) and t-test comparisons for age and education between the two groups.

	Patients (32)		Controls (32)				
	M	*SD*	*M*	*SD*	*t*	*df*	*p-value*
Age	75	6.4	77	6.5	1.51	62	*0.13*
Education	9	4.6	7	3.2	-1.18	62	*0.06*

Table 3.1 Descriptive analyses. Patients and healthy controls matched for age and education.

All participants voluntarily took part in the study after giving their written consent and were tested in a well-lighted comfortable room, with corrected-to- normal vision. The study was approved by the Local Ethical Committee of the School of Psychology of the University of Padua and conducted in accordance with the principles of the Declaration of Helsinki.

Materials

The patients' group underwent a complete neuropsychological evaluation, but for the current study we considered the three following tests, which were the only ones administered to the healthy elderly group: 1) The Montreal Cognitive Assessment (MoCA, Nasreddine et al., 2005); 2) The Famous Faces (FF) naming test (Semenza et al., 2003), and 3) The Cognitive Reserve Index questionnaire (CRIq, Nucci et al., 2012).

1) The MoCA (from Nasreddine et al., 2005; Italian normative data in Conti et al., 2015) is a brief neuropsychological screening test consisting of eight sub-tests tapping different cognitive domains (i.e., memory, language, visuospatial skills, executive functions, and orientation), which gives a picture of global cognitive status. MoCA is widely used in clinical practice and is very sensitive to mild cognitive impairment in aging, in case of neurodegenerative diseases (e.g., Alzheimer's disease and Lewy Body Dementia; Wang et al., 2013) or in Parkinson's disease (Biundo et al., 2014). The maximum score is 30 and the administration of the test lasts about 10–15 minutes.

2) The FF naming test is made up of 16 black and white pictures of very famous people. The examiner shows the famous pictures one by one in a fixed order, and records the responses. The pictures were all 13cm×18cm, equal in visual resolution, placed in the center of a white background. The FF naming test is useful to investigate proper naming performance in patients with suspected diagnosis of Alzheimer's disease and it derives from a study of Semenza and colleagues (2003). Normally, in single case studies, it is good practice to tailor the test on the participant's experience and milieu, including items like names of relatives and friends (Semenza & Zettin, 1989). A different strategy is advisable in group studies, whereby individually tailored tests may not be easy to administer and compare across participants. Moreover, knowledge of names of famous people cannot generally be predicted by education.

The best predictor of performance on multi-item tests including names of famous persons could be the amount of exposure to television programs, irrespective of education (indeed, highly educated people might not be the most proficient in such a task). To make sure that each single character was known by the large majority of people belonging to the age range of our patients, the FF naming test included a variety of international and local cultural settings: famous actors (e.g., Sophia Loren), political figures (e.g., Benito Mussolini, Queen Elizabeth, Silvio Berlusconi), TV characters (e.g., Mike Bongiorno, an anchor man who appeared on Italian TV for decades), widely known outside their specific domain of fame.

The FF naming test administered here has a maximum score of 16 and it derives from a preliminary study based on a group of 33 healthy Italian elderly persons (mean age 72 ± 6.3, years of education 4.12 ± 0.9) who obtained a mean score of 12.9 ± 2. With respect to the original 2003 version, some items (e.g., characters who may have faded in the collective memory) were updated to suit the present time. We also administered a control test for the retrieval of common nouns made up of 30 pictures portraying living and nonliving entities. However, the test was performed almost at ceiling even by our patients, and thus was not entered in the statistics. It is known in the field that it is difficult in a naming test to match proper names and common nouns, because the knowledge of the former varies widely among individuals, while the knowledge of the latter is more equally distributed. However, the ways adopted in various tests to overcome this problem are not easily applicable in an investigation like the present one (see Semenza et al., 2009; for a further discussion).

3) The CRIq is a semi-structured interview used to measure cognitive reserve. For a description, see paragraph 2.2.1 in the Method section of Study 1 above.

Statistical Analyses

Comparisons (t-tests) between patients with cognitive decline and healthy controls were carried out. Neuropsychological test scores were converted into percentages to compare the performance of MoCA and FF naming tests. Welch's test was applied when homogeneity of variance was significant. Two different linear regression analyses were carried out with raw scores of FF naming test (in Model 1) and MoCA test (in Model 2) as dependent variables. A null model was built as a baseline for Model 1 and Model 2. In Model 1, CRI and Group (i.e., Patients and Healthy controls) were entered as predictors of interest, and the FF naming score was the dependent variable. In Model 2, CRI and Group (i.e., Patients and Healthy controls) were entered as predictors of interest, and the MoCA score was the dependent variable.

Bayes Factors were obtained for Model 1 and Model 2 respectively, and then a Bayesian model comparison was computed. A series of Pearson's correlational analyses were performed across the three CRIq sub-scores (CRI-Education, CRI-WorkingActivity, CRI-LeisureTime), considering both the FF naming test and the MoCA test in patients and healthy elderly. All the analyses were performed by using R Software (R Core Team. Version 3.3.1, 2017) and the α level of 0.05 was set to determine significance.

3.2.2 Results

As reported above, patients and healthy elderly were not significantly different for education (see Table 3.2) and for CRI [$t(62)=0.72$, $p=0.46$]. Patients obtained a mean MoCA score of 18.5/30 (range 8–27), a mean FF naming score of 8.2/16 (range 1–16) and a mean CRI of 105.1 (range 67–149). Healthy participants showed a mean MoCA score of 26/30 (range 23–30), a mean FF naming score of 13.4/16 (range 9–16) and a CRI mean score of 108.6 (range 84–151) (see Table 3.2). As expected, patients and controls significantly differed in both MoCA [t(62)=8.00, p<.001; Cohen's d=2.01] and in FF naming test [t(62)=6.69, p<.001; Cohen's d = 1.67].

	Patients (32)		Controls (32)				
	M	*SD*	*M*	*SD*	*t*	*df*	*p-value*
CRIq	105.1	22	108.6	14.6	0.72	62	*0.46*
MoCA	18.5	5	26	1.77	8	62	*<0.001*
FF naming test	8.2	4.1	13.4	1.5	6.69	62	*<0.001*

Table 3.2. Group comparisons. Patients and healthy controls (i.e., healthy elderly) on the Cognitive Reserve Index questionnaire (CRIq), Montreal Cognitive Assessment (MoCA) task, and the FF naming test.

Figure 3.1 shows accuracy scores of patients at their first neuropsychological evaluation and accuracy scores of healthy controls, in both MoCA test and FF naming test.

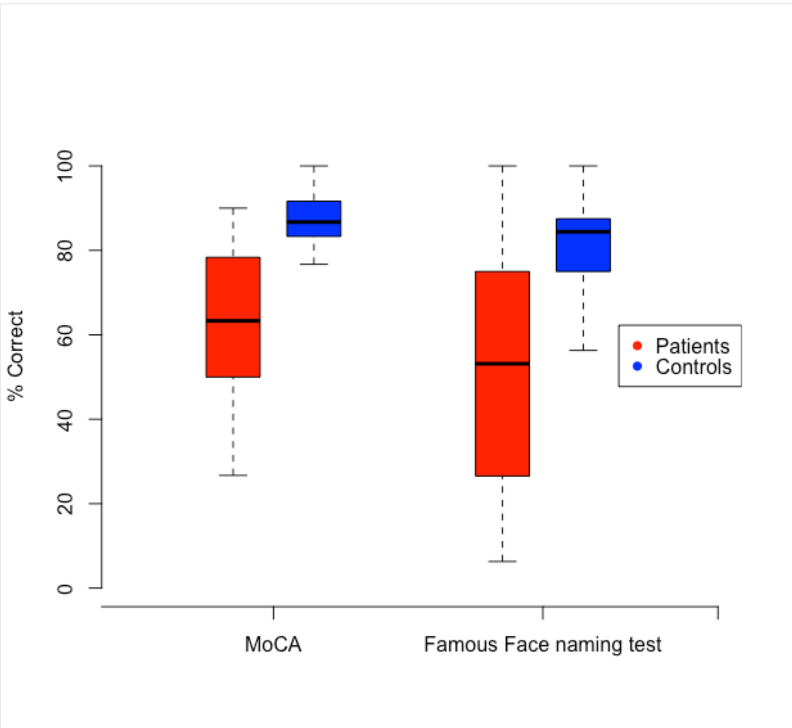

Figure 3.1. Cognitive tasks in patients and healthy controls. Tasks: Montreal Cognitive Assessment (MoCA) and the Famous Face naming test.

In Model 1, CRI and Group were entered in the model as predictors of the scoring on the FF naming task scores. Entering only the CRI score did not produce a significant improvement in the model fit (*B* =0.06, p=0.29). CRI and Group were then considered as interaction terms in the same model, and the Bayesian model comparison showed that the model that did not include the interaction between CRI and Group was 2.5 times more plausible than the model with the interaction between CRI and Group (see Figure 3.2), suggesting that CR did not influence the performance on FF naming task and did not explain any difference across Patients and Controls on this task.

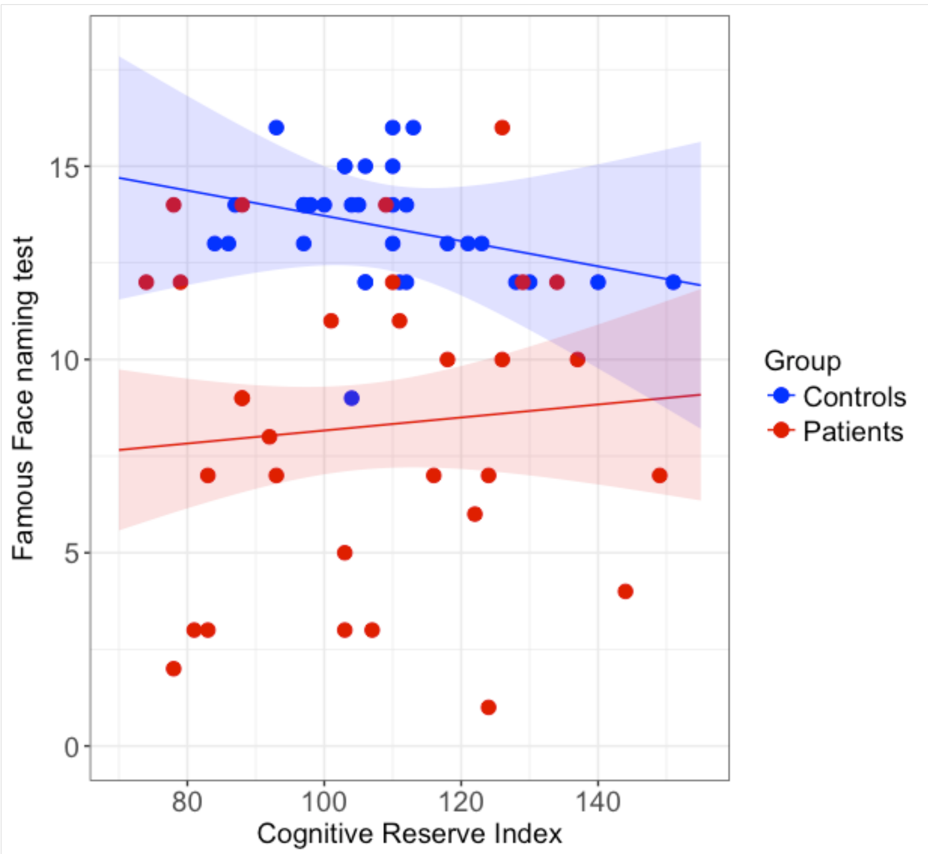

Figure 3.2 Interaction between Group and CR on performance in the FF naming test. Results of linear regression analyses based on the performance of patients (red line) and controls (blue line).

In Model 2, entering the CRI score produced a significant improvement in the model fit (B = 0.25, p<0.001) and the interaction between CRI and Group was significant ($B = -0.13$, $p < 0.01$). Bayesian model comparison showed that the model with the interaction between CRI and Group was 6.3 times more plausible compared to the model without this interaction (Figure 3.3). This suggested that CR influenced the performance on the MoCA, and it explained significantly differences between Patients and Controls on this task. Results of linear regression analyses are reported in Table 3.3.

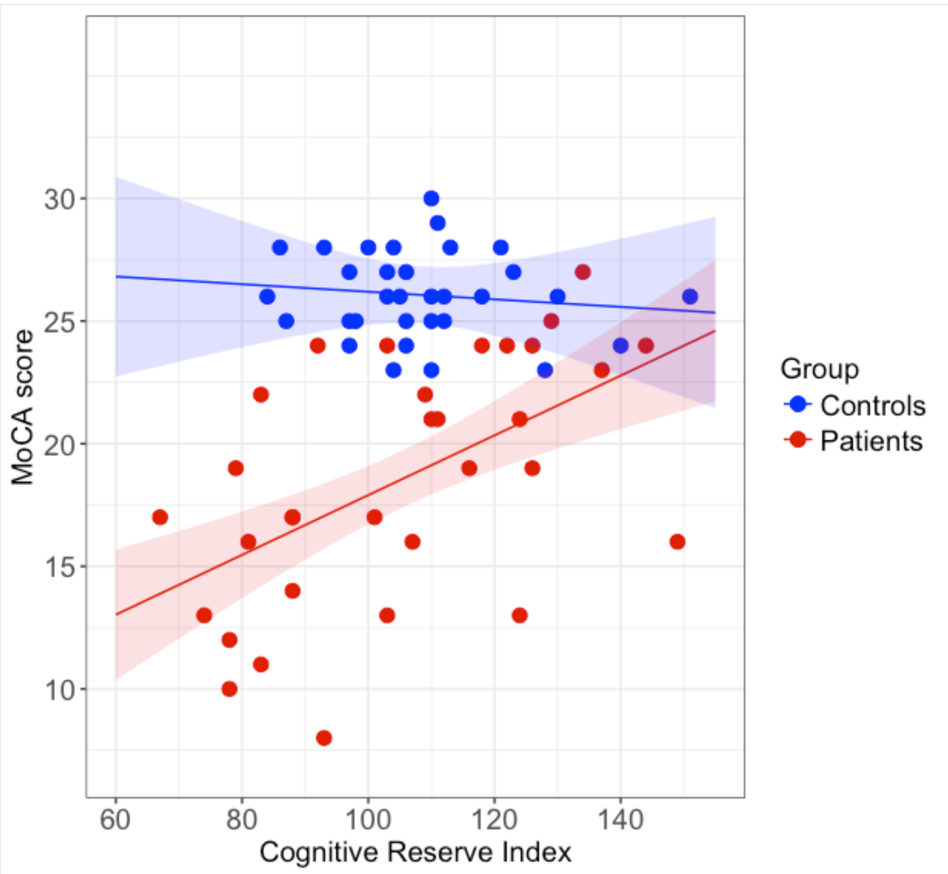

Figure 3.3. Interaction between Group and CR on performance in the MoCA test. Results of linear regression analyses based on the performance of patients (red line) and controls (blue line).

	FF naming test				MoCA			
	Beta	SE	t	p-value	Beta	SE	t	p-value
(Intercept)	-4.02	6.82	-0.58	0.55	-16.3	7.18	-2.3	0.02
CRI	0.066	0.06	1.05	0.29	0.26	0.06	3.9	< 0.01
Group	10.5	4.97	2.11	0.03	22.02	5.23	4.2	< 0.001
CRI*Group	-0.04	0.04	-1.08	0.28	-0.13	0.04	-2.8	< 0.01

Table 3.3 Linear regression models and results for predictors of interest. Dependent variables: FF naming test, Montreal Cognitive Assessment test (MoCA), and CRI = Cognitive Reserve Index questionnaire; Group = older persons with cognitive decline matched with healthy elderly.

As expected, CRI total score of all participants correlated with its sub-scores, [CRI-Education ($r(64) = 0.70$), CRI-WorkingActivity ($r(64) = 0.77$), CRI-LeisureTime ($r(64) = 0.65$)]. In the patients' group, CRI sub-scores correlated with MoCA [CRI-Education: $r(32) = 0.34$; CRI-WorkingActivitiy: $r(32) = 0.42$; CRI-LeisureTime: $r(32) = 0.54$], but not with FF naming test [CRI-Education: $r(32) = 0.002$; CRI-WorkingActivity: $r(32) = 0.09$; CRI-LeisureTime: $r(32) = 0.10$]. The control group showed a very heterogeneous pattern of results with a few negative not clearly interpretable correlations between CRI sub-scores and MoCA [CRI-Education: $r(30)=-0.17$, CRI-WorkingActivity: $r(30)=0.10$, CRI-LeisureTime: $r(32)=-0.31$], and also between CRI and FF naming test [CRI-Education: $r(30) = -0.13$; CRI-WorkingActivity: $r(30) = -0.37$; CRI-LeisureTime: $r(30) = -0.09$].

3.2.3 Discussion

The purpose of Study 2 was to verify whether proper name retrieval and global cognitive performance might be affected by CR. Results show that CR affects patients' global cognitive performance (that is, the status of their cognitive profile), but not their ability to retrieve proper names. The reason for this absence of correlation between CR and proper name retrieval in patients may be related, on the one hand, to the strong link between CR and semantic memory

(Darby et al., 2017; Reed et al., 2011) and, on the other, to the peculiar nature of proper names. As distinct from common nouns (whose attributes interact with each other in complex semantic connections), proper names can be considered purely referring expressions, labeling unique entities: their link with these entities is weaker than the link between common nouns and the entities they label (Burke et al., 1991; Semenza, 2009; Semenza & Zettin, 1989). In other words, proper names designate individual features rather than conceptual categories (e.g., Burke, et al., 1991). Compared with common nouns, which are strongly related with conceptual categories interacting with each other via high-probability connections, the semantic network labeled by proper names is purely incidental (Semenza, 2009). Consequently, while compensatory processes might be very efficient in many everyday life tasks "masking" cognitive symptoms when a pathology is underway (e.g., Mortimer et al., 2005; Spitznagel & Tremont, 2005), the same processes may not be of any help in proper name retrieval.

However, the present study shows that CR is associated with general cognitive functioning (i.e., the MoCA score), but only in the patients' group. This result may be simply due to the fact that MoCA is performed at ceiling by healthy participants. Only when pathology and/or age-related changes occur, primary task-related networks may need additional, compensatory networks to maintain those cognitive functions (Barulli & Stern, 2013). In healthy people CR may only be recruited when a task is very demanding (see Ansado et al., 2013).

In the patients' group, the association between each CRI sub-component and the performance at the MoCA and the FF naming test shows very homogenous pattern of correlation. Instead, in the group of healthy elderly no clear correlation emerges between CRI sub-components and performance in both the MoCA and the FF naming test. A high negative correlation was found between CRI-WorkingActivity and FF naming test. This is hard to interpret, but it may be related to the fact – observed but never demonstrated – that knowledge of famous persons in the media seems to be higher in people with less demanding occupations. Further investigation should address this point. A limitation of this study is the absence of a comparable common noun retrieval test, which, according to our assumptions, should be significantly influenced by CR due to the richer semantic connections of common nouns. The common noun retrieval test used in this study was performed at ceiling by most patients and thus experimentally useless. Future research should focus on the development of graduated tests of equal difficulty to compare the performance on proper names and on common nouns considering CR as a factor of interest.

3.3. Study 3. Different Cognitive Reserve effects across Proper Name, Common Noun, and Logo Name retrieval in aging[1]

Compared to Study 2, in which name retrieval ability was investigated considering only proper names through a paper-and-pencil task, in Study 3 the effect of CR on name retrieval was investigated comparing proper names with other name categories, through a computerized task developed ad-hoc for this study. Finally, in Study 3 we wanted to test older adults without clinical signs of dementia, but with varying degrees of cognitive functioning to see how the effect of CR on ability to retrieve names differed depending on cognitive conditions.

[1] Part of results of Study 3 have been reported in the following article: Montemurro S, Mondini, S, Crovace, C, & Jarema, G (2019). Cognitive Reserve and its effect in older adults on retrieval of Proper Names, Logo Names and Common Nouns. *Frontiers in Communication*, 4, 14. doi: 10.3389/fcomm.2019.00014.

3.3.1. Method

Participants

A total of forty-six Italian native speakers (28 women, 18 men) aged from 65 to 96 years and with 3 to 21 years of education participated in the study (Table 3.4). An informal interview allowed to record information about their medical history, which showed no symptoms of psychiatric disease or neurological impairment. They were administered the MoCA, the Cognitive Reserve Index questionnaire (CRIq, Nucci et al., 2012) and a Picture Naming task.

	Participants (N = 46)		
	M	*SD*	*Range*
AGE	81.09	7.73	65 - 96
EDUCATION	8.89	4.61	3 - 21
MoCA	20.63	4.01	14 - 27
CRI	97.91	23.63	59 - 152

Table 3.4. Descriptive data of participants: AGE = years; EDUCATION = years of formal education; MoCA = raw scores at the MoCA test (Nasreddine et al., 2005); CRI = Cognitive Reserve Index (from the Cognitive Reserve Index questionnaire; Nucci et al., 2012); M = mean; SD = standard deviation.

Materials and Procedure

The MoCA test is a brief neuropsychological tool, which provides a global cognitive profile. It consists of eight sub-tests tapping different cognitive domains (i.e., memory, language, visuospatial skills, executive functions, and orientation in time and space). For a description of the MoCA test, see the descriptions of materials in paragraphs 2.2.1 and 3.2.1 of Study 1 and Study 2. As reported in Table 3.4, the range of participants' raw scores on the MoCA test ranged from 14 to 27. Each raw score was then adjusted for age and education according to the Italian normative data of Conti et al. (2015). All participants' scores fell within the non-clinical population (i.e., above the adjusted Italian cut-off of 17.36). More specifically, considering the global cognitive performance of our participants, the 19.56% of their adjusted scores fell within the borderline/fragile (but not pathological) group, and the rest of the participants fell within the preserved elderly.

Cognitive Reserve was measured with the Cognitive Reserve Index questionnaire (Nucci et al., 2012), which is a semi-structured interview. It requires approximately 10 min to complete and includes 20 questions grouped into three sections: Education (CRI-Education), Working activities (CRI-WorkingActivity), and Leisure time activities (CRI-LeisureTime). For a description of the CRIq, see the descriptions of materials in paragraphs 2.2.1 and 3.2.1 of Study 1 and Study 2.

The Picture Naming task was a computer task to measure naming Latency and naming Accuracy. We decided to build this test ad-hoc for the present study, based on evidence that computer-based tasks are more precise and suitable for stimulus control and repeated measure analysis (e.g., (Maruish & Moses, 1996). Picture selection was based on a total of 159 colored images, preliminarily rated on a 1–7 Likert scale according to Familiarity, Difficulty of naming and Age of Acquisition. Pictures represented three categories of entities: very famous persons, well-known Logos, and living, and non-living things. Pictures of famous persons were chosen from a variety of settings, such as movies (e.g., "Sean Connery," "Marilyn Monroe"), politics (e.g., "Vladimir Putin," "Angela Merkel"), and religious contexts (e.g., "Pope Francis," "Mother Teresa"), to make sure that each of them would have been known by a large majority of people. Logos were chosen from a wide range of international and local symbols whose visual representation was very frequent both in Italian and International settings (e.g., sport brands such as "Nike," "Adidas"), car companies (e.g., "Audi" and "Mercedes"), commercial products (e.g., "Rolex" and "Benetton"). We excluded Logos whose visual representation carries the meaning of the name (e.g., "Apple") and Logos whose visual representation carries the initial letter of the name (e.g., "McDonald's"). The pictures of living and non-living things for Common Nouns derived (with few adjustments) from a set of 360 high-quality color images (Moreno-Martínez & Montoro, 2012). A group of forty healthy Italian individuals (15 women, 25 men), with no history of neurological or psychiatric disease (mean age = 73.5 ± 7.6; mean education = 10.2 ± 5.1) rated all the pictures. Participants were asked to judge them on a 1– 7 Likert scale according to Familiarity, Difficulty of naming and Age of Acquisition. For Familiarity, participants were asked to rate each picture from 1 to 7, where 1 indicated "completely unknown" and 7 indicated "highly familiar" (Moore & Valentine, 1998; Salmon, McMullen, & Filliter, 2010). For Difficulty, participants were asked to rate each image from 1 to 7, where 1 indicated "impossible to name" and 7 indicated "very easy to name" pictures (e.g., Moreno-Martínez & Montoro, 2012). For Age of Acquisition, participants were asked to rate each image from 1 to 7, where 1 indicated "never acquired" and 7 indicated "acquired very early": before 3 years of age (e.g., Valentine, 1998; Salmon et al., 2010). Examples were provided before starting the rating phase. A 1–7 Likert scale was visually available to participants, for each variable, during the entire scoring process. The rating allowed to eventually select 30 pictures for each of the three categories (i.e., Proper Names, Logo Names, and Common Nouns) for the computerized Picture Naming task. See Table 3.5.

Name Categories	**Familiarity**				**Difficulty**				**Age of Acquisition**			
	Mean	SD	MIN	MAX	Mean	SD	MIN	MAX	Mean	SD	MIN	MAX
Proper Names	6.14	0.58	5.05	7.01	5.16	0.54	4.15	6.25	2.08	0.22	1.75	2.65
Common Nouns	5.89	0.98	3.33	6.93	5.08	0.79	3.2	5.98	3.97	0.97	2.2	5.73
Logo Names	3.68	1.59	1.53	6.53	2.89	1.41	0.9	5.53	1.68	0.44	1.13	2.6

Table 3.5. Results of the Likert scale rating for item selection. Familiarity of images, Difficulty of naming and Age of Acquisition of images of Proper Names, Common Nouns and Logo Names.

As expected, Logo Name pictures were rated as less familiar than both Proper Names ($B = -2.47$, $p < 0.001$) and Common Noun pictures ($B = -2.47$, $p < 0.001$), which did not differ from each other ($B = 0.26$, $p = 0.36$). Logo Name images have been judged as the most difficult to retrieve compared to both famous faces ($B = 2.27$, $p < 0.001$) and Common object images ($B = 2.18$, $p < 0.001$), which did not differ from each other ($B = 0.09$, $p < 0.71$). Finally, Common Noun pictures were acquired significantly earlier than both famous face images ($B = -1.88$, $p < 0.001$) and Logo pictures ($B = -2.3$, $p < 0.001$), while famous face images were acquired earlier than Logo Name pictures ($B = -0.4$, $p < 0.01$).

To sum up, Logo pictures were less familiar, later acquired and they have been judges as more difficult to name than the other two categories. While pictures of famous faces and pictures of common objects were balanced for the two first psycholinguistic variables (Familiarity and Difficulty of naming), Age of Acquisition was, as expected, higher for famous faces. The final set of the computerized Picture Naming task consisted of 90 colored images: 30 famous faces for Proper Names, balanced across international/local and male/female characters; 30 pictures for Common Nouns, balanced across living/non-living things; 30 pictures of logos for Logo Names, balanced across international/local subjects (see Figure 3.4 for some examples).

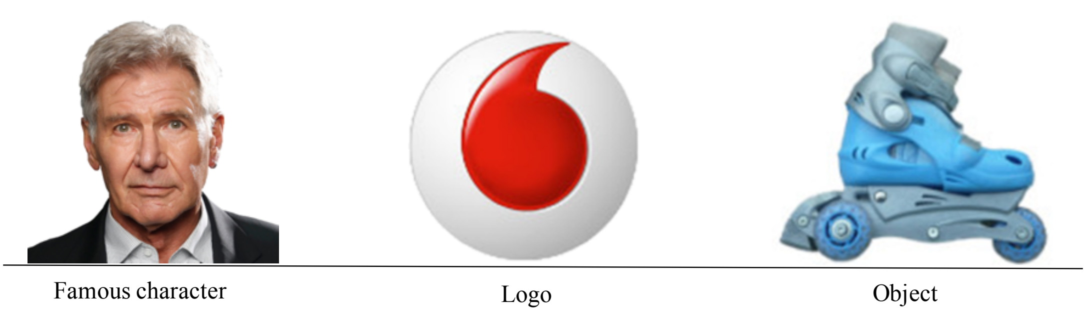

Figure 3.4. Example of figures of the Picture Naming task: famous character on the left hand-side for proper name retrieval; logo image at the center for logo name retrieval (source: https://www.istockphoto.com/ca). Object image on the right hand-side for common noun retrieval; no permission is required for the use of this image (Moreno-Martínez & Montoro, 2012).

Each participant attended a training session before performing the experimental session. Instructions were presented in written and in verbal form; they were repeated if necessary. Image dimension was standardized with GIMP software in a 400×400 pixel-frame. A fixation point appeared on the center of the computer screen for 500 milliseconds (ms), followed by a blank of 150 ms; then the picture was shown in the center of the screen on a white background and remained on the screen until the participant gave a verbal response through the microphone (via voice-key), either naming the picture (correctly or incorrectly) or giving an "I don't know" answer[1]. Pictures were presented randomly, both inter-category and across categories. Latency and Accuracy were recorded. The Picture Naming task was built in E-Prime®, and the administration lasted about 10 min. The participants took part in the study voluntarily. The consent obtained from all participants was both written and informed. The study was approved by the Local Ethical Committee of the School of Psychology of the University of Padua and conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analyses

Analyses were computed through mixed-effects models (Pinheiro & Bates, 2000) which have been shown to provide awareness about factors that potentially contribute to the structure of our data (Baayen et al., 2008). In particular, Generalized Linear mixed-effect models (GLMM) were used for modelling response times and accuracies (Baayen et al., 2008; Quené & van den

[1] A limitation of our study is that the picture naming task did not register different types of errors. Name retrieval errors and recognition errors are two different responses based on different cognitive mechanisms (see Semenza, 2006 for a discussion of recognition and name retrieval errors).

Bergh, 2008). Random effects for all GLMMs were ID (i.e., subject identity) and TrialList (i.e., picture identity). All Latency analyses were made on participants' correct scores. Accuracy was entered as binomial dependent variable in which the whole set of responses (4,140 data-points, both correct and incorrect) were considered in a repeated-measure design, which avoids the proportion aggregation of binomial data and provide a balanced method of analysis in psycholinguistic (Quené & Van den Bergh, 2008). Fixed effects (i.e., independent variables) for Latency and Accuracy analyses were CRI (as a continuous variable), MoCA score (as a continuous variable) adjusted for age and education, and Category (i.e., Proper Names, Logo Names and Common Nouns). All GLMM analyses started from a null model that included only an intercept; then all the independent variables were added. Likelihood Ratio Test was used for model comparison. Akaike's Information Criterion (AIC; Sakamoto et al., 1986) and Delta-AIC (Burnham and Anderson, 2003) were used to examine model plausibility. Cook's distance (Cook & Weisberg, 1982) was measured to detect influential data and next the whole dataset was considered without excluding any observations. For the analysis of Latency on the naming task, CRI and MoCA were first entered separately in the null model. Next, CRI and MoCA were considered as additional terms and as interaction terms, respectively, in two separate models. The same procedure was followed for the Latency analysis considering CRI and Category as predictors of interest. See Table 3.6a for more details about each model. For the analysis of Accuracy of responses at the naming task, CRI and MoCA were first entered separately as independent variables in the null model. Next, CRI and MoCA were considered as additional terms and as interaction terms, respectively, in two separate models. The same procedure was followed for Accuracy considering CRI and Category as independent variables (see Table 3.6b for more details about each model).

	Cognitive Reserve and global cognitive profile	AIC	AIC w	*Pr(>Chisq)*
Model 0	RT ~ 1 + (1|ID) + (1|TrialList)	22,867.2	0.10	-
Model 1	RT ~ MoCA + (1|ID) + (1|TrialList)	228,58.9	0.65	< 0.001
Model 2	RT ~ CRI + (1|ID) + (1|TrialList)	22,869.1	0.01	< 0.001
Model 3	RT ~ CRI + MoCA + (1|ID) + (1|TrialList)	22,860.9	0.24	0.024
Model 4	RT ~ CRI * MoCA + (1|ID) + (1|TrialList)	22,862.7	0.09	< 0.001
	Cognitive reserve and name categories			
Model 1	RT ~ CAT + (1|ID) + (1|TrialList)	22,864.8	0.46	< 0.001
Model 3	RT ~ CRI + CAT + (1|ID) + (1|TrialList)	22,866.7	0.18	< 0.001
Model 4	RT ~ CRI * CAT + (1|ID) + (1|TrialList)	22,867	0.15	0.15

Table 3.6a General Linear Mixed Effect Models. Dependent Variable: RT (i.e., name retrieval time response in milliseconds. Fixed effects: MoCA = Montreal Cognitive Assessment test (Nasreddine et al., 2005); CRI = Cognitive Reserve Index (Nucci et al., 2012); CAT = name categories (i.e., Proper Names, Logo Names, and Common Nouns). Random Effects: ID = subject identity; Trials = picture identity. AIC = Akaike's Information Criterion; AIC w = AIC weight; Pr(>Chisq) = Chi-Square probability associated to the model.

	Cognitive Reserve and global cognitive profile	AIC	AIC w	*Pr(>Chisq)*
Model 0	ACC ~ 1 + (1|ID) + (1|TrialList)	3,995.4	0.01	-
Model 1	ACC ~ MoCA + (1|ID) + (1|TrialList)	3,982.1	0.01	< 0.001
Model 2	ACC ~ CRI + (1|ID) + (1|TrialList)	3,988.7	0.01	< 0.001
Model 3	ACC ~ CRI + MoCA + (1|ID) + (1|TrialList)	3,974.7	0.54	< 0.001
Model 4	ACC ~ CRI * MoCA + (1|ID) + (1|TrialList)	3,975.1	0.43	< 0.21
	Cognitive reserve and name categories			
Model 1	ACC ~ CAT + (1|ID) + (1|TrialList)	3,958.1	0.01	< 0.001
Model 3	ACC ~ CRI + CAT + (1|ID) + (1|TrialList)	3,951.4	0.01	0.002
Model 4	ACC ~ CRI * CAT + (1|ID) + (1|TrialList)	3,943	0.98	< 0.01

Table 3.6b General Linear Mixed Effect Models. Dependent Variable: ACC (i.e., accuracy of name retrieval). Fixed effects: MoCA = Montreal Cognitive Assessment test (Nasreddine et al., 2005); CRI = Cognitive Reserve Index (Nucci et al., 2012); CAT = name categories (i.e., Proper Names, Logo Names, and Common Nouns). Random Effects: ID = subject identity; Trials (picture identity). AIC = Akaike's Information Criterion; AIC w = model averaging; Pr(>Chisq) = Chi-Square probability associated to the model.

We assessed the relationship between CRI (i.e., our predictor of interest) and psycholinguistic measures related to the pictures on naming performance, in order to evaluate if higher CRI was correlated with better performance in the case of items that were judged less familiar, more difficult to name and acquired later, compared to lower CRI. In addition, we assessed the relationship between Category and Psycholinguistic variables on naming performance, without entering the CRI. All the analyses were performed by means of R Software (R Core Team, 2016 version 3.3.1) and GLMM was run by means of lme4-package (Bates et al., 2014), with an α level of 0.05 defining significance.

3.3.2 Results

Results are grouped in separate sections considering Latency and Accuracy as measures of performance in the Picture Naming task. In the first section, we report results about the effect of Cognitive Reserve on naming performance; in the second, we report the results of Cognitive Reserve and the global cognitive profile as predictors of naming performance; in the third, we report the results of Cognitive Reserve and Category as predictors of naming performance; and finally in the fourth, we report the results of the analyses in which Cognitive Reserve, Psycholinguistic variables, and Category are entered as predictors of naming performance.

Cognitive Reserve on Naming Performance

CRI was our measure of CR and was entered as a continuous variable. CRI significantly predicted both naming Latency ($B = -0.01$, $t = -11$; $p < 0.01$) and naming Accuracy ($B = 0.54$, $z = 3.09$; $p < 0.01$), with participants performing better when CRI was higher; see Figure 3.5. Based on Delta-AIC as a measure to check model plausibility (Burnham & Anderson, 2002), the model with CRI as the only independent variable was 63 times more plausible than the null model for the Latency analysis, and 813 times more plausible than the null model for the Accuracy analysis.

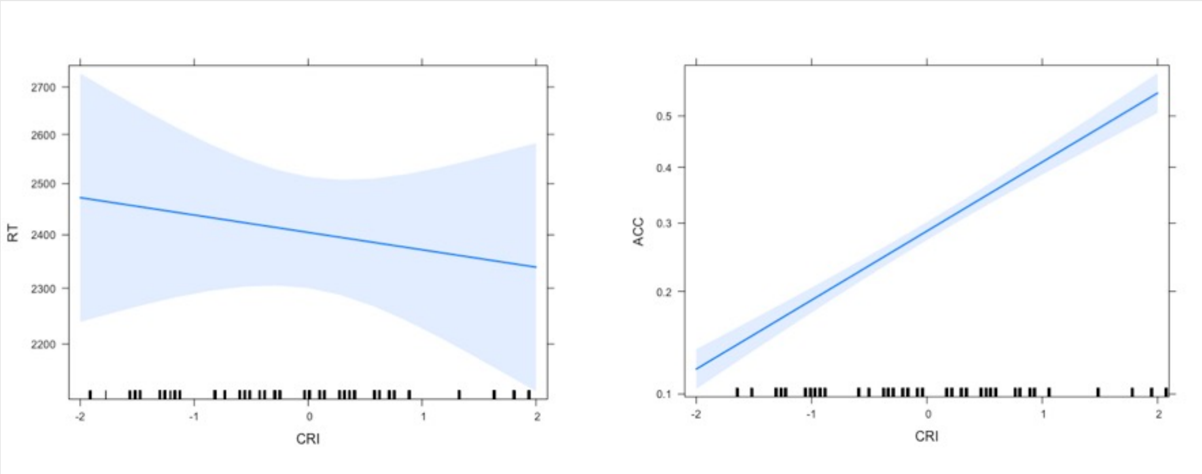

Figure 3.5 CRI as predictor of name retrieval Latency and Accuracy. Response Times and Accuracies were significantly predicted by the amount of CR in the group of older adults. RT = response times; ACC = accuracy.

Cognitive Reserve and Global Cognitive Profile on Naming Performance

MoCA (Montreal Cognitive Assessment, a measure of global cognitive profile) was a continuous variable entered in the null model. Based on the interaction between CRI and MoCA, these two independent variables improved the model fit and predicted name retrieval Latency ($B = 0.005$, $t = 7$; $p < 0.001$) with a stronger CRI effect when the cognitive profile score was in the low range (MoCA < 23). The model with the interaction between CRI and MoCA was about 24 times more plausible than the model with CRI as the only independent variable [$\chi2(2) = 10.35$, $p < 0.01$]. This suggests that global cognitive profile and CRI taken together strongly predicted name retrieval Latency in older adults. The MoCA score predicted the overall Accuracy of name retrieval when it was the only independent variable ($B = 0.23$, $z = 4.24$; $p < 0.01$), and adding the CRI to the MoCA improved the model fit [$\chi2$ (2) = 9.32, $p < 0.001$]. These two variables were then considered as interaction terms and no significant improvement was found ($B = -0.06$, $z = -1.25$; $p = 0.21$). However, the Likelihood Ratio Test carried out to compare the model with CRI and MoCA as interaction terms and the model with

MoCA as a single variable showed a better fit for the former [$\chi2$ (2) = 10.85, p = 0.004], with a stronger CRI effect when the MoCA score was in the low range (MoCA < 23; Figure 3.6).

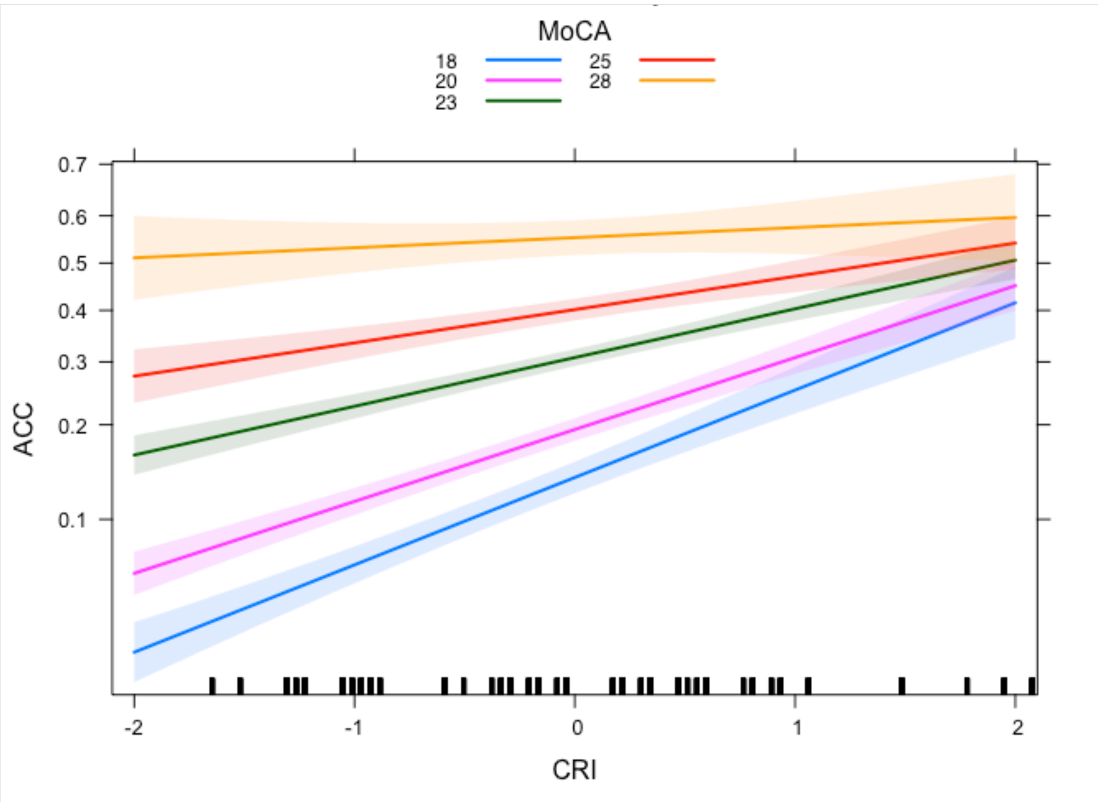

Figure 3.6. CRI and MoCA[1] as predictors of name retrieval Accuracy. ACC = accuracy. Compensatory effects of CR on name retrieval accuracy outcomes was significantly stronger when the cognitive profile was in the lower ranges.

Cognitive Reserve on Naming Performance According to Category (Proper Names, Logo Names and Common Nouns)

Entering in the null model Category as the factorial variable (three levels: Proper Names, Logo Names, and Common Nouns) significantly improved the model fit compared with the null model in both Latency [$\chi2$ (2) = 6.35, p = 0.04], and Accuracy $\chi2$ (2) = 41.26, p < 0.001). Common Nouns were retrieved faster and more accurately than Proper Names (Latency: B =

[1] MoCA ranges generated by default through the analyses in R.

0.15, t = 126; p < 0.001; Accuracy: B = −0.64, z = −2.05; p = 0.04) and also than Logo Names (Latency: B = 0.16, t = 130; p < 0.001; Accuracy: B = −2.23, z = −6.94; p < 0.001). Proper Names, on the other hand, were retrieved faster and more accurately than Logo Names (Latency: B = 0.004, t = 4; p < 0.001; Accuracy: B = −1.59, z = −4.95; p = 0.001); see Figure 3.7. for more details about Accuracy results across the three categories.

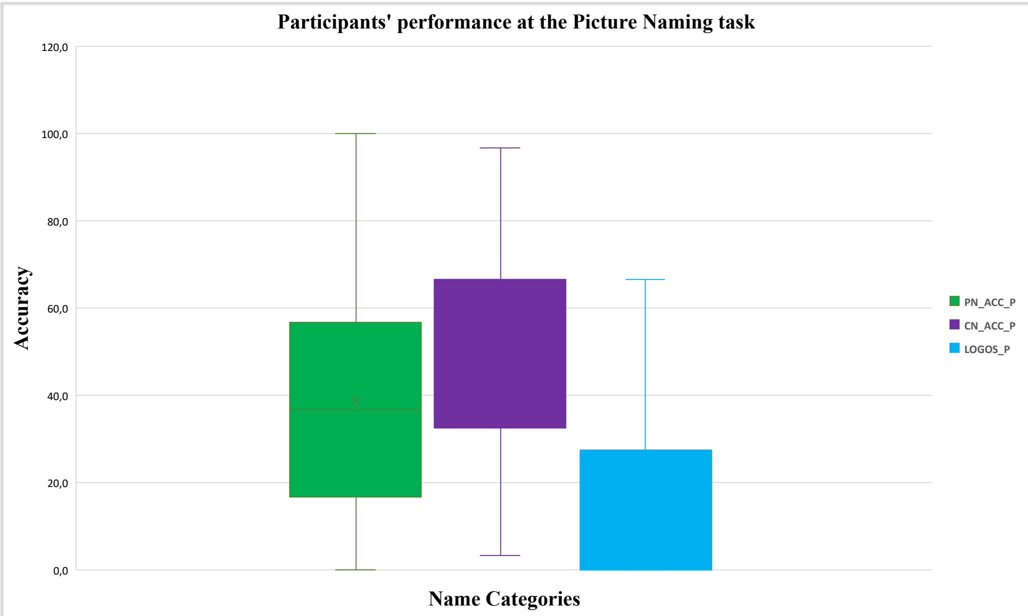

Figure 3.7 Accuracy on Picture Naming task. Three different name categories considered. PN_ACC_P = Proper Names; CN_ACC_P = Common Nouns; LOGOS_P = Logo Names.

When Category and CRI were entered as independent variables, no effect of CRI was found on Latency across the three categories, either in the case of CRI and Category as additional terms [$\chi 2$ (1) = 0.09, p = 0.75], or when CRI and Category were considered as interaction terms [$\chi 2$ (1) = 3.75, p = 0.15]. These results suggest that having higher or lower CR does not significantly affect the speediness of name retrieval across the three categories. Noteworthy, Figure 3.8 shows similar trends between Common Noun and Logo Name retrieval, compared to Proper Name retrieval.

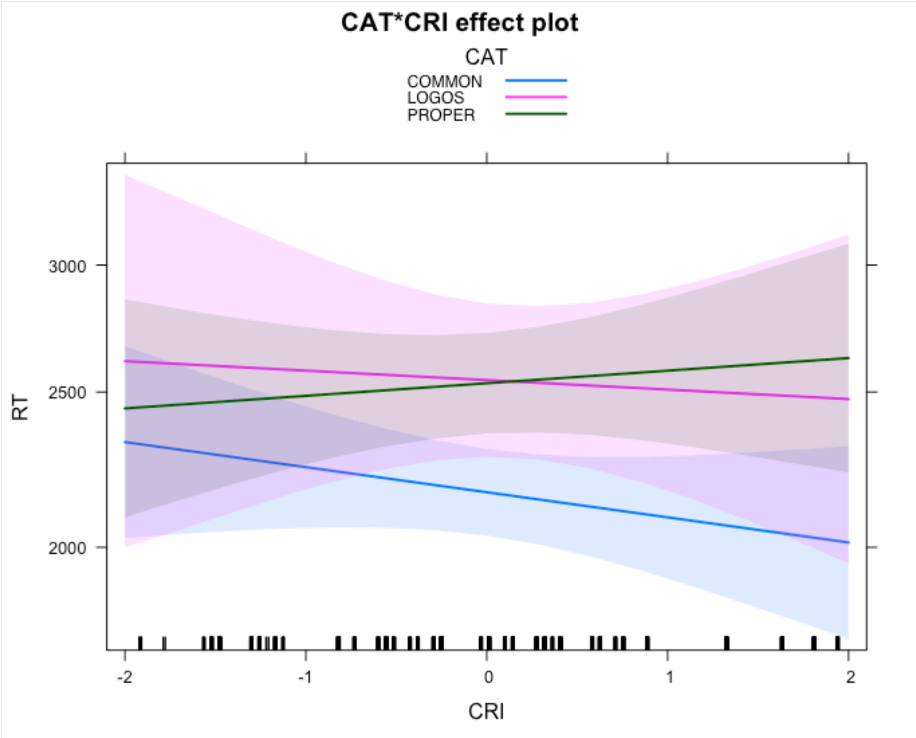

Figure 3.8. CRI and Category as predictors of latency of responses: CAT = category. RT = response times expressed in milliseconds.

Table 3.7. shows the summary result of the model of interest, (i.e., where CRI and Category are entered as interaction terms and Latency is the dependent variable).

	CR and Category (Latency)			
	Beta	SE	Z	p-value
(Intercept)	7.68	0.07	105.58	< 0.001
LN	0.16	0.07	2.14	0.03*
PN	0.15	0.07	2.23	0.02*
CRI	-0.03	0.04	-0.75	0.45
CRI: LN-CN	0.02	0.03	-0.56	0.57
CRI:PN-CN	-0.05	0.02	-1.94	0.05
CRI:PN-LN	-0.03	0.04	0.76	0.44

Table 3.7. Generalized Linear Mixed Models analyses and results. Dependent variable: Latency for name retrieval (milliseconds). Fixed effects: CRI = Cognitive Reserve Index and name Category (CN = Common Nouns; PN = Proper Names; LN = Logo Names). Random effects: subject identity and trial list. CRI:PN-CN was obtained in the relevel function in R.

Results on Accuracy showed a significant effect of CRI across name categories. CRI and Category as interaction terms predicted Accuracy (B = −0.35, z = −3.24; $p < 0.01$) and this model was about 68 times more plausible than the model with CRI and Category entered as additional terms. Entering CRI and Category as interaction terms showed significant improvement in the model fit, compared with entering name Category as the only variable of interest [$\chi 2$ (1) = 21.19, $p < 0.001$]. Table 3.8 shows summary results of the model of interest (i.e., based on the model with CRI and Category as interaction terms and Accuracy as dependent variable).

	CRI and Category (Accuracy)			
	Beta	**SE**	**Z**	**p-value**
(Intercept)	-0.58	0.28	-2.06	0.03
CN	0.62	0.31	1.97	< 0.4*
LN	-1.66	0.32	-5.11	< 0.001***
CRI	0.36	0.18	1.97	0.4*
CRI:LN-PN	0.35	0.11	3.24	< 0.01**
CRI:NC-PN	0.26	0.09	2.69	< 0.01**
CRI:NC-LN	-0.09	0.11	-0.81	0.41

Table 3.8 Generalized Linear Mixed Models analyses and results. Dependent variable: Accuracy of name retrieval. Fixed effects: CRI = Cognitive Reserve Index and name Category (CN = Common Nouns; PN = Proper Names; LN = Logo Names). CRI:NC-LN was obtained by the relevel function in R. Random effects: subject identity and trial list.

In line with our hypothesis, the effect of CRI on name retrieval Accuracy was significantly lower for Proper Names than for Common Nouns (B = 0.26, z = 2.69, $p < 0.01$) and Logo Names (B = 0.35, z = 3.24, $p < 0.01$). The effect of CRI on Accuracy did not differ when comparing Logo Names and Common Nouns (B = −0.09, z = −0.81, p = 0.41) (Figure 3.9).

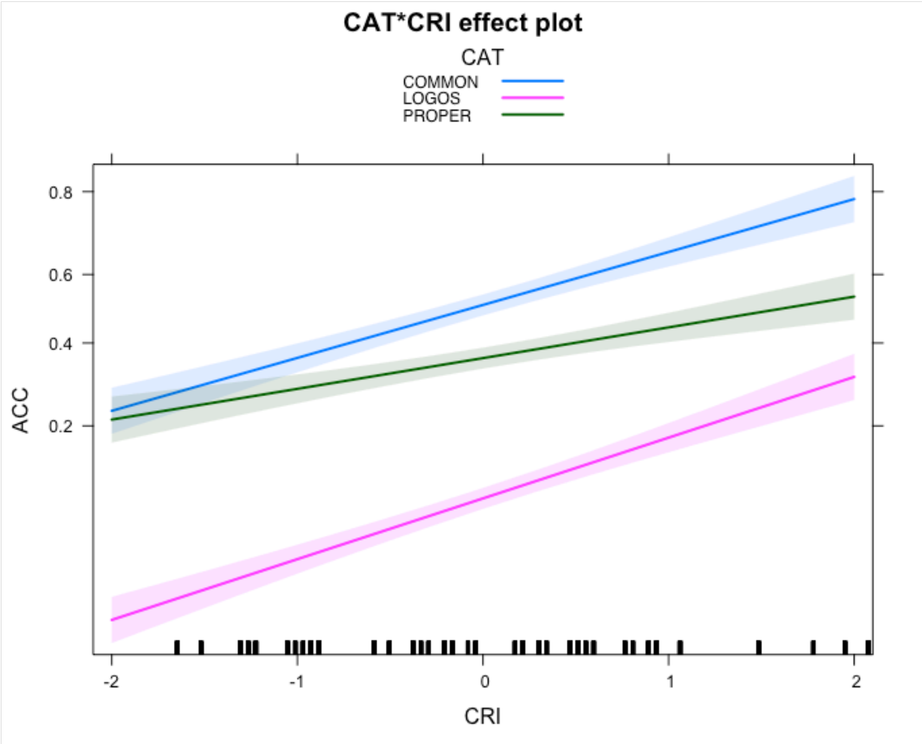

Figure 3.9 CRI AND CATEGORY FOR ACCURACY ANALYSIS: Generalized Linear Mixed Models results. CRI = Cognitive Reserve Index questionnaire; CAT = category. ACC = accuracy.

Cognitive Reserve and Psycholinguistic Variables

Psycholinguistic variables had a different role in the three categories on Accuracy. Participants' performance in the picture naming task was better for higher familiar pictures (B = 0.38, z = 3.05, p < 0.01) and for those whose names that were judged easier to retrieve (B = 0.36, z = −2.37, p = 0.01), with no significant effect of Age of Acquisition (B = 0.27, z = 1.82, p = 0.06). Post-hoc analyses showed that Familiarity predicted Accuracy in Proper Names (B = 0.66, z = 2.42, p = 0.01), but not in Common Nouns (B = −0.03, z = −0.24, p = 0.81) and not in Logo Names (B = 0.03, z = 0.24, p = 0.81). In a similar way, Difficulty predicted Accuracy in Proper Names (B = −4.58, z = −2.91, p < 0.01), but not in Common Nouns (B = 0.98, z = 1.04, p = 0.29) and not in Logo Names (B = 0.96, z = 1.03, p = 0.31). We evaluated if higher CR predicted Accuracy of Names that were less familiar, more difficult to retrieve and acquired later. Entering CRI and

Familiarity as interaction terms predicted Accuracy (B = −0.002, z = −1.96, p = 0.04), showing that when Familiarity was low, the name retrieval performance of participants with higher CRI was better. Similarly, CRI and Difficulty of naming as interaction terms significantly predicted Accuracy (B = −0.003, z = −2.29, p = 0.02), whereas no interaction was found between CRI and Age of acquisition (B = 0.003, z = 0.81, p = 0.41).

3.3.3 Discussion

This research aimed at investigating whether language, in particular name retrieval processing, can be influenced by the degree of CR acquired throughout the lifespan. Some evidence of beneficial effects of CR in the domain of language has already been reported in previous studies. For instance, years of education has been shown to predict verbal comprehension skills (Schaie, 1989) and the amount of vocabulary in adulthood (Arbuckle, Maag, Pushkar, & Chaikelson, 1998; Christensen et al., 1997). However, more recent studies have reported that the effect of CR is not evident in some other cases, as in proper name retrieval tasks (Semenza & Mondini, 2016). Among the group of older adults that took part in this study, those with high CR performed better in name retrieval compared with people with low CR. A previous study (Le Carret et al., 2003) reported that high CR is associated with the more successful general cognitive performance of older adults with early symptoms of dementia. Consistent with that, the present study shows that CR can affect naming performance, depending on the degree of cognitive decline. In particular, name retrieval of participants with early signs of decline seems to have benefitted more from CR, than name retrieval of healthy participants. This result could be explained by the two mechanisms of neural reserve and neural compensation (Barulli & Stern, 2013), where the strong association between CR and name retrieval in case of cognitive decline may reflect the necessity to recruit additional networks to cope with a relatively simple task. Evidence from previous research based on a comparison between younger and older adults has shown that as the task load increases, healthy older adults recruit brain networks in the same way as their younger counterpart (Ansado et al., 2013). The authors suggested that healthy older adults may first adopt cognitive compensatory mechanisms and then, when compensatory processes are not enough to cope with an increased task demand, they make use of their neural reserve (Ansado et al., 2013). Interestingly, their findings suggest that, in older adults, the neural substrates of CR are based on flexible and adaptive neural processes; however, such adaptation of neural responses can be more or less successful depending on both global cognitive condition and difficulty of the task. In the present study we used a simple name retrieval task, which might require additional resources only in persons with an impaired global condition, whereas such additional resources might be needed in healthy older adults only if task demand got higher. We analyzed the role of CR in name retrieval, which is frequently impaired in adults who often refer to this problem in terms of "memory loss." Difficulties in retrieving names can be one of the first symptoms reported at the early clinical assessments and may generally depend on a physiological decline (Rastle & Burke, 1996; Semenza, 2006). In our study we found that naming performance across categories showed Logo Names as the most demanding items, but when CR was entered in the model, high CR predicted a better name retrieval performance in both the Logo Name and the Common Noun categories. In naming Proper Names, high vs. low CR did not influence performance as it did in the two other name categories. In other words, CR is correlated with better performance in retrieving Common Nouns and Logo Names, which may be both conceptually categorized due to their greater environmental pervasiveness, rather than with naming Proper Names, which are pure referential expressions. Thus, these results underline that CR matters for naming performance only in some cases.

To the best of my knowledge, this is the first study exploring the relationship between CR and name retrieval using the three name categories of Proper Names, Logo Names, and Common Nouns. The interest in this relationship derives from previous findings, where proper name anomia was proposed to be a predictor for the onset of dementia (Semenza et al., 2003). In their study, the authors suggested that proper name anomia at the very early stages of dementia might be due to lexical semantic disruption. Although the impact of age-related naming deficits has already been reported in previous studies (Evrard, 2002; Flicker, Ferris, Crook, & Bartus, 1987), the contribution of CR on name retrieval processing in older adults has been addressed only recently (e.g., Mondini & Semenza, 2016). Proper Names and Common Nouns were considered in light of the well-documented dissociation between proper name and common noun retrieval in older adults (e.g., Cohen & Burke, 1993; Evrard, 2002; Rastle & Burke, 1996) even if the evidence of a disproportionate deficit for proper names as compared to common nouns has been shown to be controversial (see Maylor, 2007). In line with our hypothesis, we demonstrated that the effect of CR on name retrieval Accuracy was weaker for Proper Names compared to Logo Names and Common Nouns. This result seems to be reflected in the analysis of Response Times (see Figure 3.8), although no statistical difference across name categories was found when considering CR as a predictor. Common Nouns and Logo Names could highly benefit from CR, as shown in previous studies where CR was associated with semantic task components (see Reed et al., 2011; Darby et al., 2017). Our results showed differences across the three categories for Accuracy but not for Latency, possibly because name retrieval speediness is more generally affected by age-related synaptic delay (Jackson, Balota, Duchek, & Head, 2012; MacKay & Burke, 1990; Rastle & Burke, 1996). The difference between Accuracy and Latency might be due to high age-related variability when performing a cognitive task that requires reaction speediness (Anstey, 1999; Bielak, Hultsch, Strauss, MacDonald, & Hunter, 2010; Christensen et al., 1999). For example, in a longitudinal study employing a series of cognitive tasks conducted with 760 elderly individuals, Christensen et al. (1999) found a heterogeneous pattern of speed performance along with increased age-related inter-individual variability.

Our results show that high CR is a predictor of name retrieval Accuracy in the case of less familiar and more difficult names. However, no association was found between CRI and Age of Acquisition. The same result was obtained when excluding Logo Names from the analysis, as they were generally rated as acquired later in life. This suggests that name retrieval accuracy does not appear to be sensitive to CR at the point in time when names were acquired, and that CR could be associated with frequency of occurrence of certain names throughout lifespan experiences. Interestingly, our analysis of the association between psycholinguistic variables and Accuracy across categories shows that Proper Names can be more sensitive to image Familiarity and Difficulty of naming, compared to Common Nouns and Logo Names. These findings suggest that name retrieval Accuracy seems to be modulated not only by Familiarity and Difficulty, but also by CR. Categories, however, showed that name retrieval of those names that refer to repeated and shared knowledge (Common Nouns and Logo Names) benefitted from high CR, whereas name retrieval of items with poor semantic attributes (Proper Names) benefitted from high image Familiarity and low Difficulty of naming.

It might be the case that high CR can help context-driven information processing, as in the case of real living/non-living entities and commercial products, instead of information that is arbitrarily assigned to unique entities, despite their familiarity or ease of accessing their representation. With this interpretation, context availability might be a very interesting target to explore in association with the possible effects of CR.

Future investigations might further address the proposition that having an active and socially integrated lifestyle in adulthood may not only enrich cognitive resources in general, but also strengthen some specific cognitive processes, such as name retrieval.

CHAPTER 4. COGNITIVE RESERVE AND ITS POTENTIAL EFFECT ON PRAGMATIC COMMUNICATION IN PARKINSON'S DISEASE[1]

4.1 Introduction

The aim of Study 4 was to sketch a pragmatic profile in patients with Parkinson's Disease (PD), addressing the effects CR on pragmatic skills. Pragmatic abilities of communication refer to human ability to communicate in different contexts, with different speakers, recognizing and expressing communicative intentions (Bara, 2010; Grice, 1975). The role of pragmatics is especially evident when a major discrepancy between the literal and the intended meaning occurs, for example in metaphors, idioms, irony, or proverbs. In the phrase: "He's as nice as a lion to his prey", for example, the literal meaning has to be processed at a higher level, to grasp the sense of the utterance. Indeed, pragmatic abilities rely on a high-order interplay among cognitive functions supporting context-dependent language processing (Martin & McDonald, 2003).

As previously reported in Study 1 and in Study 3 of this project, context-driven aspects of language can be modulated by CR. Since pragmatic abilities are strictly associated with the use of context for efficiency in the use of language, in Study 4, pragmatics and CR have been studied in a population of Parkinson's Disease (PD) patients.

Different neurological diseases can affect the "pragmatic system" at different levels (Martin & McDonald, 2003) but, as far as I am aware, no study to date has investigated the pragmatic profile of patients with PD and its relationship with CR. PD is characterized by a disorder at the level of the dopaminergic neurons of the substantia nigra, causing a reduction of dopamine

[1] Part of results of Study 4 have been described in the following article: Montemurro, S., Mondini, S., Signorini, M., Marchetto, A., Bambini, V., Arcara, G. (2018). Pragmatic language disorder in Parkinson's Disease and its relationship with Cognitive Reserve. *Front. Psychol.* 10:1220. doi: 10.3389/fpsyg.2019.01220.

availability for neurotransmission in the corpus striatum. This biochemical imbalance results in the typical motor symptoms of PD (e.g., bradykinesia, muscular rigidity, resting tremor, and postural instability; Barone et al., 2009; Litvan et al., 2003). PD patients, moreover, may also present executive dysfunctions, visuospatial difficulties and memory difficulties, sometimes generating the symptomatic patterns of dementia (Biundo et al., 2014; Kehagia, Barker, & Robbins, 2010), so that an executive impairment in PD has been hypothesized as being associated with pragmatic difficulties (Holtgraves & McNamara, 2010).

Traditionally, right hemisphere damage (RHD) was one of the first clinical conditions associated with pragmatic impairment (Joanette, Goulet, Hannequin, & Boeglin, 1990; McDonald, 2000). Furthermore, pragmatic impairments have been found in populations with Traumatic Brain Injury (TBI; (Bosco, Parola, Sacco, Zettin, & Angeleri, 2017; Marini, Zettin, & Galetto, 2014), schizophrenia (Bambini et al., 2016a; Bosco & Parola, 2017; DeLisi, 2001; Parola, Berardinelli, & Bosco, 2018) and within neurodevelopmental disorders (see Cappelli, Noccetti, Arcara, & Bambini, 2018; Cummings, 2014). With regard to neurodegenerative diseases, pragmatic deficits seem to be widespread. (Amanzio, Geminiani, Leotta, and Cappa, (2008) have shown, for example, that patients with AD have poor understanding of novel metaphors, possibly associated with executive deficits.

Several studies have highlighted a pragmatic impairment in PD (Holtgraves & Giordano, 2017; McNamara & Durso, 2003) and investigated this disruption in relation with attentional, short-term memory, and executive deficits (Grossman, Carvell, Stern, Gollomp, & Hurtig, 1992; McKinlay, Grace, Roger, & Zealand, 2009). However, patients with PD may often present other relevant deficits in language, such as verbal fluency, voice articulation (Ho, Iansek, Marigliani, Bradshaw, & Gates, 1999), and verb inflection, which could also be at the core of a pragmatic impairment. The literature still lacks a comprehensive description of the pragmatic profile characteristic of PD, and some crucial aspects associated with pragmatic abilities have been neglected in this disease. One of these aspects refers to the Theory of Mind (Martin & McDonald, 2003), which has been linked to pragmatic disruption in other neurodegenerative diseases (e.g., Carotenuto et al., 2018). Finally, and crucially from a clinical perspective, little is known about those factors that might help to maintain pragmatic abilities in patients with PD as the disease progresses. In this context, one of the best candidates is CR, which can modulate the progression of degenerative disorders (Bonner-Jackson et al., 2013; Roe, Xiong, Miller, & Morris, 2007; Sumowski, Chiaravalloti, Wylie, & Deluca, 2009). Studying CR and pragmatics in PD could help understand how pragmatic abilities are supported and interlaced with new learnings acquired throughout the lifespan. Moreover, if a strong association between CR and pragmatic performance is assumed, whenever pragmatic abilities are clinically assessed in PD, CR should also be considered.

Higher CR has been shown to predict global cognitive performance, especially in executive function tasks. However, this is not always the case, since (as shown above) some studies have failed to show a positive impact of CR on cognitive functioning. Thus, it is not known whether possible beneficial effects of CR are homogenous across distinct aspects of pragmatics. Assuming that both pragmatic abilities and CR are fundamentally developed and enhanced throughout social life experiences, and that high CR is typically associated with better cognitive performance, the hypothesis was that high CR would be associated with better pragmatic abilities. Moreover, we expected the relationship with CR to be stronger for pragmatic aspects such as figurative language comprehension, as compared with discourse production, given previously reported education effects on non-literal speech comprehension (Champagne-Lavau, Monetta, & Moreau, 2012). In the following sections, the methodological procedure and results of Study 4 (i.e., pragmatics and CR in Parkinson's Disease) are presented.

4.2 Cognitive Reserve on Pragmatic Communication in Parkinson's Disease

4.2.1 Method

Participants

A series of 47 consecutive patients with PD coming for neurological rehabilitation after initial diagnosis were recruited at the Gruppo Veneto Diagnostica e Riabilitazione (Padua, Italy). We excluded patients who had clinically severe cardiovascular, metabolic, and psychiatric diseases or neurosurgical implants (e.g., deep brain stimulation, also called "brain pacemaker"). We also enrolled a sample of 45 healthy controls matched, as much as possible, with the patient group. All participants were monolingual native speakers of Italian.

Patients with PD had a mean Age of 72 years (SD = 7.36) and a mean Education of 10.36 years (SD = 4.82), 12 were females and 35 males. The healthy control individuals had a mean Age of 70.47 (SD = 7.50) and a mean education of 10.42 (SD = 4.65), 13 were females and 32 males. Between-group differences on age and education were not significant at t-tests [age: $t(90) = -0.98$, $p = 0.32$; education: $t(90) = 0.06$, $p = 0.95$]. As a more robust test for matching of demographic variables we also employed the Test of Equivalence, which assesses if two groups can be considered significantly equivalent. We found that patients with PD and healthy controls were significantly equivalent for Age when the threshold was 5 years ($p = 0.014$), and significantly equivalent for Education with a threshold of 2 years ($p = 0.03$). Finally, the two groups were not different in terms of proportion of female/male participants [$\chi2\ (1) = 0.01$, $p = 0.89$, with Yates correction]. Concerning clinical variables, patients had a mean Unified Parkinson Disease Rating Scale (UPDRS-III) score of 34.52 (SD = 13.30), a mean Hoehn and Yahr (H&Y) score of 2.15 (SD = 0.94), and a mean number of Years from Onset of the disease of 7.5 (SD = 3.86). The patients with PD showed different degrees of cognitive impairment: using a stratification based on MoCA scores (Biundo et al., 2014), our sample was composed of 31 patients with PD without cognitive disorders (PD-CNT, MoCA > 25), 10 patients with PD with Mild Cognitive Impairment (PD-MCI, MoCA > 20 and ≤25), and 6 patients with PD Dementia (PDD, MoCA < 20). The study was approved by the ethics committee of the University of Padua (Italy). All participants signed an informed consent explaining the nature of the study. The research was completed in accordance with the Declaration of Helsinki.

Procedure

Patients were assessed for clinical characteristics of the diseases, pragmatic abilities, general cognitive abilities, and Cognitive Reserve. Two main demographic variables were considered in the analysis: age, as number of years, and education. For the patients with PD, three additional clinical variables were included: two of them measured the severity of extrapyramidal symptoms, which was evaluated with the H&Y (Hoehn & Yahr, 1967) and with the motor UPDRS-III (Fahn & Elton, 1987). The H&Y system is based on a scale from 1 to 5, with higher scores indicating a more severe impairment, which can be associated with a variety of neurocognitive issues such as depression or dementia, and poorer quality of life. The motor UPDRS-III ranges from 0 to 108 and classifies the severity of the disease based on tremor, slowness (bradykinesia), stiffness (rigidity) and balance, with higher scores suggesting a more severe impairment. Finally, the third variable was the duration of illness was considered and quantified as number of Years from Onset (after first diagnosis).

All participants were administered the APACS (Arcara & Bambini, 2016).

From the theoretical point of view, the APACS test is grounded in Neo-Gricean pragmatics, assuming that communication involves not only coding and decoding, but rather it is a rational, cooperative activity (Grice, 1975), involving also inferential processes to derive the speaker's meaning and to link different information in the text, as well as the ability to meet the interlocutor's needs. More specifically, inferential abilities are especially evident when there is a gap between the literal and the intended meaning, as in figurative language, and in the textual dimension, when inferences are needed to bridge different aspects of a text. Conversely, the ability to meet the interlocutor's need is especially evident in conversation, as reflected in skills such as providing the appropriate amount of information, taking verbal initiative when appropriate, etc.

Materials

The *Assessment of Pragmatic Abilities and Cognitive Substrates (APACS)*

APACS is a test that investigates pragmatic skills in both expressive and receptive modalities through six tasks, two dedicated to production (Interview and Description) and four dedicated to comprehension (Narratives, Figurative Language 1, Humor, Figurative Language 2).

- The Interview task measures discourse organization and engagement in conversation based on autobiographical topics. The frequency of communication difficulties is reported (i.e., always/sometimes/never) and then converted into scores (0/1/2). Various dimensions of discourse are evaluated (e.g., repetition, incomplete utterances, echolalia), informativeness (over- or under-informativeness, loss of verbal initiative), information flow (e.g., missing referents, wrong order of the discourse elements, abrupt topic shift), paralinguistic dimensions (e.g., altered intonation, loss of eye-contact, fixed facial expression, abuse of gesture). Errors in grammar and vocabulary are also annotated, as they affect the communicative effectiveness of the discourse. Maximal score: 44.

- The Description task measures the ability of producing and sharing information of everyday life situations, based on the description of photographs that represent scenes of daily life (e.g., a person waiting the bus).

- The Narratives task measures the ability to understand the main aspects of a narrative text. A series of stories inspired by real newspaper, radio, and TV news are read to the participants, and followed by comprehension questions on explicit and implicit contents, with the latter based on inferential processes. Each question is scored for accuracy (either 0/1 or 0/1/2). Maximal score: 56.

- The Figurative Language 1 task measures the ability to infer non-literal meanings through multiple-choice questions following the presentation of idioms, novel metaphors, and proverbs. Each item is scored either 1 or 0 according to the accuracy. Maximal score: 15.

- The Humor task measures the ability to comprehend verbal humor through multiple-choice questions. The participant is asked to select the best punch line of a story. Each item is scored either 1 or 0 according to the accuracy. Maximal score: 7.

- The Figurative Language 2 task measures the ability to infer non-literal meanings through verbal explanation of idioms, novel metaphors, and proverbs. The maximal score of 2 is given to an item when the subject provides a good description of the meaning of the figurative expression; a score of 1 is given when the participant provides an incomplete explanation, such as concrete examples, but fails in providing an abstract meaning; a score of 0 is given when the participant provides a literal explanation, paraphrases the figurative expression or does not know it. Maximal score: 30. Three composite pragmatic scores are derived from the six APACS single task scores. The Pragmatic Production score is calculated from Interview and Description, whereas the Pragmatic Comprehension score is calculated from Narratives, Figurative Language 1, Figurative Language 2, and Humor. Each composite score is obtained by transforming the original task scores in proportion and averaging these proportions, so that each task equally contributes to the final composite score. APACS Total score is calculated by averaging Pragmatic Production and Pragmatic Comprehension scores.

Besides APACS, participants were administered a series of cognitive tasks:

MoCA test, a brief neuropsychological tool, which provides a global cognitive profile (Nasreddine et al., 2005). It consists of eight sub-tests tapping different cognitive domains (i.e., memory, language, visuospatial skills, executive functions, and orientation in time and space). Its administration lasts about 10 min and the maximum score is 30.

Digit Span Backward, which assesses working memory ability, participants. In this task each item consists of a list of digits. Participants are required to immediately repeat the list of digits in reverse order (Monaco, Costa, Caltagirone, & Carlesimo, 2013). After each list, if the subject has succeeded in repeating it, another list one digit longer is presented. If the subject has failed, a second list of the same length is presented. If the participant is successful on the second item list, a list one digit longer is given, as before. However, if the participant fails on the second list too, the test is ended. The length of the digit sequences gradually increases starting with a sequence of three numbers to a sequence of maximum eight items. The span is established as the length of the longest list recalled correctly. Maximal score: 8.

Theory of Mind test. Specifically, we used the *Story-Based Empathy Task* (SET; Dodich et al., 2015), which is a non-verbal test developed for the assessment of intention and emotion attribution in neurodegenerative diseases. The total SET score is the result of performance in 18 stimuli, grouped into three conditions that assess the ability to infer others' intentions (Story-Based Empathy Task: Intention Attribution, SET-IA) and emotions (Story-Based Empathy Task: Emotion Attribution, SET-EA), compared to a control condition testing causal inference (Story-Based Empathy Task: Causal Inference, SET-CI). Each condition is made of six trials in which the participant is asked to select the correct ending of a sequence of pictures. Score 1 is assigned only for the selection of the correct ending, and the global score is computed based on the total of correct answers. Maximal score of each subtask: 6, maximum total score: 18.

Token Test: to examine language comprehension.; the 36-item-version of the Token Test was administered (De Renzi & Vignolo, 1962). The participant is required to perform some actions in response to simple verbal commands. This test detects receptive language disorders. All commands consist of not redundant words referring to different tokens, which are circles and rectangles in different colors and sizes. Maximal score: 36.

Then, we evaluated the Cognitive Reserve Index through the CRIq (Nucci et al., 2012), which is grouped into three sections: Education (CRI-Education = years of formal education and additional training courses), Working activity (CRI-WorkingActivity = years and cognitive load of an occupation), and Leisure time activities (CRI-LeisureTime = based on intellectual, social and physical activities). See *Procedure and Materials* in par. 2.2.1 for a broader description of the questionnaire.

Statistical Analysis

First, the performance of patients with PD and healthy controls in the APACS test and in the other cognitive tasks (MoCA, Token, Digit Span Backward, SET) was compared through separate independents t-tests, with false discovery rate (FDR) correction (Benjamini and Hochberg, 1995). In order to analyze individual performance, APACS scores of each patient were compared to cut-off values calculated as 5th percentile of the healthy control matched sample (for an analogous approach, see (Bambini, Arcara, Martinelli, et al., 2016)[1].

[1] Additional analyses restricted to PD-CNT patients (i.e., patients without cognitive impairment as measured by MoCA, Biundo et al., 2014) in Montemurro, S., Mondini, S., Signorini, M., Marchetto, A., Bambini, V., Arcara, G. (2018). Pragmatic language disorder in Parkinson's Disease and its relationship with Cognitive Reserve. Front. Psychol. 10:1220. doi: 10.3389/fpsyg.2019.01220.

Furthermore, a correlation analysis[1] and a Random Forest analysis were performed to evaluate which scores were mostly associated with the performance in APACS among Demographic and Clinical variables, General Cognitive variables, and CR. Then, the correlation coefficients between PD patients and healthy controls were compared with the test for difference of independent correlations (r.pair function of the psych R package; Revelle, 2017). Two Random Forests[2] were performed: one with the Pragmatic Production and the other with the Pragmatic Comprehension as dependent variables, respectively. The predictors of each Random Forest were: Demographic (i.e., Age, Education) and Clinical variables (UPDRS-III, H&Y, Years from Onset), General Cognitive variables (i.e., MoCA, Token Test, Digit Span Backward, SET), and Cognitive Reserve (i.e., CRIq)[3]. Statistical analyses were performed with R, release 3.3.2 (R Core Team, 2016).

4.2.2 Results

Descriptive statistics and t-tests comparing patients with PD and healthy controls in all administered tests are reported in Tables 4.1 and 4.2.

APACS task or composite score	Mean Parkinson (SD)	Mean Controls (SD)	df	t	Cohen's d	p-value
Interview	35.09 (6.15)	38.82 (2.45)	90	-3.8	-0.79	<0.001
Description	37.26 (5.85)	46.4 (1.99)	90	-9.9	-2.1	<0.001
Narratives	42.87 (8.25)	49.6 (4.33)	90	-4.9	-1	<0.001
Figur. Lang. 1	12.91 (1.87)	13.24 (2.09)	90	-0.8	-0.17	0.48
Humor	5.21 (1.94)	6.09 (1.24)	90	-2.6	-0.53	0.015
Figur. Lang. 2	20.38 (5.66)	21.09 (4.04)	90	-0.69	-0.14	0.49
Pragmatic Prod.	0.78 (0.1)	0.92 (0.03)	90	-9	-1.9	<0.001

[1] In the Correlation analysis, Pearson's correlations corrected with FDR were used.
[2] A machine learning method allowing to predict values of a variable from a large set of other variables.
[3] Each forest consisted of 500 trees. Random Forests were calculated using unbiased partitioning as implemented in the cforest function included in the party package (Strobl et al., 2009a,b).

Pragmatic Compr.	0.77 (0.15)	0.83 (0.1)	90	-2.6	-0.54	0.015
APACS Total	0.77 (0.11)	0.88 (0.06)	90	-5.9	-1.2	<0.001

Table 4.1. Descriptive statistics and results for t-tests comparing patients with PD and healthy controls in the pragmatic assessment.

Task	**Mean Parkinson (SD)**	**Mean Controls (SD)**	**df**	**t**	**Cohen's d**	**p-value**
MoCA	25.4 (4.55)	25.18 (2.56)	90	0.29	0.061	0.77
Token	33.11 (2.97)	33.92 (1.69)	89	-1.6	-0.33	0.11
Digit SPAN BW	3.65 (1.4)	4.47 (0.94)	89	-3.2	-0.68	0.0017
SET TOT	13.71 (2.99)	16.02 (1.5)	88	-4.6	-0.97	<0.001
SET IA	4.62 (1.25)	5.44 (0.72)	88	-3.8	-0.8	<0.001
SET EA	4.62 (1.28)	5.31 (0.82)	88	-3	-0.63	0.003
SET CI	4.44 (1.37)	5.16 (0.98)	88	-2.8	-0.59	0.006
CRIq-Education	102.6 (17.14)	104.36 (16.1)	88	-0.5	-0.1	0.62
CRIq-WorkingAct	106.91 (23.32)	104.91 (16.8)	88	0.47	0.097	0.64
CRIq-LeisureTime	104.67 (24.22)	124.91 (17.07)	88	-4.6	-0.96	<0.001
CRIq-Total	107.62 (21.38)	115.13 (19.21)	88	-1.8	-0.37	0.083

Table 4.2. Descriptive statistics and results for t-test comparing patients with PD and healthy controls in all neuropsychological tests. The table shows the results of t-tests comparing patients with PD and healthy controls on the neuropsychological tests taken into account in our study.

The analysis comparing the patients with PD and healthy controls in the APACS scores showed significant differences in the Interview, Description, Narratives, Humor, Pragmatic Production, Pragmatic Comprehension, and APACS Total composite scores (FDR correction; $p < 0.05$). The highest effect size was found for Description (Cohen's d = 2.1). No significant differences between patients with PD and controls were observed in Figurative Language 1 and Figurative Language 2. See the barplot showing the results of patients with PD and controls in APACS scores in Figure 4.1.

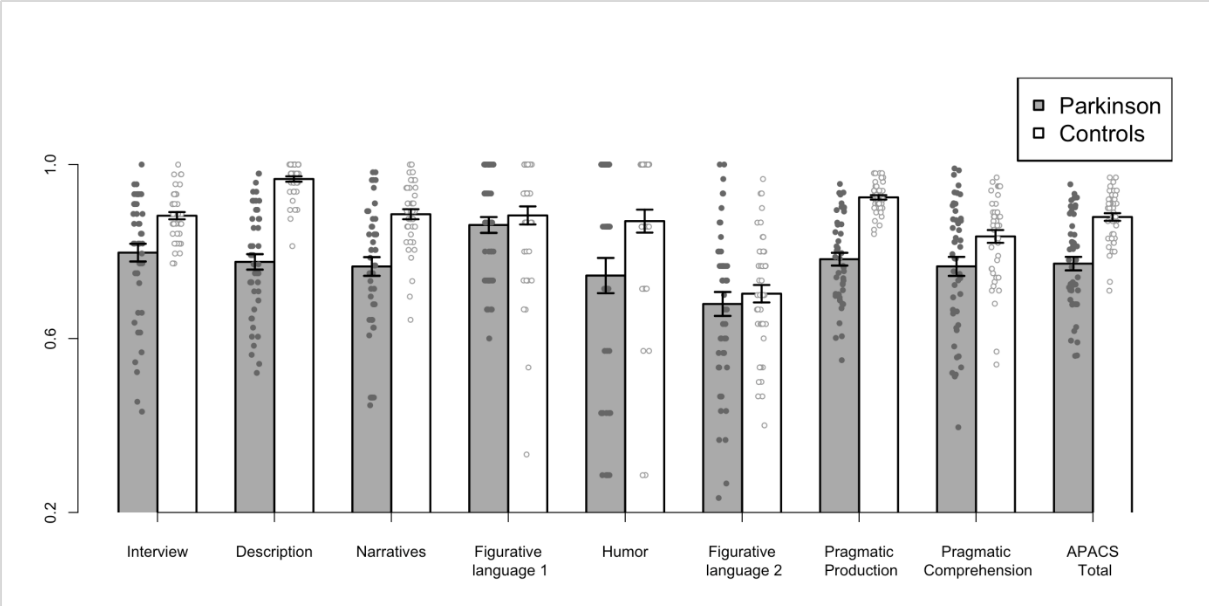

Figure 4.1. Performance of patients with PD and Controls in Pragmatic tasks and composite scores. All raw scores were transformed in proportion (relative to the maximum obtainable score) before plotting. Grey bars indicate the mean performance of patients with PD, whereas white bars indicate the mean performance of healthy controls. The small circles denote the scores for each participant (a small jitter was added in the x-axis to improve visibility of individual scores).

Moreover, patients with PD had a significantly lower performance than healthy controls in the Digit Span Backward, as also in the SET-Tot, SET-IA, SET-EA, SET-CI, and in the CRI-LeisureTime (Table 4.2). Analyses performed on a group of 31 patients with PD without clear signs of cognitive impairment (PD-CNT) generated a similar profile, with significant lower performance compared to controls on the Interview, Description, Narratives tasks and Pragmatic Production. Differing from the complete sample, here no difference in performance compared to healthy controls was observed in Humor, Pragmatic Comprehension, and APACS Total[1].

[1] More details in Montemurro, S., Mondini, S., Signorini, M., Marchetto, A., Bambini, V., Arcara, G. (2018). Pragmatic language disorder in Parkinson's Disease and its relationship with Cognitive Reserve. Front. Psychol. 10:1220. doi: 10.3389/fpsyg.2019.01220.

Individual performance of patients with PD in the APACS Tasks

To better assess individual performance separately for each patient, we took into account whether the score in each APACS task, and in each composite score, was below the normative cut-off. Several patients showed a performance below cut-off, especially in the production tasks (i.e., Interview and Description) and in the Pragmatic Production composite score. However, performance below cut-off was widespread (Number of Patients below cut-off/Total number of patients: Interview: 18/47; Description: 36/47; Narratives: 17/47 Figurative Language 1: 1/47; Humor: 13/47, Figurative Language 2: 8/47; Pragmatic Production: 34/47, Pragmatic Comprehension: 14/47; APACS Total: 25/47). Figure 4.2 shows patients with PD who scored below cut-off (i.e. below 5th percentile of healthy control data) in the APACS tasks and in the three composite scores.).

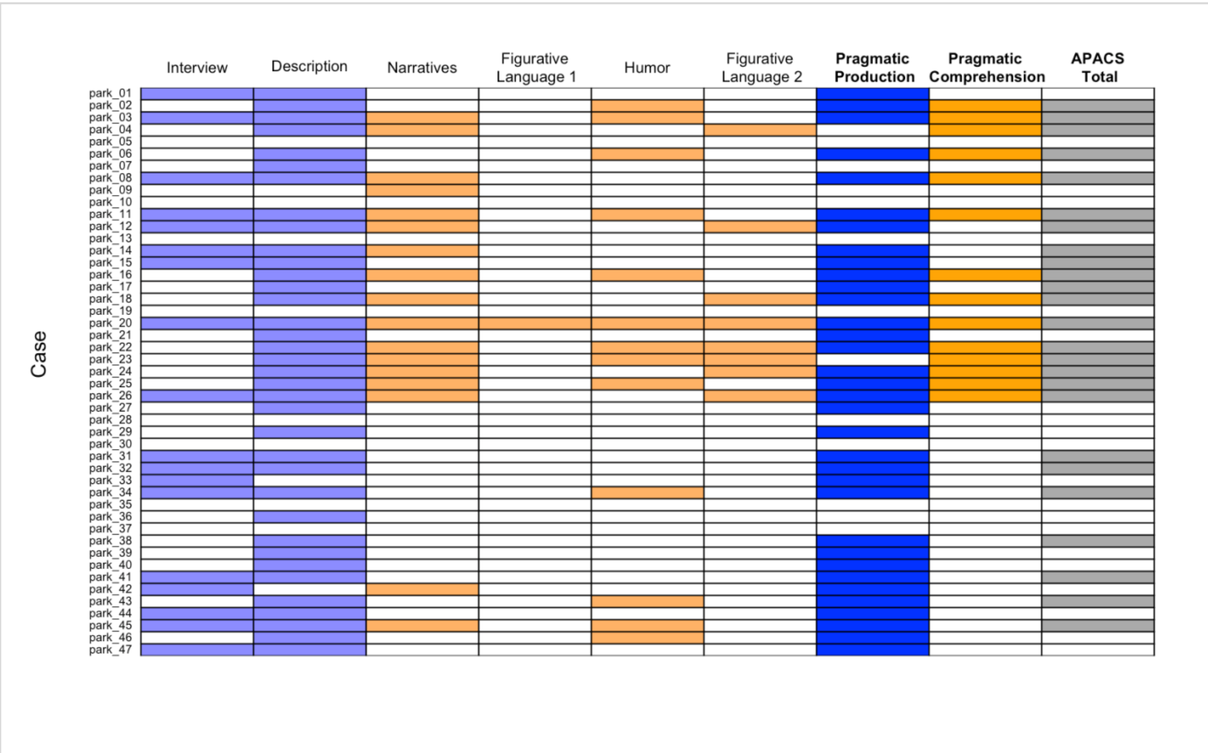

Figure 4.2. Performance below cut-off of Parkinson Patients in Pragmatic tasks and composite scores. Each row denotes a patient, whose case number is reported in the left part of the figure. White cells indicate a performance equal to or above cut-off, whereas colored cells indicate a performance below cut-off.

Pairwise Correlation Analysis Between Pragmatic and Neuropsychological Tests in Patients with PD and Controls

Pairwise correlations between APACS scores and neuropsychological variables were performed separately for patients with PD and healthy controls. Detailed results on the correlations are reported in Table 4.3. Both PD patients and healthy controls showed several significant correlations. Concerning the Demographic variables, Education was positively associated with several APACS scores in patients with PD and controls, while Age showed only a few significant negative correlations. With regard to the Clinical variables (available only for patients with PD), both UPDRS-III and H&Y were negatively correlated with Interview scores and APACS Production scores. Years from onset did not show any significant correlation.

Patients with Parkinson's Disease

	Age	Edu	UPDRS-III	H&Y	Years From Onset	MoCA	Token Test	Digit Span BW	SET-Tot	SET-IA	SET-EA	SET-CI	CRI *Education*	CRI *WorkingAct*	CRI *LeisureTime*	Cri-Tot
Interview	0	0.22	-0.49 *	-0.46 *	0	0.26	0.26	0.18	0.07	-0.03	0.04	0.15	0.26	0.3	0.16	0.29
Description	-0.23	0.15	-0.29	-0.2	-0.14	0.29	0.38 *	0.17	0.41 *	0.23	0.28	0.46 *	0.14	0.16	0.13	0.18
Narratives	-0.09	0.51 *	0.08	-0.16	-0.28	0.49 *	0.48 *	0.24	0.47 *	0.29	0.42 *	0.41 *	0.51 *	0.55 *	0.36 *	0.56 *
FL1	-0.14	0.66 *	0	0.01	-0.15	0.41 *	0.49 *	0.11	0.51 *	0.24	0.45 *	0.5 *	0.59 *	0.6 *	0.3	0.55 *
Humor	-0.12	0.43 *	-0.06	-0.06	-0.02	0.34 *	0.52 *	0.31	0.41 *	0.17	0.48 *	0.31	0.35 *	0.35 *	0.37 *	0.47 *
FL2	-0.11	0.62 *	0.1	-0.02	-0.06	0.55 *	0.56 *	0.14	0.48 *	0.21	0.54 *	0.39 *	0.55 *	0.49 *	0.37 *	0.55 *
PP	-0.09	0.68 *	0.05	-0.08	-0.17	0.55 *	0.67 *	0.27	0.59 *	0.3	0.57 *	0.5 *	0.63 *	0.55 *	0.49 *	0.67 *
PC	-0.27	0.17	-0.57 *	-0.49 *	-0.03	0.33 *	0.36 *	0.17	0.26	0.07	0.15	0.38 *	0.17	0.25	0.09	0.21
APACS_Total	-0.21	0.56 *	-0.24	-0.29	-0.15	0.55 *	0.63 *	0.29	0.52 *	0.22	0.47 *	0.52 *	0.51 *	0.51 *	0.39 *	0.57 *

Healthy Controls

	Age	Edu	UPDRS-II	H&Y	Years From Onset	MoCA	Token Test	Digit Span BW	SET-Tot	SET-IA	SET-EA	SET-CI	CRI *Education*	CRI *WorkingAct*	CRI *LeisureTime*	Cri-Tot
Interview	-0.3	0.37 *	-	-	-	0.48 *	0.38 *	0.29	0.18	0.13	-0.01	0.19	0.29	0.35 *	0.48 *	0.43 *
Description	-0.3	-0.11	-	-	-	0.16	0.07	-0.09	0.17	0.3	0.08	-0.1	-0.17	-0.02	-0.02	-0.08
Narratives	-0.43 *	0.29	-	-	-	0.72 *	0.47 *	0.32	0.47 *	0.43 *	0.13	0.28	0.18	0.3	0.29	0.3
FL1	-0.26	0.57 *	-	-	-	0.54 *	0.41 *	0.51 *	0.35 *	0.21	0.11	0.26	0.5 *	0.41 *	0.46 *	0.53 *
Humor	-0.29	0.03	-	-	-	0.22	0.29	0.31	0.22	0.49 *	-0.12	-0.01	-0.02	0	0.08	0.03
FL2	=0.25	0.46 *	-	-	-	0.64 *	0.41 *	0.42 *	0.54 *	0.2	0.41 *	0.33	0.43 *	0.54 *	0.52 *	0.57 *
PP	-0.4 *	0.43 *	-	-	-	0.65 *	0.51 *	0.53 *	0.49 *	0.44 *	0.15	0.25	0.35 *	0.38 *	0.44 *	0.45 *
PC	-0.41 *	0.25	-	-	-	0.47 *	0.39 *	0.19	0.24	0.26	0.05	0.11	0.15	0.29	0.39 *	0.32
APACS_Total	-0.44 *	0.41 *	-	-	-	0.68 *	0.53 *	0.48 *	0.49 *	0.44 *	0.15	0.25	0.32	0.39 *	0.47 *	0.45 *

Table 4.3 Correlations in Patients and in healthy controls, between APACS tasks and variables from Clinical Assessment. The table reports the Pearson's r-values for the correlation among APACS tasks and scores and all the other variables included in the study. Asterisks (*) denote correlations with p-value < 0.05 after FDR multiple comparison correction. FL1 = Figurative Language 1; FL2 = Figurative Language 2; PP = Pragmatic Production composite score; PC = Pragmatic Comprehension composite score.

Overall, variables belonging to the pool of Neuropsychological tasks showed several significant correlations both in patients with PD and in healthy controls, with a qualitatively similar pattern of performances on these tasks. These correlations involved especially the comprehension tasks of APACS (i.e., Narratives, Figurative Language 1, Humor, Figurative Language 2, and consequently Pragmatic Comprehension) and were rarely associated with production scores (i.e., Interview, Description, and Pragmatic Production). Importantly, Cognitive Reserve scores showed several significant correlations especially with the comprehension tasks of APACS (both in patients with PD and in healthy controls). The analysis that compared the difference in correlations between patients with PD and healthy controls did not show any significant difference, confirming a similarity in the pattern of the two groups. Given the high number of significant correlations, to better understand these results, two exploratory Principal Component Analyses (PCA)[1], not planned from the beginning of the study were run. These PCA included only a subset of the relevant scores: MoCA, Token Test, SET-Total, CRI Total, and Pragmatic Comprehension score[2]. The PCA on patients with PD showed that a single component was able to explain 62% of the variability in all scores, while the PCA on controls showed that a single component was able to explain 52%. Both these results suggest a common underlying association across all the variables.

With regard to the Random Forest analysis, results are interpreted by checking the Importance associated with each predictor in the model. Importance indicates how much each model worsens (i.e., lowers the ability to predict data) if a given variable is taken out from the model. In the Random Forest with Pragmatic Production as dependent variable, the most important predictors were the UPDRS- III, the H&Y, the SET-CI, and the Token Test (Figure 4.3; Random Forest $R^2 = 0.33$). In the Random Forest with Pragmatic Comprehension as dependent

[1] One for patients with PD and one for healthy controls.
[2] This analysis was restricted to a limited number of scores because in PCA the number of variables that can be included is limited by the number of observations (i.e., in our case the number of patients).

variable, the most important predictors were: Education, the Token Test, the CRI-Total, and the SET-Tot (Figure 4.4; Random Forest $R^2 = 0.61$).

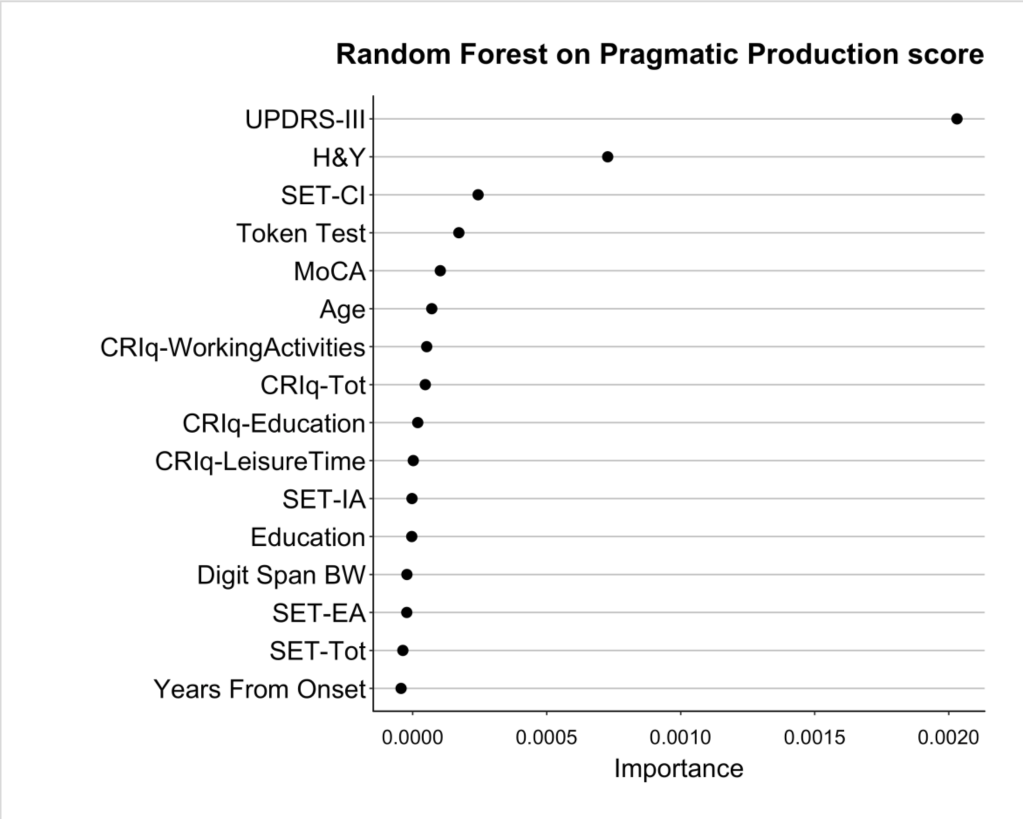

Figure 4.3 Importance of all variables in Random Forests with Pragmatic Production as dependent variable. The figure shows the Importance associated to each variable in the Random Forests with Pragmatic Production score from APACS as dependent variable. Variables are sorted from top to bottom according to Importance, so that the variables on top are the ones with the highest Importance.

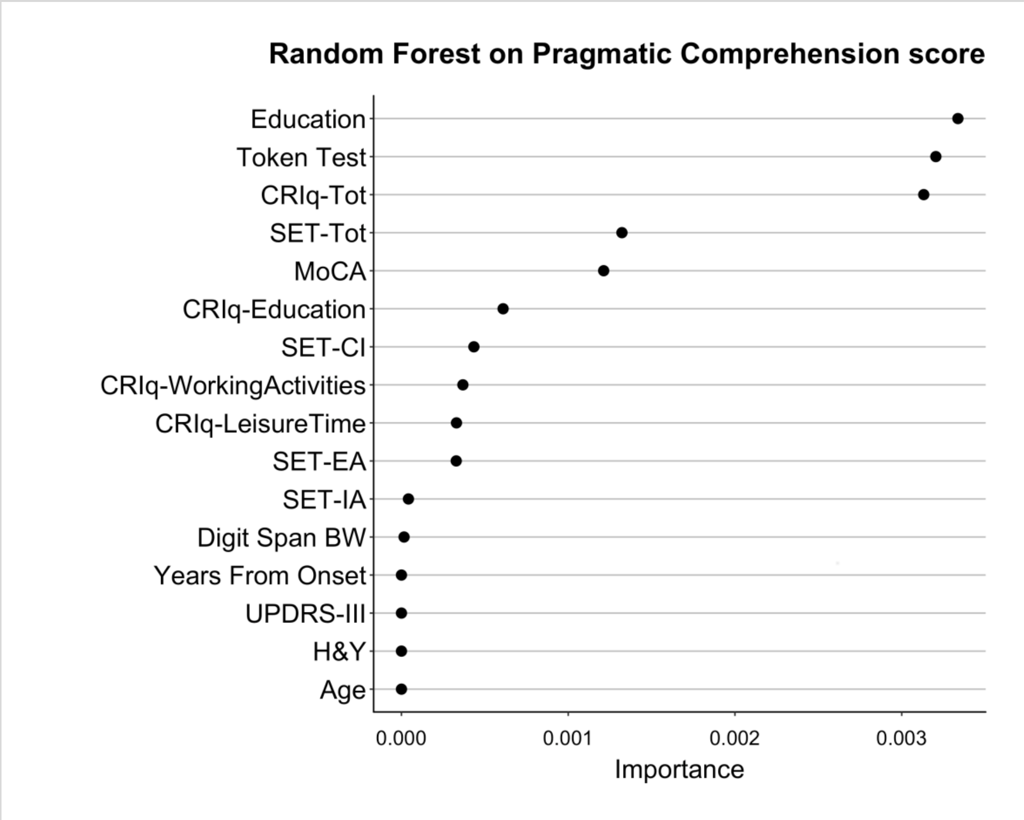

Figure 4.4 Importance of all variables in Random Forests with Pragmatic Comprehension as dependent variable. The figure shows the Importance associated to each variable in the Random Forest with Pragmatic Production score from APACS as dependent variable. Variables are sorted from top to bottom according to Importance, so that the variables on top are the ones with the highest Importance.

4.2.3 Discussion

Study 4 aimed at delineating the pragmatic profile of patients with PD, the association between pragmatics and cognitive variables and the impact of CR on pragmatic performance of this clinical population. At the group level, the performance of patients with PD was worse than that of matched healthy controls in several pragmatic tasks of APACS and its composite scores. In patients with PD, performance was not significantly different from performance of healthy controls in Figurative Language 1 and Figurative Language 2, two tasks assessing the ability to understand figurative language expressions. Significant differences were found between patients and controls in Digit Span, some subscales of SET (Story-based Empathy Test), and in CRI-LeisureTime.

The pattern of results on pragmatic abilities was investigated not only at group level but also at individual level, showing that 82% of patients with PD fell below the cut-off in at least one pragmatic task, with 53% of patients presenting an overall pragmatic language disorder (defined in terms of APACS Total score).

In the Interview task, patients' performance was mainly impaired in discourse organization, with a lack of important details in the produced speech. Similar problems were found in the Description task, where participants were required to provide information about photographs of everyday life scenes. These problems in production are in line with previous studies, in which patients with PD showed major deficits in discourse organization in terms of under-informativeness, turn-taking disruption, inappropriate levels of politeness, and paralinguistic deficits (Holtgraves & Giordano, 2017; Illes, 1989; McNamara & Durso, 2003). Post-hoc exploratory analysis showed that patients with PD often did not report the main referents of the discourse, lacked verbal initiative, showed impairment in paralinguistic aspects (e.g., fixed facial expression), making frequent grammatical mistakes. In line with previous findings, both correlations and Random Forests analyses indicated a very clear-cut relationship of the production abilities of patients with PD with their motor impairment (Hall, Ouyang, Lonnquist, & Newcombe, 2011; Ho et al., 1999). Grammatical impairment was just one of the many facets of the deficits in discourse production shown by patients with PD, and indeed these patients did not show an impairment in the Token Test and there was no evidence of phonological paraphasia.

Concerning the pragmatic abilities in the comprehension modality, PD patients had worse performance than healthy controls: Narratives and Humor. Interestingly, the impairment in comprehension was not generalized, as patients with PD did not show problems in the two other tasks targeting receptive aspects, that is Figurative Language 1 and 2, devoted to assessing the ability to understand idioms, metaphors, and proverbs.

A potential explanation of these differences within the comprehension pragmatic dimension can be found in the communalities between Narratives and Humor, since both include stories. It is possible, then, that patients with PD show impairment whenever information about a story (including the monitoring of different aspects such as protagonists and relations) have to be kept "on-line" to make correct inferences. The hypothesis of a problem in the inferential aspects of processing a story is confirmed by the performance of patients with PD in the control SET-CI task of the SET (a test of Theory of Mind; Dodich et al., 2015). SET-CI is a control condition of the SET and assesses the ability to understand causal inferences (e.g., a short scenario in which a person with a hat walks against a strong blowing wind, with several possible endings on what could happen to the hat). The difficulties in all the SET sub-scores and also in the SET-CI control condition suggest that the low SET-total performance could be considered as linked to the difficulties in inferring from stories (Martin and McDonald, 2005), rather than to problems of Theory of Mind.

In line with the findings of (Monetta & Pell, 2007), PD patients showed no impairment in figurative language tasks. In Study 4 we tested a sample of patients with different cognitive profiles (the majority were not cognitively impaired), which might be the reason of the spared figurative language skills. Performance of PD patients in pragmatic comprehension tasks showed several correlations with CRIq scales and with all the other cognitive variables. The PCA analysis indicated that a single component was able to capture more than 50% of variance in all these scores. In other words, people who obtained a low score in one of the tasks considered in the PCA (i.e., MoCA, Token Test, SET-Total, CRI Total, and Pragmatic Comprehension score) obtained low scores in all the other tasks and people who obtained a high score in one of these tasks obtained high scores in all the other tasks. This suggests that most of these correlations with comprehension scores might be considered as different facets of the same phenomenon. This pattern was similar for patients with PD and healthy controls, suggesting that the pattern of association of cognitive and pragmatic abilities in patients with PD could be quantitatively rather than qualitatively different from healthy controls. Besides showing several significant correlations with almost all pragmatic tasks, the Token Test showed the second highest Importance in Random Forest analysis with Pragmatic Comprehension as the dependent variable. This result indicates that, even when considering several predictors and their interaction, the Token Test is strongly associated with Pragmatic Comprehension, possibly due to ability of the Token Test to correlate with global cognitive status (e.g., Agrell, Dehlin, & Nilsson, 1995).

Interestingly, we did not find any significant correlation between the pragmatic tasks and the Digit Span Backward, although, as shown in the literature, patients with PD had a lower performance in working memory tasks than healthy controls (Gilbert, Belleville, Bherer, & Chouinard, 2005). This result suggests that at least one major aspect of executive functioning (i.e., working memory) is not strictly related to the pragmatic profile of patients with PD. However, this should not be taken to imply that executive functions in general are not related to pragmatic abilities in PD, as several aspects of executive functioning were not included in our assessment and might be compromised in PD, for example set maintenance (D'Aniello, Scarpina, Albani, Castelnuovo, & Mauro, 2015; Holtgraves & Giordano, 2017; Kehagia et al., 2010). Beyond the aim of sketching the pragmatic profile -and the relative cognitive features- associated to PD, a further aim of Study 4 was to investigate the potential compensatory role of CR in pragmatic skills. In an initial analysis, comparing CR in patients with PD and healthy controls, there were no differences on the CRI total scores and the two sub-scores CRI-Education and CRI-WorkingActivity (Nucci et al., 2012). However, the two groups showed a significant difference in the CRI-LeisureTime sub-score. Rather than a problem arising from group matching, this difference might be related to the impact that PD has on the health-related quality of life of patients. As reported by some patients, coping with the disease and trying to "re-set" the lifestyle can at some point lead to increasing social embarrassment and isolation, which could possibly explain a reduction of leisure time activities (Karlsen, Tandberg, Årsland, & Larsen, 2000; Martinez-Martin, 1998).

Since CR is reported to be associated with better performances in high-order cognitive tasks, and since both are developed and enhanced through social life experiences (Tucker & Stern, 2011), we expected significant high correlations between CR indices and performance on pragmatic tasks. In particular, we expected an association of education with figurative language comprehension (in line with Champagne-Lavau et al., 2012). This expectation was confirmed for the pragmatic comprehension abilities both by correlations and Random Forests. These two analyses, in fact, evidenced a strong relationship between CR and Pragmatic Comprehension. All tasks and composite scores in the comprehension section of APACS showed significant correlations with CR, and in the Random Forest with Pragmatic Comprehension as the dependent variable, the CRI-Total was among the variables with the highest Importance. Interestingly, the variable with the highest Importance (i.e., the variable that best predicted the Pragmatic Comprehension score) was Education, which is a crucial demographic variable and also part of Cognitive Reserve itself (Nucci et al., 2012; see also Arcara et al., 2017 for considerations on education). This strong association between CR variables and performance in Pragmatic Comprehension suggests that having a socially rich and active lifestyle may have a compensatory effect on the decline of pragmatic abilities associated with neurodegeneration and may protect the ability to understand non-literal speech as well as narrative texts. Importantly, as the correlation between CR and neuropsychological variables was similar in healthy controls, it can be argued that comparable protective mechanisms act in normal aging as well.

CHAPTER 5. AN INTER-DISCIPLINARY APPROACH IN DEVELOPING NEW SOFTWARE FOR PRAGMATIC ASSESSMENT[1]

5.1 Introduction

The most recent literature has reported that neuropsychological tests need to be updated, in order to improve efficiency and utility of assessment (Fernandez, 2019). The aim of Study 5 was to develop a new user-friendly tool to assess pragmatic abilities of discourse. In particular, we transformed the paper-and-pencil Interview task, which is part of the Assessment of Pragmatic Abilities and Cognitive Substrates (APACS, Arcara & Bambini, 2016), into a software-based task. The assessment of speech features in a patient with a neurological disease (for example, with possible disorganized discourse and disruptions in conversation) can be very challenging for the examiner, whose work consists in a multi-tasking operation in which the full observation of the patient has to be combined with their scoring performance, based on different parameters of their speech.

Successful results have arisen from studies based on the interdisciplinary work of cognitive sciences, medical sciences and Information Technology (Kumar, Helgeson, & White, 1994; Kushniruk, Patel, & Cimino, 1997; Saxton et al., 2009; Singleton, Thomas, & Horne, 2000; Smith & Caputi, 2007). For example, Saxton and colleagues (2009) realized a Computer Assessment of Mild Cognitive Impairment (CAMCI) and compared this tool with the Mini-Mental State Examination in its original paper-and-pencil version (MMSE; Folstein, Folstein, & McHugh, 1975). Then, the authors checked the sensitivity of CAMCI in the identification of Mild Cognitive Impairment (MCI) based on 524 non-demented 60 year-olds. The comparison

[1] Part of results of Study 5 have been reported in the following article: Begolo M., Gaggi O., Mondini S., Montemurro S. (2019). Digital Neuropsychological assessment of discourse production: An Interdisciplinary approach. GoodTechs 2019: 5th EAI International Conference on Smart Objects and Technologies for Social Good, Valencia, Spain. ACM, New York, NY, USA, 5 pages. https://doi.org/10.1145/1122445.1122456

between the two tests showed that CAMCI can provide suitable rates of sensitivity (86%) and specificity (94%). In another study, Singleton and colleagues (2000) realized a Computer-based task to assess reading abilities in developmental stages. In particular, they tested 5 year-olds, showing that this task was a satisfactory predictor of poor reading skills, with very low or zero rates for false positives and false negatives. However, from age 6 to 8, the task turned out to be unsatisfactory in predicting reading skills, with a false positive rate of 21%.

In the language domain, the digitalization of cognitive tasks is especially relevant for discourse analysis, and certainly requires multidisciplinary work, mainly across linguists, psychologists and experts in the IT field (Van Dijk, 2011). Evaluation of discourse production in pathological populations requires ability to identify the possible presence of a number of variables, such as repetitions, incomplete sentences, over- and under-informativeness of discourse, loss of verbal initiative, wrong order of the discourse elements, abrupt topic shift, but also abuse of gesture, altered intonation, fixed-facial expression, loss of eye-contact (see Arcara & Bambini, 2016; Marini, Andreetta, del Tin, & Carlomagno, 2011). In this study, the Interview task, which lasts 5 minutes, is used to examine discourse production. The examiner has a single paper sheet (a checklist) where to record the frequency of occurrences of discourse anomalies. The task may be demanding for those who administer it, who have not only to identify the anomalies (which can be numerous and occur simultaneously), but at the same time note down their frequency.

It seemed appropriate, then, to make this task more user-friendly by turning it into a digital format and to help its administration by drawing on neuropsychology and IT disciplines. To our knowledge, this is the first attempt to transform a highly professional paper-and-pencil tool for the evaluation of several dimensions of pragmatic and paralinguistic features of discourse (i.e., the Interview task) into a digital version. This new tool was developed in Italian.

5.2 Implementation of the Interview Application[1]

5.2.1. Method

Study 5 aimed at describing the development of new software for the assessment of discourse production and was realized through a fruitful collaboration between neuropsychologists and IT specialists. The paper-and-pencil Interview task, transformed into a software application for tablets and PC, consists in an oral interview to evaluate the patient's discourse by means of a series of informal questions. The Interview does not require the patient to perform a particular task, since most of the work is entrusted to the examiner. The examiner has to lead the talk, listen carefully to the patient and simultaneously recognize, count and take note of any of the 22 discourse anomalies that may occur. More specifically, the examiner has to assign a score to the frequency of occurrence of a given anomaly (0 = anomaly occurred three or more times; 1 = anomaly occurred one or two times; and 2 = never occurred). At the same time, the examiner monitors the duration of the total Interview time (5 minutes) and encourages the patient to produce the discourse in case he/she is not keen to speak. The 22 anomalies that have to be considered during the Interview task are reported in Table 5.1.

[1] Since Study 5 aimed at transforming a paper-and-pencil neuropsychological task into a software-based task, the Method and the Result sections of this study follows a different conceptual format than the other four studies.

	Analysis of discourse during the Interview		OCCURRENCE (SCORING)			
	Parameters to measure	*Brief Description*	VERY OFTEN	SOMETIMES	NEVER	TOTAL
		GRAMMAR AND VOCABULARY				
1	**Anomias**	*Inability to recall words*				
2	**Agrammatisms**	*Lacking grammatical structure*				
3	**Phonemic Paraphasias**	*Incorrect selection of phonemic units*				
4	**Semantic Paraphasias**	*Incorrect selection in the word meaning*				
5	**Circumlocutions**	*More words than necessary to express an idea*				
		SPEECH				
6	**Repetitions / Passe-partout expressions**	*Stereotyped Repetition of words*				
7	**Incomplete utterances**	*Tendency to produce utterances unfinished*				
8	**Echolalia**	*Meaningless repetition of one's spoken words*				
9	**Coprolalia**	*Involuntary and repetitive use of obscene language*				
		INFORMATIVENESS				
10	**Difficulty in Yes / No answers**	*Inability to respond to questions that only require yes/no*				
11	**Under-informative**	*Tendency to speak telegraphically*				
12	**Over-informative**	*Tentency to provide excess of information*				
13	**Loss of verbal initiative**	*Loss of spontaneity in absence of articulatory impairment*				
		INFORMATION FLOW				
14	**Loss of- / Wrong use of cohesive ties**	*Speech with weak "train of thought" support*				
15	**Missing referents**	*Pronouns often missing or unknown to the interlocutor*				
16	**Wrong order of the discourse elements**	*Wrong order of the (correct) sentence elements*				
17	**Abrupt topic shift**	*Abruptions due to distractions*				
		PARALINGUISTIC FEATURES				
18	**Altered speech pace**					
19	**Altered intonation**					
20	**Loss of Eye-contact**					
21	**Fixed Facial expression**					
22	**Abuse of Gesture**					

Figure 5.1. Parameters discourse analysis included in the Interview task (see Arcara & Bambini, 2016 for more details).

To administer the task accurately and keep to the allotted 5 minutes, the examiner should simultaneously focus on the possible presence of any of the above-listed anomalies (Figure 5.1). Both in the paper-and-pencil version and the digital version of the task, the examiner can make audio-recordings of the patient’s speech and assign the scores later (off-line). This, however, increases the time needed to obtain a final global score.

For this reason, we wanted to develop an application that could help reduce the examiner’s stress by attempting to optimize the procedure needed for the assessment of the Interview task, and possibly refine objectivity of scoring.

5.2.2 Results

The Interview application is made up of a server that records the personal data of the examinee, the audio-recordings of the Interview and the scores assigned to the patient by the examiner. First of all, the examiner has to access the dedicated website and log into the platform or register (Figure 5.2), which allows to use the app and save all the data that are put in.

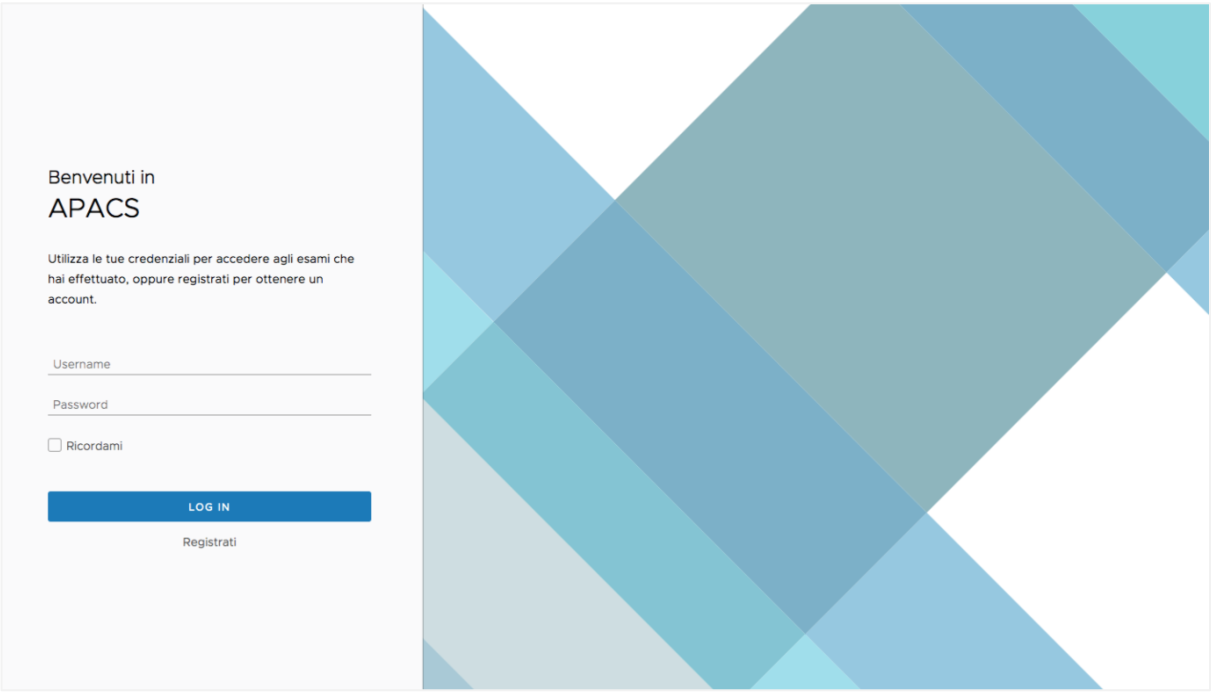

Figure 5.2. Log-in and registration page of the APACS Interview App.

Once logged in, the user can input some personal information about the patient for future follow-ups or can access the file of a patient previously "saved" on the system. If the examiner does not have a previous registration of a patient, he/she can click on "Nuova Valutazione" (Figure 5.3) in order to insert the patient's information (e.g., age, years of education, nationality, presence or absence of a neurological disease, type of disease, etc.; see Figure 5.3).

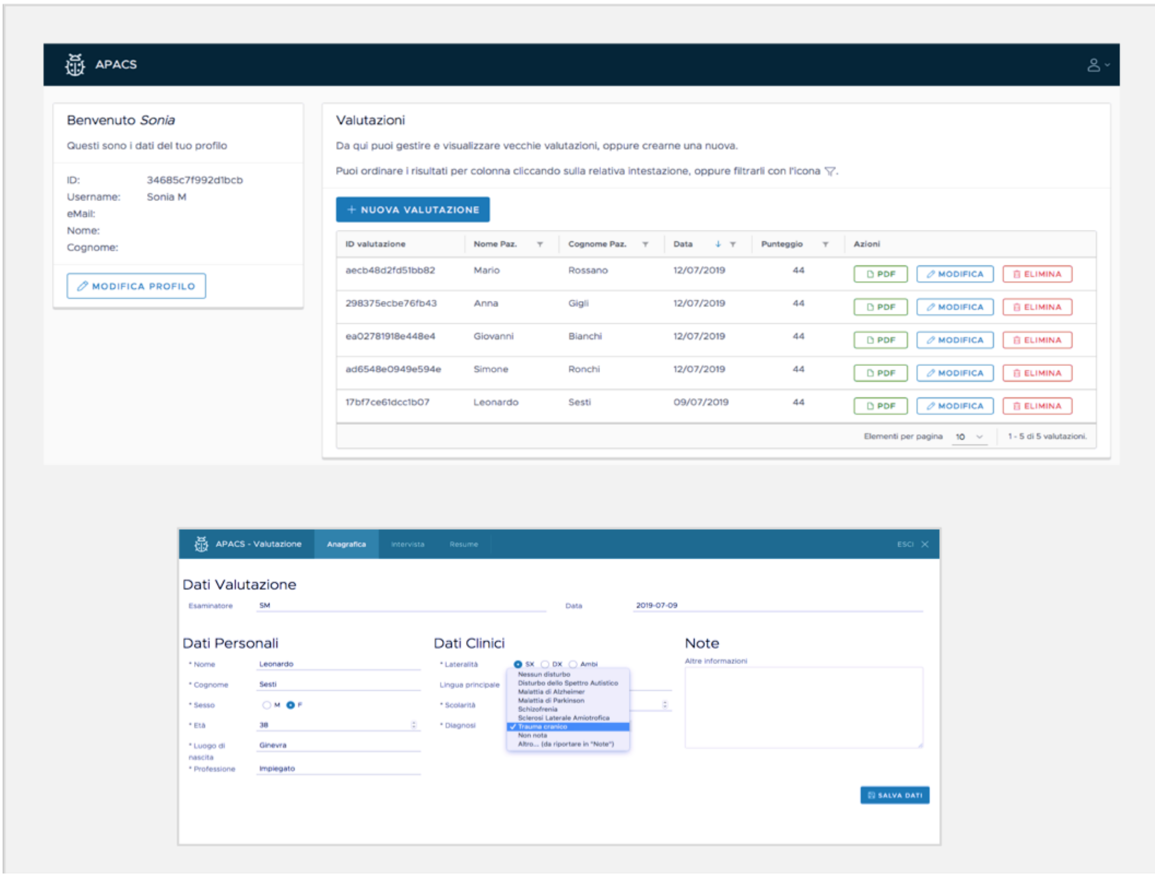

Figure 5.3. First interface of the Interview task; New Assessment interface; Creation of a page to save the patient's general information

At the end of each evaluation, information about the patient is reported in a resume document, in which each of the 22 single scores and the final score are automatically generated by the system, with the possibility to save the material in a PDF document. During the Interview task, the user clicks on the colored buttons, each of them corresponding to one discourse feature. Figure 5.7 shows the Interview task in its original paper-and-pencil form (paper-and-pencil score sheet at the top of Figure 5.7) and its digitalized form (at the bottom of Figure 5.7). The buttons associated to each of the 22 discourse features and present on the panel are divided in 5 groups, following the original format of the test (i.e., Grammar and Vocabulary, Speech, Informativeness, Information flow, and Paralinguistic features; see Figure 5.1). The panel has been developed with a *point-and-click interaction*, so that the examiner clicks on the relative button each time an anomaly of discourse is detected. After any anomaly has been clicked for the first time, each following click will count as one occurrence of that specific anomaly. Frequency of occurrence is thus automatically computed. If the examiner realizes that he/she has made a mistake (e.g., a false positive judgment), it is possible to click on “undo” near each of the 22 discourse features buttons to remove the error. The *point-and-click interaction* in the digital version of the task is particularly important for the purpose of this study since the examiner no longer needs to keep track of the occurrences of the anomaly, and can concentrate more on the patient’s performance.

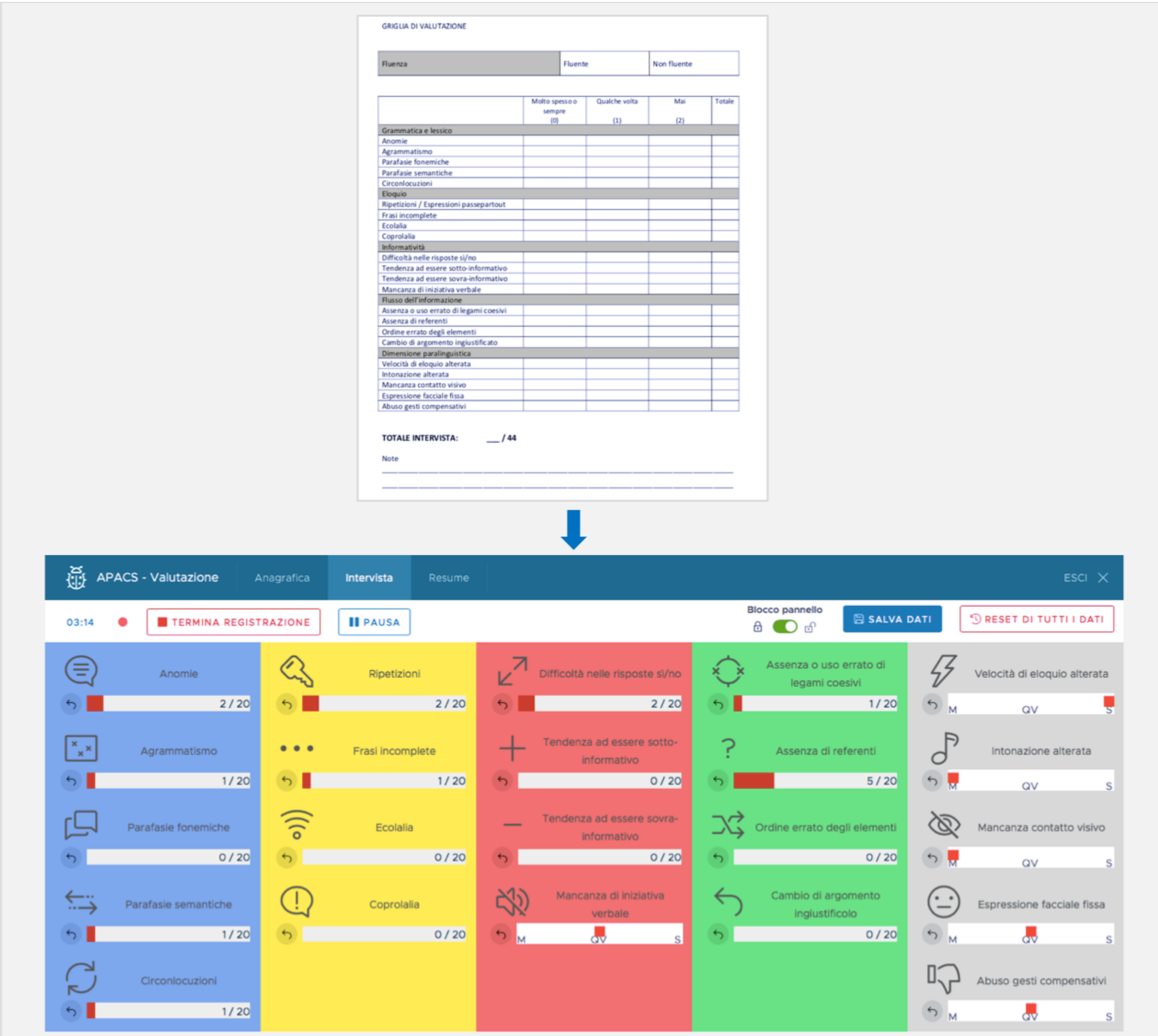

Fig. 5.7 APACS Interview from paper-and-pencil to digitalization; a) Interview task in its paper-and-pencil form at the top of the figure; b) Interview task in digitalized form at the bottom of the figure.

During the Interview task it is important to record the audio of the examinee to check for any possible incongruence in the score. The digital version of this task requires a click on the "record" button before starting the assessment, and, if the user wants to interrupt the Interview, the recording can be stopped to reduce the chance of any possible alterations in the scoring (Figure 5.8).

The support of the app in the automatization of the scoring phase is believed to represent a stress-reducing aspect of this new digital tool. In this digital version, the examiner only needs 'to react' each time he/she recognizes an anomaly, then the software gives the correct score according to the rules set out in the manual (Arcara & Bambini, 2016). Figure 5.8 shows an example of a patient's resume, which always appears on the final page of the testing phase.

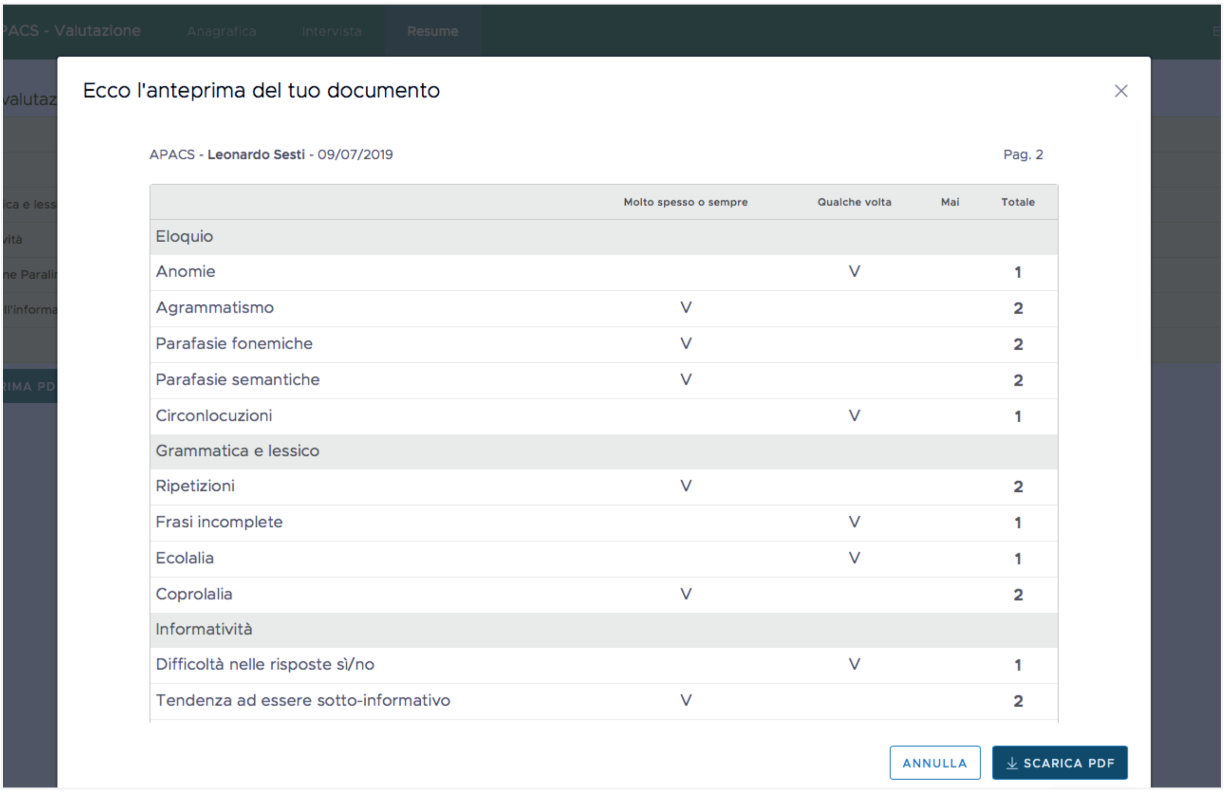

Figure 5.8 Resume of the results.

5.2.3 Observations, technological limitations, and further proposals

We collected a set of audio-recordings on the Interview task. This would serve as an initial pool of data for comparing the patients' and healthy controls' speech, to possibly automatize the recognition of parts of the speech. The audio-recordings we collected were transcribed from audio to text. Among the 22 discourse features assessed by the Interview task, only the parameters of discourse that seemed suitable for automatic error recognition (e.g., repetitions or agrammatisms; Figure 5.1) were entered in this audio-text transcription. Three services were used for transcription: *Google*, *Microsoft Azure,* and *Trint*. However, none of them was able to transcript the conversation with acceptable accuracy. The difficulty associated with the audio-text transcription was related to some technical limitations -worth to be refined in the future- due to differences in audio-quality across recordings and most importantly to the use of dialect by some participants. Dialect is still used by the elderly in this part of Italy for informal conversations and participants often switched from dialect to standard Italian during the task. This made automatic detection of anomalies challenging to the sophisticated automatic speech-recognition systems which were set on standard Italian.

It goes without saying that, although the digitalization of cognitive tasks could optimize the resources needed to assess the performance of patients, this cannot substitute the clinician's observation, which remains essential for a reliable neuropsychological diagnosis.

Through the collaboration of IT professionals and neuropsychologists, we reached the important first goal of realizing a tool that can be tested and adopted in its ready-to-use version, although I am aware that further work is needed to refine it. It is important to note that Study 5 was possible thanks to finding a shared language between the two disciplines. Future testing and refinements of the digital Interview task are believed to be necessary to get this tool used in clinical contexts. In a traditional neuropsychological assessment, in fact, the analysis of discourse does not always have a precise structure and it only serves for obtaining a qualitative picture of the patient's profile before administering psychometric tests. The agile use of the digital Interview task (which lasts only 5 minutes) could make this preliminary observation more structured and allow the collection of valid information about the patient's ability to communicate. In order to use this tool to its full potential, more inter-disciplinary collaborations, discussions and clinicians' feedback will be necessary in the future.

CHAPTER 6. CONCLUSIONS

The studies reported in this project resulted from the inter-connected work of neuropsychologists, medical doctors, linguists, and IT specialists. The main purpose was to advance knowledge on the relationship between CR and language. The findings of Studies 1 to 4 highlighted the role of CR, showing that keeping the cognitive system active along adulthood maintains a more skillful language in the later stages of life, which is undoubtedly a resource for social interactions and well-being. The interdisciplinary approach, with particular interest in the digitalization of cognitive tasks, was another relevant aspect addressed in this project, leading to the development (and use) of language and CR digital measurements, particularly in Study 1, Study 3, and Study 5.

5.1. Summary of the findings and of their implications

In Study 1 the important role of CR was analyzed in a Lexical Decision task, a Semantic Matching task and a Sentence Reading task. The computerized Lexical Decision and the Semantic Matching tasks were created ad hoc for the purpose of this study. The words entered in the first two tasks were well-balanced across different degrees of lexical frequency (high vs. low) and lexical semantics (concrete vs. abstract words) to examine possible variation of the CR effect across different task demands. In the Sentence Reading task, the CR effect was investigated by comparing syntactically and semantically incongruent sentences to their correct and plausible counterparts, to assess how CR modulates the resolution of grammatical and pragmatic/contextual incongruencies based on reading times as the dependent variable. Results emerged from Study 1 highlighted the fact that high CR predicts faster and more accurate responses in the lexical decision, semantic matching and reading performances. CR played different roles across the language processes involved, with low-frequency, abstract words and detection of grammatical anomalies strongly dependent on CR, compared to high-frequency, concrete words and semantic anomalies. Study 1 indicates that abstract words and low-frequency words, which require more efforts to be processed, can be well preserved by keeping an active lifestyle in aging. Based on the Sentence Reading outcomes, Study 1 underlines that high CR not only maintains higher knowledge of grammar rules but also better monitoring of these rules "on-line" during the reading processing.

Study 2 and Study 3 revealed the weak role of CR in processing some cognitive tasks and specific lexical items. In Study 2, in fact, words that convey poor semantic/contextual information, that is proper names, were not dependent on CR, possibly due to their pure referential characteristics and their scarce semantic connections with their bearers. This supports the distinct status of proper names in the processing of nominal lexical items. Study 3 is strictly connected to the results obtained in Study 2 and shows that, although CR can predict overall name retrieval (with stronger effects in the early symptoms of decline), some name categories (Logo Names and Common Nouns) benefit more from CR than others (Proper names). Thus, this may support the idea that nominal lexical items involved in denser semantic networks benefit from the contextual and semantic information conveyed by CR. A possible implication emerging from the results of Study 2 and Study 3 is that the weak dependence of Proper Name retrieval on CR can make the former especially useful to detect early symptoms of dementia.

Study 4 was dedicated to the pragmatic abilities of language and their relationship with CR. The effect of CR on pragmatics was observed in patients with Parkinson's Disease (PD) matched with healthy controls. We first sketched the pragmatic profile of this clinical population showing, that compared to controls, PD patients manifested a pragmatic disorder in discourse production and in inferring from narrative and humorous stories. Study 4 also showed that in PD patients CR is strongly associated with pragmatic comprehension. Overall, the findings of Study 4 suggest that in this population high CR may not be sufficient to compensate problems in the production dimension of pragmatics. Further investigation is needed to understand what can possibly be influential factors of pragmatic production in PD (e.g., personality traits and the presence of depression).

In Study 5, a tablet and PC application was developed for assessing several components of discourse by means of a user-friendly digital interface. As far as I am aware, to date this is the first attempt to make the digital version of a tool that includes several dimensions of pragmatic and paralinguistic features of discourse. From the point of view of the user of this tool (the examiner), this new digital task represents a useful and innovative way for assessment. The digital version of the Interview task can allow the clinician to better focus on what the patient is saying in the interview, while its automatic score calculation can help reduce errors that might occur with the manual procedure. Finally, a PDF final resume with a run of complete information about the patient implies a reduction in paper consumption that can have a small but welcome environmental impact.

5.2. Limitations and suggestions for future research

I am aware of some limitations of the studies described above. Analyzing the influence of CR on cognitive performance in longitudinal studies would be ideal for the comprehension of resilience over time. However, the previous literature and the studies presented in this project show that various other factors can influence cross-sectional studies, allowing to outline the relationship between some behavioral outcomes (like speediness and accuracy in the aging language) and CR measures, including a wide range of adulthood activities. The influence of comprehensive CR indices on performance is an important issue to consider in the clinical neuropsychological assessment, where education (with age) is frequently used as the only proxy for CR, without taking into account other important learning experiences.

Good language skills undoubtedly contribute to CR. For example, as reported above, multilingualism can preserve brain functioning from age-related alterations. However, there is an ongoing debate on this matter. It might be that old people with good language skills have a high CR level because they have always had such good skills, or it may be that their CR prevented language deterioration. For this reason, a future research question should focus more in depth on the refinement of the CR concept and on its disentanglement from other factors that impact cognition like Intelligent Quotient (IQ) or socioeconomic status. Importantly, in this project CR has been considered as distinct from IQ measures, which refer to abilities tested on a certain performance. CR, instead, has been considered as an index of learning experiences that can enrich cognitive functioning over time.

This study does not include structural or functional neuroimaging data for measuring CR (Studies 1 to 4). Nonetheless, this project highlights several interesting relationships which are new in the literature, between language processing and pragmatic processing with CR (conceived in terms of composite measure), drawing an interesting picture of ability resources' interplay with cognition. A second limitation specifically concerns Study 1 and Study 3, in which a strong relationship was hypothesized between CR and semantic name categories, and also with more difficult words (i.e., abstract and low-frequency words). The results were in line with this hypothesis with regard to accuracy, but not with response times. Duration of visual presentation of stimuli was adapted to possible time constraints related to the age of participants. A possible explanation of the difference between accuracy and response times could reflect a physiological, age-related, synaptic delay (Rastle and Burke, 1996; Jackson et al., 2012), and high age-related variability (e.g., Hultsch et al., 2002; Bielak et al., 2010). Study 5 also has some limitations, one of which specifically concerns the amount of usability feedback from clinicians, who are the potential users of this application. Getting more feedback would allow, in the future, to refine this app based on the necessities of the clinical practices. Study 5 is a very important part of this project as it succeeded in connecting different disciplines and finding a shared language between IT and clinical neuropsychological professionals. This positive collaboration will hopefully be continued in the future.

In conclusion, the whole project also raises future research questions about CR: how are CR and its underlying neural resources interlaced with the *availability* and *usability* of contextual information in the environment? Are there other factors (e.g., stress monitoring) implied in the actual possibility to tap into CR? Are CR and its use associated with degrees of self-consciousness with regard to symptom manifestation? Finding answers to these questions is extremely important for the well-being of individuals, especially in our current society, in which the possibility to acquire new learning is exponentially increasing over generations thanks, for example, to technological progress. What this whole project has taught me is that, although everyone has a certain amount of cognitive reserve, resilience does not depend only on how many experiences ones makes across the lifespan or on how many years of education one has; it is a much more complex concept, worth to be acknowledged.

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APPENDIX

APPENDIX A. Items included in the computer-based task developed for Study 1

A.1 Items used in the *Lexical Decision Task*

LEXICAL DECISION TASK

REAL WORDS			Translation	PSEUDO WORDS
HF	CONCRETE	CUSCINO	PILLOW	IUNO
	CONCRETE	UFFICIO	OFFICE	CORZO
	CONCRETE	MARTELLO	HAMMER	LETO
	CONCRETE	TELEFONO	TELEPHONE	TECEBONO
	CONCRETE	LIBRO	BOOK	RIBRO
	CONCRETE	PISTOLA	GUN	RENTOLA
	CONCRETE	CASSETTO	DRAWER	GESTETTO
	CONCRETE	CAMERA	ROOM	PADORA
	CONCRETE	NAVE	SHIP	BACE
	CONCRETE	ACQUA	WATER	AFURA
LF	CONCRETE	PALCO	STAGE	CANCO
	CONCRETE	TANICA	CONTAINER	VADISA
	CONCRETE	MANTO	MANTLE	RENTO
	CONCRETE	CANTIERE	SITE	RESSIERE
	CONCRETE	BROCCA	PITCHER	PRACCA
	CONCRETE	CABINA	CABIN	CENSANA
	CONCRETE	AMMONIACA	AMMONIA	ANGELIAVA
	CONCRETE	COPPA	BOWL	COMBA
	CONCRETE	ALTARE	ALTAR	ITTALE
	CONCRETE	PLACCA	SLAB	FLOCCA
HF	ABSTRACT	SEGRETO	SECRET	DEBLOTO
	ABSTRACT	MUSICA	MUSIC	DUCISA
	ABSTRACT	MOTIVO	REASON	SOCAVO
	ABSTRACT	SENSO	SENSE	SERNO
	ABSTRACT	FUTURO	FUTURE	TUNURI
	ABSTRACT	DOMANDA	QUESTION	FOLENDA
	ABSTRACT	PACE	PEACE	MABE
	ABSTRACT	SICUREZZA	SAFETY	PIMURECCA
	ABSTRACT	ERRORE	ERROR	INFORE
	ABSTRACT	GENERE	GENDER	NEVORE
LF	ABSTRACT	SINTOMO	SYMPTOM	SANDOCO
	ABSTRACT	SAPORE	FLAVOR	RASERE
	ABSTRACT	ISTINTO	INSTINCT	ETTISTO
	ABSTRACT	ALIBI	ALIBI	ADAZI
	ABSTRACT	RISORSA	RESOURCE	DICORVA
	ABSTRACT	SIMPATIA	SYMPATHY	DOLLATIA
	ABSTRACT	PUDORE	MODESTY	RUVERE
	ABSTRACT	DETTAGLIO	DETAIL	PICCAGLIO
	ABSTRACT	LITE	QUARREL	NETE
	ABSTRACT	FRENESIA	FRENZY	GRISURA

APPENDIX A.1 Stimuli used in the Lexical Decision task. HF = High Lexical Frequency words; LF = Low lexical Frequency words.

A.2 Items used in the *Semantic Matching Task*

SEMANTIC ASSOCIATION TASK					
		PAIRS OF WORDS		Translation	
		RESTARE	RIMANERE	TO REMAIN	TO STAY
		ENTRARE	ACCEDERE	TO ENTER	TO GO IN
	HF	AIUTARE	ASSISTERE	TO HELP	TO ASSIST
		DORMIRE	RIPOSARE	TO SLEEP	TO REST
CONCRETE		GUARDAR	OSSERVARE	TO WATCH	TO OBSERVE
		SEGNARE	MARCARE	TO MARK	TO SCRATCH
		SPEDIRE	MANDARE	TO SEND	TO DISPATCH
	LF	SVEGLIAR	DESTARE	TO WAKE	TO ROUSE
		BOLLIRE	LESSARE	TO BOIL	TO SIMMER
		SCUOTERE	AGITARE	TO SHAKE	TO JOLT
		PENSARE	MEDITARE	TO THINK	TO REFLECT
		CREDERE	REPUTARE	TO BELIEVE	TO CONSIDER
	HF	ASPETTAR	ATTENDERE	TO WAIT	TO LINGER
		DIVENTAR	DIVENIRE	TO BECOME	TO DEVELOP
ABSTRACT		CAPIRE	INTENDERE	TO UNDERSTAND	TO COMPREHEND
		ESPLORAR	INDAGARE	TO EXPLORE	TO EXAMINE
		ISOLARE	CONFINARE	TO ISOLATE	TO CONFINE
	LF	ODIARE	DETESTARE	TO HATE	TO LOATHE
		TRIONFAR	VINCERE	TO TRIUMPH	TO WIN
		ACCADERI	CAPITARE	TO HAPPEN	TO OCCUR
		CIBO	PASTO	FOOD	MEAL
		PRIGIONE	GALERA	JAIL	PRISON
	HF	OSPEDALE	CLINICA	HOSPITAL	CLINIC
		PARETE	MURO	WALL	PARTITION
CONCRETE		SACCO	BORSA	SACK	BAG
		SPINA	ACULEO	THORN	NEEDLE
		ASTRO	STELLA	STAR	CELESTIAL BODY
	LF	PILASTRO	COLONNA	PILLAR	COLUMN
		TANA	COVO	DEN	HIDEOUT
		MEMBRAN	INVOLUCRO	WRAPPING	COVERING
		MESSAGGI	NOTIFICA	MESSAGE	NOTIFICATION
		SCELTA	OPZIONE	CHOICE	OPTION
	HF	NUMERO	CIFRA	NUMBER	FIGURE
		ATTIMO	ISTANTE	MOMENT	INSTANT
ABSTRACT		FRETTA	PREMURA	HURRY	HASTE
		SELEZIONI	CERNITA	SELECTION	PICK
		ARBITRIO	GIUDIZIO	REASONING	JUDGEMENT
	LF	AUDACIA	CORAGGIO	PLUCK	BRAVERY
		AUSPICIO	AUGURIO	DESIRE	WISH
		INGEGNO	ACUME	INTELLECT	ACUTENESS

APPENDIX A.2 Stimuli used in the Semantic Matching task. HF = High Lexical Frequency words; LF = Low lexical Frequency words.

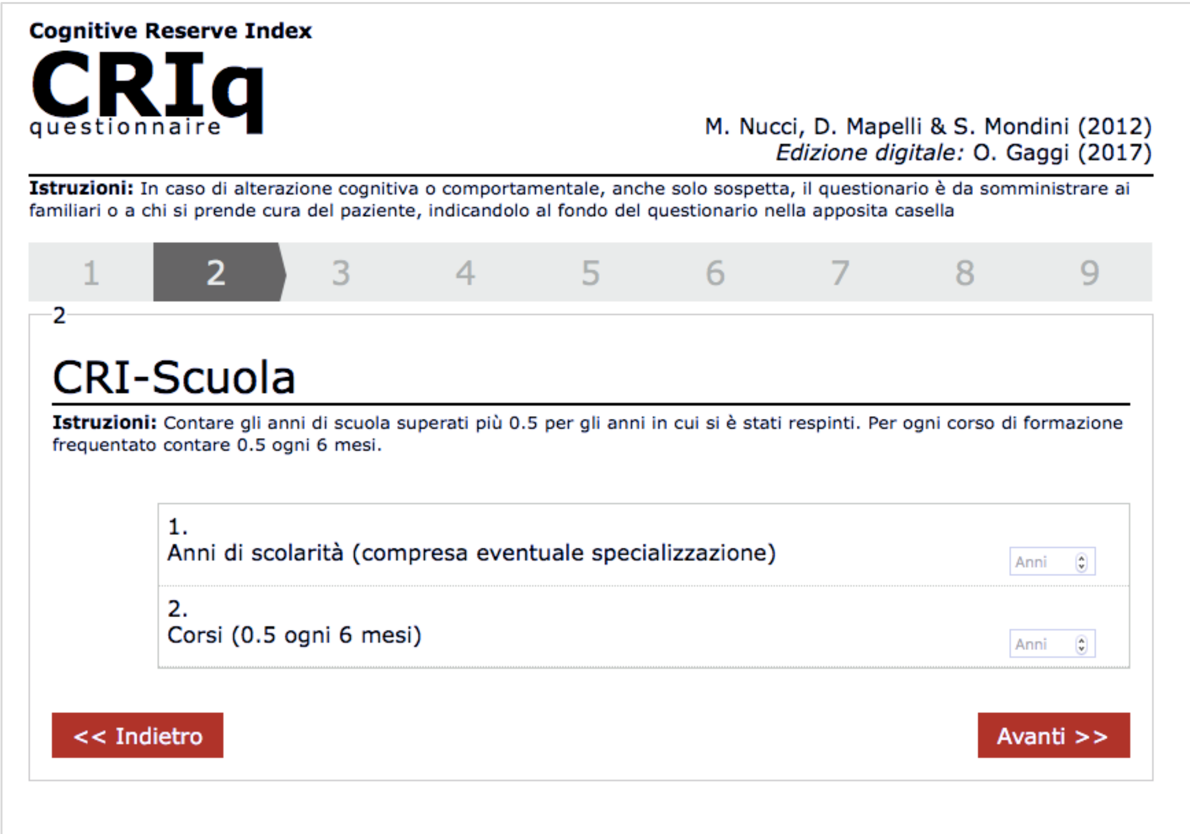
A.3 Items used in the *Sentence Reading task*

SENTENCE READING TASK									Translation
	Il	treno	espresso	parte	in	perfetto	orario		The express train leaves/leave on perfect time
	Il	treno	espresso	**partono**	in	perfetto	orario		
	Il	gelsomino	fiorito	profuma	nella	notte	calda		The blossoming jasmine scents/scent in the
	Il	gelsomino	fiorito	**profumano**	nella	notte	calda		warm night
	Il	ceppo	odoroso	crepita	nel	nuovo	caminetto		The fragrant stump crackles /crackle in the
	Il	ceppo	odoroso	**crepitano**	nel	nuovo	caminetto		new fireplace
	La	macchina	sportiva	viaggia	sulla	strada	montana		The sports car travels /travel along the
	La	macchina	sportiva	**viaggiano**	sulla	strada	montana		mountain road
	Il	faro	lontano	appare	nella	fitta	nebbia		The far lighthouse appears /appear in the thick fog
SYNTACTIC	Il	faro	lontano	**appaiono**	nella	fitta	nebbia		
VIOLATION	La	palla	rossa	rotola	tra	la	folla		The red
	La	palla	rossa	**rotolano**	tra	la	folla		ball rolls /roll into the crowd
	La	telefonata	inattesa	arriva	dagli	Stati	Uniti		The unexpected phone call comes /come
	La	telefonata	inattesa	**arrivano**	dagli	Stati	Uniti		from the United States
	Il	vetro	blindato	protegge	dal	rumore	esterno		The bulletproof glass protects /protect
	Il	vetro	blindato	**proteggono**	dal	rumore	esterno		from the external noise
	Il	libro	si	bagna	sotto	la	pioggia		The
	Il	libro	si	**bagnano**	sotto	la	pioggia		book[self] wets /wet under the rain
	Lo	scaffale	polveroso	crolla	per	il	peso		The dusty shelf collapses/collapse for the weight
	Lo	scaffale	polveroso	**crollano**	per	il	peso		
	La	lampada	fluorescente	illumina	senza	dare	alcun	calore	The fluorescent lamp
	La	lampada	fluorescente	**dimentica**	senza	dare	alcun	calore	lights /forgets without giving any warmth
	La	penna	stilografica	cade	dal	vecchio	tavolo	inclinato	The fountain pen falls /smokes from the
	La	penna	stilografica	**fuma**	dal	vecchio	tavolo	inclinato	old tilted table
	La	valanga	si	ferma	contro	un	muro	resistente	The avalanche [self] stops /regrets against a resistant
	La	valanga	si	**pente**	contro	un	muro	resistente	wall
	La	terra	si	spacca	sotto	il	solleone	estivo	The ground [self] breaks /hangs under the summer
	La	terra	si	**appende**	sotto	il	solleone	estivo	heat
	La	cassettiera	antica	cede	a	causa	dei	tarli	The ancient chest of drawers caves in /runs because
SEMANTIC	La	cassettiera	antica	**corre**	a	causa	dei	tarli	of the woodworms
VIOLATION	La	torre	medievale	resiste	nonostante	il	violento	terremoto	The medieval tower stands up /
	La	torre	medievale	**studia**	nonostante	il	violento	terremoto	studies despite the violent earthquake
	Il	vecchio	disco	fruscia	gia	da	molto	tempo	The old record rustles /hopes already from a long
	Il	vecchio	disco	**spera**	gia	da	molto	tempo	time
	La	roccia	si	sgretola	col	taglio	degli	alberi	The rock [self] crumbles /combs because of the
	La	roccia	si	**pettina**	col	taglio	degli	alberi	cutting
	L'incendio	nel	villaggio	divampa	violento	in	un	attimo	The fire in the village blazes /plays violently
	L'incendio	nel	villaggio	**recita**	violento	in	un	attimo	in a moment
	La	campana	bronzea	invita	alla	messa	della	domenica	The bronzy bell invites /swears to the
	La	campana	bronzea	**giura**	alla	messa	della	domenica	Sunday mass

APPENDIX A.3 Stimuli used in the Sentence Reading task. SYNT VIOL = sentenced used to compare correct sentences and syntactically violated sentences. SEM VIOL = sentences used to compare correct sentences and semantically violated sentences. Adapted from De Vincenzi et al., (2003).

APPENDIX B. Items included in the Cognitive Reserve Index questionnaire

B.1 Cognitive Reserve Index-Education (CRI-Education)


Cognitive Reserve Index

CRIq

questionnaire

M. Nucci, D. Mapelli & S. Mondini (2012)
Edizione digitale: O. Gaggi (2017)

Istruzioni: In caso di alterazione cognitiva o comportamentale, anche solo sospetta, il questionario è da somministrare ai familiari o a chi si prende cura del paziente, indicandolo al fondo del questionario nella apposita casella

1 2 3 4 5 6 7 8 9

2

CRI-Scuola

Istruzioni: Contare gli anni di scuola superati più 0.5 per gli anni in cui si è stati respinti. Per ogni corso di formazione frequentato contare 0.5 ogni 6 mesi.

1.
Anni di scolarità (compresa eventuale specializzazione) Anni

2.
Corsi (0.5 ogni 6 mesi) Anni

<< Indietro Avanti >>

B.2 Cognitive Reserve Index-Working Activity (CRI-WorkingActivity)

Cognitive Reserve Index

CRIq
questionnaire

M. Nucci, D. Mapelli & S. Mondini (2012)
Edizione digitale: O. Gaggi (2017)

Istruzioni: In caso di alterazione cognitiva o comportamentale, anche solo sospetta, il questionario è da somministrare ai familiari o a chi si prende cura del paziente, indicandolo al fondo del questionario nella apposita casella

1 2 **3** 4 5 6 7 8 9

3

CRI-Lavoro

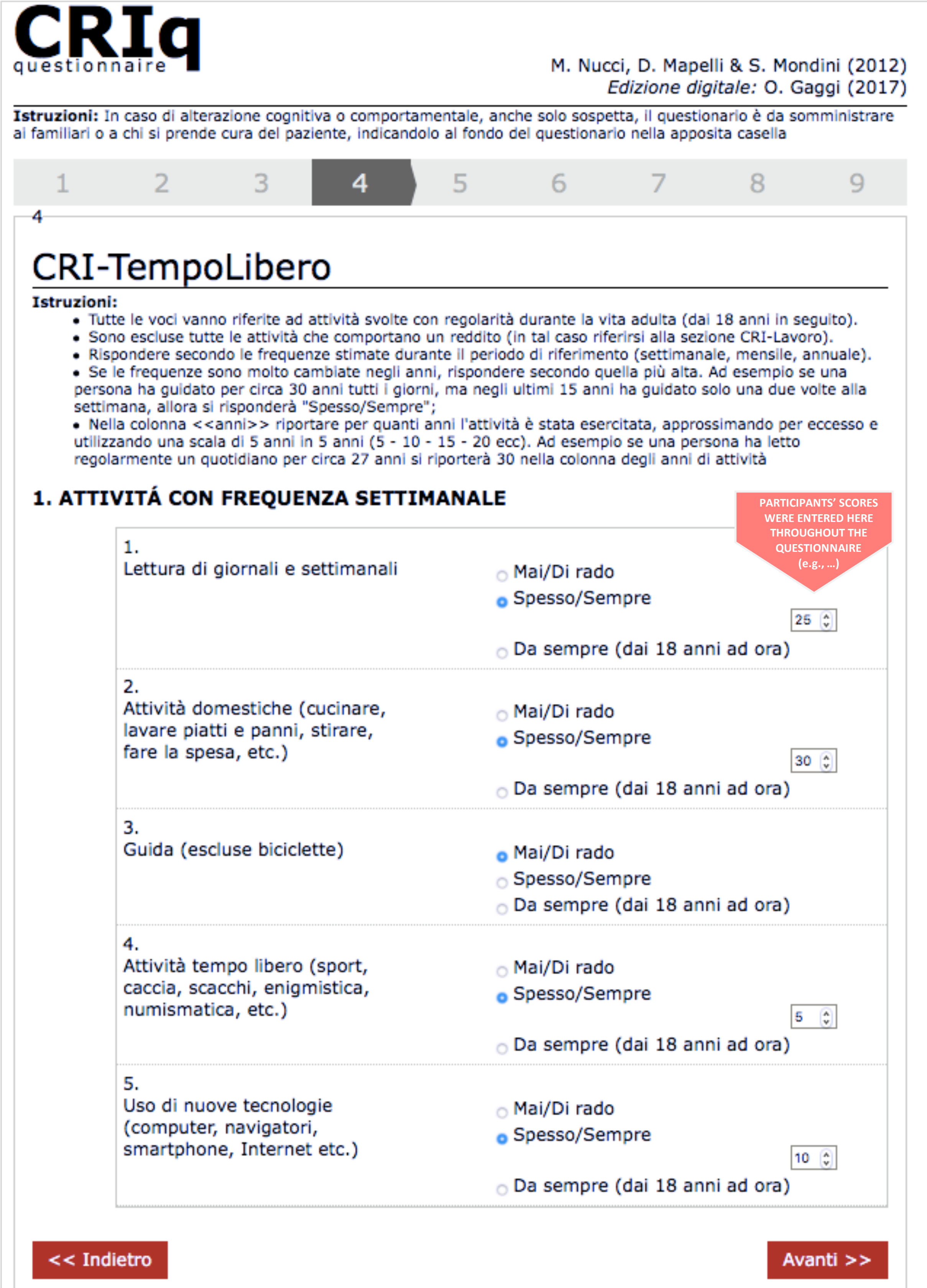
Istruzioni: Indicare gli anni lavorativi per eccesso, utilizzando una scala di 5 anni in 5 anni(0 - 5 - 10 - 15 - 20 ecc; ad esempio, se una persona ha lavorato per 17 anni, indicare 20). I cinque livelli sono suddivisi per il grado di impegno cognitivo richiesto e di responsabilità personale assunta. Riportare ogni professione esercitata, anche se svolta in contemporanea con altre.

1. Operaio non specializzato, lavoro in campagna, giardiniere, badante, cameriere, autista, operatore call center, baby-sitter, colf, ecc.	Anni
2. Artigiano o operaio specializzato, impiegato semplice, cuoco, commesso, sarto, idraulico, infermiere, militare (basso grado), parrucchiere, ecc.	Anni
3. Commerciante, impiegato di concetto, religioso, agente di commercio, agente immobiliare, maestra d'asilo, musicista, tecnico specializzato, ecc.	Anni
4. Dirigente di piccola azienda, libero professionista qualificato, insegnante, imprenditore, medico, avvocato, psicologo, ingegnere ecc.	Anni
5. Dirigente di grande azienda, direttore con alta responsabilità, giudice, politico, docente universitario, magistrato, chirurgo, ricercatore, ecc.	Anni

<< Indietro   Avanti >>

B.3 Cognitive Reserve Index-Leisure Time Activity (CRI-LT)

B.3.1. Activities with weekly frequency



CRIq
questionnaire

M. Nucci, D. Mapelli & S. Mondini (2012)
Edizione digitale: O. Gaggi (2017)

Istruzioni: In caso di alterazione cognitiva o comportamentale, anche solo sospetta, il questionario è da somministrare ai familiari o a chi si prende cura del paziente, indicandolo al fondo del questionario nella apposita casella

1 2 3 **4** 5 6 7 8 9

4

CRI-TempoLibero

Istruzioni:

- Tutte le voci vanno riferite ad attività svolte con regolarità durante la vita adulta (dai 18 anni in seguito).
- Sono escluse tutte le attività che comportano un reddito (in tal caso riferirsi alla sezione CRI-Lavoro).
- Rispondere secondo le frequenze stimate durante il periodo di riferimento (settimanale, mensile, annuale).
- Se le frequenze sono molto cambiate negli anni, rispondere secondo quella più alta. Ad esempio se una persona ha guidato per circa 30 anni tutti i giorni, ma negli ultimi 15 anni ha guidato solo una due volte alla settimana, allora si risponderà "Spesso/Sempre";
- Nella colonna <<anni>> riportare per quanti anni l'attività è stata esercitata, approssimando per eccesso e utilizzando una scala di 5 anni in 5 anni (5 - 10 - 15 - 20 ecc). Ad esempio se una persona ha letto regolarmente un quotidiano per circa 27 anni si riporterà 30 nella colonna degli anni di attività

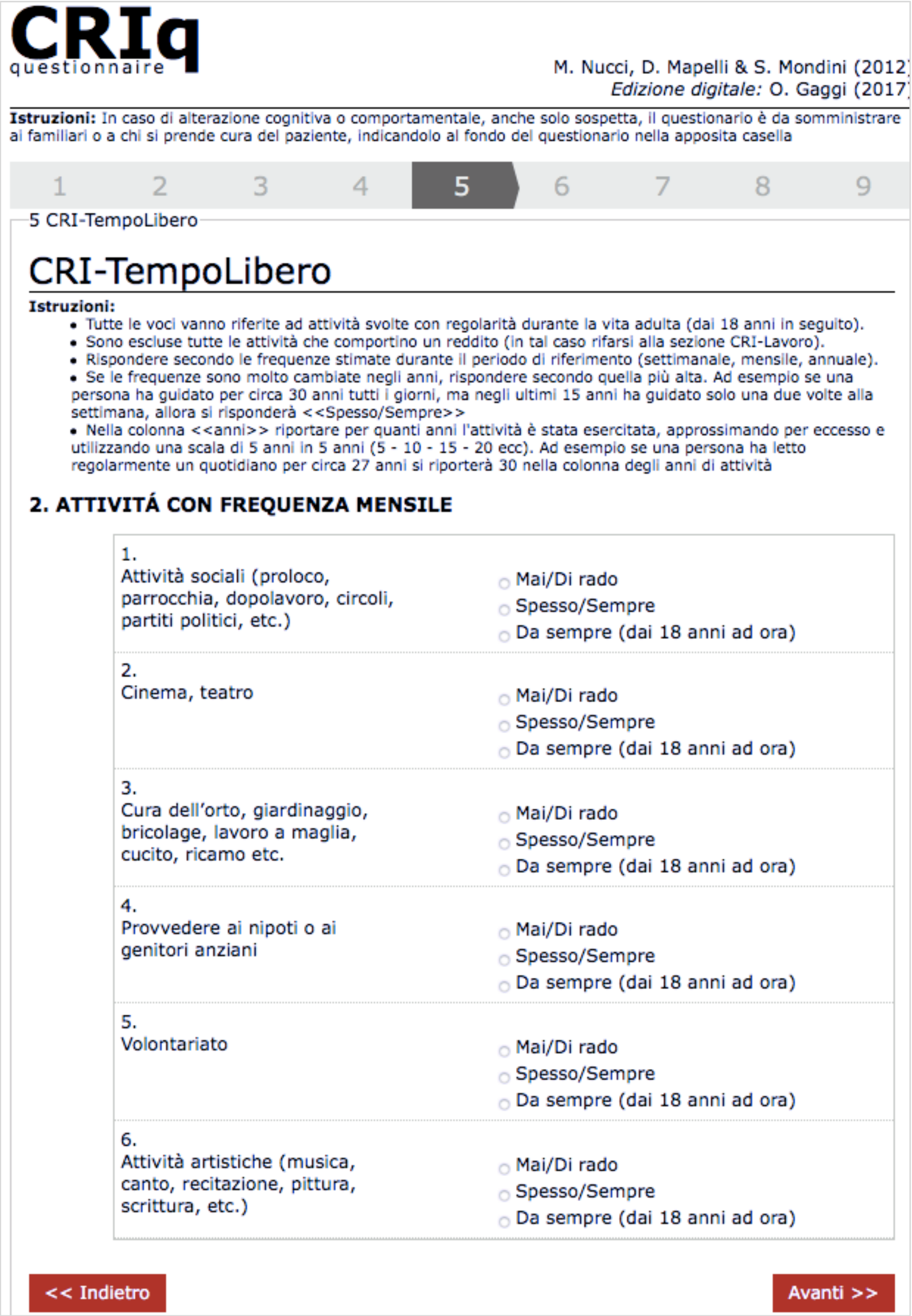
1. ATTIVITÁ CON FREQUENZA SETTIMANALE

PARTICIPANTS' SCORES WERE ENTERED HERE THROUGHOUT THE QUESTIONNAIRE (e.g., ...)

1. Lettura di giornali e settimanali	○ Mai/Di rado ● Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)	25
2. Attività domestiche (cucinare, lavare piatti e panni, stirare, fare la spesa, etc.)	○ Mai/Di rado ● Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)	30
3. Guida (escluse biciclette)	● Mai/Di rado ○ Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)	
4. Attività tempo libero (sport, caccia, scacchi, enigmistica, numismatica, etc.)	○ Mai/Di rado ● Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)	5
5. Uso di nuove tecnologie (computer, navigatori, smartphone, Internet etc.)	○ Mai/Di rado ● Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)	10

<< Indietro Avanti >>

B.3.2. Activities with montly frequency



CRIq
questionnaire

M. Nucci, D. Mapelli & S. Mondini (2012)
Edizione digitale: O. Gaggi (2017)

Istruzioni: In caso di alterazione cognitiva o comportamentale, anche solo sospetta, il questionario è da somministrare ai familiari o a chi si prende cura del paziente, indicandolo al fondo del questionario nella apposita casella

1 2 3 4 **5** 6 7 8 9

5 CRI-TempoLibero

CRI-TempoLibero

Istruzioni:

- Tutte le voci vanno riferite ad attività svolte con regolarità durante la vita adulta (dai 18 anni in seguito).
- Sono escluse tutte le attività che comportino un reddito (in tal caso rifarsi alla sezione CRI-Lavoro).
- Rispondere secondo le frequenze stimate durante il periodo di riferimento (settimanale, mensile, annuale).
- Se le frequenze sono molto cambiate negli anni, rispondere secondo quella più alta. Ad esempio se una persona ha guidato per circa 30 anni tutti i giorni, ma negli ultimi 15 anni ha guidato solo una due volte alla settimana, allora si risponderà <<Spesso/Sempre>>
- Nella colonna <<anni>> riportare per quanti anni l'attività è stata esercitata, approssimando per eccesso e utilizzando una scala di 5 anni in 5 anni (5 - 10 - 15 - 20 ecc). Ad esempio se una persona ha letto regolarmente un quotidiano per circa 27 anni si riporterà 30 nella colonna degli anni di attività

2. ATTIVITÁ CON FREQUENZA MENSILE

1. Attività sociali (proloco, parrocchia, dopolavoro, circoli, partiti politici, etc.)	○ Mai/Di rado ○ Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)
2. Cinema, teatro	○ Mai/Di rado ○ Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)
3. Cura dell'orto, giardinaggio, bricolage, lavoro a maglia, cucito, ricamo etc.	○ Mai/Di rado ○ Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)
4. Provvedere ai nipoti o ai genitori anziani	○ Mai/Di rado ○ Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)
5. Volontariato	○ Mai/Di rado ○ Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)
6. Attività artistiche (musica, canto, recitazione, pittura, scrittura, etc.)	○ Mai/Di rado ○ Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)

<< Indietro   Avanti >>

B.3.3. Activities with annual frequency

Cognitive Reserve Index

CRIq
questionnaire

M. Nucci, D. Mapelli & S. Mondini (2012)
Edizione digitale: O. Gaggi (2017)

Istruzioni: In caso di alterazione cognitiva o comportamentale, anche solo sospetta, il questionario è da somministrare ai familiari o a chi si prende cura del paziente, indicandolo al fondo del questionario nella apposita casella

1 2 3 4 5 **6** 7 8 9

6 CRI-TempoLibero

CRI-TempoLibero

Istruzioni:

- Tutte le voci vanno riferite ad attività svolte con regolarità durante la vita adulta (dai 18 anni in seguito).
- Sono escluse tutte le attività che comportino un reddito (in tal caso rifarsi alla sezione CRI-Lavoro).
- Rispondere secondo le frequenze stimate durante il periodo di riferimento (settimanale, mensile, annuale).
- Se le frequenze sono molto cambiate negli anni, rispondere secondo quella più alta. Ad esempio se una persona ha guidato per circa 30 anni tutti i giorni, ma negli ultimi 15 anni ha guidato solo una due volte alla settimana, allora si risponderà <<Spesso/Sempre>>
- Nella colonna <<anni>> riportare per quanti anni l'attività è stata esercitata, approssimando per eccesso e utilizzando una scala di 5 anni in 5 anni (5 - 10 - 15 - 20 ecc). Ad esempio se una persona ha letto regolarmente un quotidiano per circa 27 anni si riporterà 30 nella colonna degli anni di attività

3. ATTIVITÁ CON FREQUENZA ANNUALE

1. Mostre, concerti, conferenze	○ Mai/Di rado ○ Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)
2. Viaggi di più giorni	○ Mai/Di rado ○ Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)
3. Lettura di libri	○ Mai/Di rado ○ Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)

<< Indietro   Avanti >>

B.3.4. Activities requiring a regular monitoring

Cognitive Reserve Index

CRIq
questionnaire

M. Nucci, D. Mapelli & S. Mondini (2012)
Edizione digitale: O. Gaggi (2017)

Istruzioni: In caso di alterazione cognitiva o comportamentale, anche solo sospetta, il questionario è da somministrare ai familiari o a chi si prende cura del paziente, indicandolo al fondo del questionario nella apposita casella

1 2 3 4 5 6 **7** 8 9

7 CRI-TempoLibero

CRI-TempoLibero

Istruzioni:

- Tutte le voci vanno riferite ad attività svolte con regolarità durante la vita adulta (dai 18 anni in seguito).
- Sono escluse tutte le attività che comportino un reddito (in tal caso rifarsi alla sezione CRI-Lavoro).
- Rispondere secondo le frequenze stimate durante il periodo di riferimento (settimanale, mensile, annuale).
- Se le frequenze sono molto cambiate negli anni, rispondere secondo quella più alta. Ad esempio se una persona ha guidato per circa 30 anni tutti i giorni, ma negli ultimi 15 anni ha guidato solo una due volte alla settimana, allora si risponderà <<Spesso/Sempre>>
- Nella colonna <<anni>> riportare per quanti anni l'attività è stata esercitata, approssimando per eccesso e utilizzando una scala di 5 anni in 5 anni (5 - 10 - 15 - 20 ecc). Ad esempio se una persona ha letto regolarmente un quotidiano per circa 27 anni si riporterà 30 nella colonna degli anni di attività

3. ATTIVITÁ CON FREQUENZA FISSA

1. Figli	○ No ○ Si
2. Cura di Animali Domestici	○ Mai/Di rado ○ Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)
3. Gestione del conto corrente in banca	○ Mai/Di rado ○ Spesso/Sempre ○ Da sempre (dai 18 anni ad ora)

<< Indietro   Avanti >>