UNIVERSIDADE DE LISBOA

FACULDADE DE MEDICINA

Lost in Time. A Neurophilosophical Quest to Understand the Perception of Time in MCI Patients

Sara Cunha Leal Rocha Coelho

Supervisor: Prof. Doutor Alexandre Valério de Mendonça
Co-Supervisor: Prof. Doutor Fabio Paglieri

Tese especialmente elaborada para a obtenção do grau de Doutor em Ciências Biomédicas – Especialidade Neurociências

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Dedico esta tese ao meu avô materno,
vítima da doença de Alzheirmer.

Como diria uma canção tradicional escocesa
cantada por Robert Wilson:

"Oh my heart is in the heart o' Loch Lomond when the sun has gone to rest;
And there beside the banks o' Loch Lomond lives the one that I love best."

“Viu que o tempo não era mais do que uma ‘irmã muda’,
uma coluna de mercúrio totalmente desprovida de escala,
para aqueles que quisessem fazer batota”

[Mann, 1924]

PUBLICATIONS

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ABSTRACT

Introduction: Mild cognitive impairment (MCI) patients often complaint about difficulties in dealing with time questions, an issue that compromises their daily planning and orientation. The conscious experience of duration has been the most studied time experience and is generally assessed through duration judgments and passage of time judgments. This temporal experience may also impact other aspects of human life, namely intertemporal decision making. In the same vein, the connexion between time and memory has long been debated among neuroscientists, psychologists and philosophers. Among these scholars, Bergson, a 20th century French philosopher, was the leading proponent of a strong bond between time and memory, through the concept of duration. Time, for Bergson, is also interwoven with other dimensions of human consciousness, such as will.

Thus, mild cognitive impairment can offer us a human disease model to see if and how memory impairments affect human time perception and to explore their broader effects upon subjects' lives. Bergson seems to favour the idea of an affective and qualitative time experience interlinked with memory issues, akin of the situation of judging time passage. These ideas contrast with an Aristotelian idea of counting time intervals, similar to interval length judgments and currently conveyed by internal clock models, which neglects the role that feelings may play in time experience. In the case that the results obtained support Bergson's intuitions, further avenues of work will be open to explore the relation between memory deficits and affective time experience.

Objectives: This study aims to investigate the perception of time in patients with Mild Cognitive Impairment. The experience of time duration, with respect to both interval length judgments and passage of time judgments, and the consequences for decision making, using an intertemporal choice, are assessed. We intend to see how the results obtained fit into a philosophical framework that interlink memory and time and make suggestions regarding future work.

Methods: Fifty-five MCI patients and fifty-seven healthy controls undergo an experimental protocol for time perception on interval length, a questionnaire for the

subjective passage of time, an intertemporal choices questionnaire and a neuropsychological evaluation.

In the experimental protocol for interval Length judgements, participants have to estimate and produce the duration of short time intervals of 7 s, 32 s, 58 s, following a prospective paradigm (they are told in advance that they will have to estimate and produce time intervals). They also have to estimate a duration of the time to draw a clock and the duration of the neuropsychological interview, following a retrospective paradigm (they are not told that they will have to estimate time intervals).

In the passage of time judgments protocol, participants are inquired about their subjective impressions about the speed of time course and have to rate their impressions into a scale ranging from the very fast to the very slow.

To check decision-making, participants are submitted to an intertemporal choice questionnaire where they have to choose between small and immediate reward or a larger but delayed reward.

Finally, participants undergo a neuropsychological evaluation, where they are submitted to tests of cognitive functions, particularly memory and executive functions, as well as scales to evaluate their emotional state, namely depressive and anxiety symptoms.

Results: Patients with MCI present no changes in the perception of interval length. However, they report the time passing slower than controls. This experience is significantly correlated with memory deficits, but not with performance in executive tests, depressive or anxiety symptoms. Patients with MCI have no alterations in temporal preferences in comparison with the healthy controls.

These results from a study in neuroscience, put into a philosophical framework, suggest that Bergson and Aristotle, at the end, consider different aspects of time perception, in the first case referring to feelings of time passage and in the second case to the estimation of time intervals. However, both philosophers highlight the connexions of different aspects of time perception with different types of memory. Thus, passage of time judgements is linked to long-term memory and interval length judgements is associated with working memory.

Conclusions: Memory deficits do not affect either the perception of interval length or temporal preferences, but are associated with alterations in the subjective experience of time. Following Bergson's footsteps, we may say that memory is associated with an

affective and qualitative experience of time. Future works investigating time perception in patients with memory deficits should careful consider this dimension when designing the experimental protocols.

Keywords: Mild cognitive Impairment, Memory, Intertemporal choices, passage of time judgments, interval length judgments.

RESUMO

Introdução: Nos dias de hoje, os pacientes com Defeito Cognitivo Ligeiro (DCL) são alvo de uma atenção crescente nos meios clínicos e académicos pois representam uma população em risco de evoluir para a doença de Alzheimer (AD). Embora as suas funções cognitivas gerais estejam preservadas, quando avaliados em entrevista neuropsicológica, o desempenho nas tarefas de memória é inferior ao esperado para a sua idade e nível de escolaridade. Os doentes com DCL queixam-se muitas vezes durante a consulta de dificuldades em lidar com experiência temporal, o que a afeta a gestão do seu dia-a-dia e a sua orientação.

A experiência consciente da duração tem sido a experiência de tempo mais estudada e é geralmente acedida através de juízos de duração, sobre quanto um evento dura, e juízos de passagem de tempo, acerca de quão depressa um indivíduo sente o tempo a passar. Esta experiência de tempo pode também ter um impacto noutros aspetos da nossa vida, nomeadamente em decisões intertemporais. Ao mesmo tempo, a conexão entre tempo e memória tem sido longamente debatida entre neurocientistas, psicólogos e filósofos. Entre estes académicos, Bergson, um filósofo francês do século XX, foi o principal proponente de uma forte ligação entre o tempo e a memória, maioritariamente através do conceito de *duração*. O tempo, para Bergson, está interligado com outras dimensões da consciência humana, nomeadamente com as livres escolhas, como o caso das decisões.

Deste modo, a patologia do Defeito Cognitivo Ligeiro, em virtude de ter as funções cognitivas gerais preservadas, excetuando a memória, pode oferecer-nos um modelo de doença humana para observar se e como os defeitos de memória afetam a perceção humana de tempo e explorar os efeitos mais latos sobre a vida dos sujeitos. A filosofia de Bergson parece favorecer a ideia de uma experiência afetiva e qualitativa de tempo ligada a questões de memória, semelhante à situação dos juízos de passagem de tempo. Estas ideias contrastam com a ideia aristotélica de contar intervalos de tempo, semelhante aos juízos de intervalos de tempo e correntemente transmitida pelos modelos de relógio interno, que esquecem o papel que os sentimentos podem desempenhar na experiência

temporal. No caso de os resultados obtidos suportarem as intuições de Bergson, direções futuras de trabalho serão abertas para explorar a relação entre os défices de memória e a experiência afetiva de tempo.

Tanto quanto sabemos, existe pouca investigação sobre a perceção de tempo em sujeitos com declínio cognitivo. O nosso estudo propõe uma análise detalhada sobre a experiência consciente da duração em sujeitos com DCL. Focamo-nos na perceção da passagem de tempo de curtas durações (segundos a minutos), de acordo com um método baseado na assunção que temos um relógio interno que pode mover-se mais rapidamente ou mais vagarosamente. O modelo de relógio interno tem sido o modelo mais proeminentemente usado nas últimas décadas para estudar a perceção de tempo. Assenta na convicção de que temos um dispositivo que está constantemente a emitir pulsos ao mesmo ritmo e que processa a informação ao longo de três estádios. No estádio do relógio, os pulsos entram num acumulador quando a porta está aberta, desempenhando a atenção um papel capital no número de pulsos absorvidos. No estádio da memória, os pulsos encerrados no acumulador, que representa o tempo corrente, são armazenados no sistema de memória de trabalho para comparação com os valores contidos na memória de referência, que é a memória de longo termo para os pulsos acumulados no passado. Por último, segue-se o estádio da decisão, no qual os valores presentes na memória de trabalho são comparados com aqueles presentes na memória de referência, permitindo que se tome uma decisão sobre a perceção de tempo. Deste modo, o modelo de relógio interno afere em que medida os juízos de intervalo de tempo se aproximam ou se afastam do tempo real medido, identificando as fontes de diferença patológica na perceção de tempo e relacionando-as com traços mnésicos, decisionais, executivos ou emocionais.

O método suportado pelo modelo supracitado tem a vantagem de usar um paradigma prospetivo e retrospetivo ao mesmo tempo, avaliando intervalos de tempo estimados e produzidos. Com estas tarefas, testamos se a perceção de tempo está alterada nos pacientes com DCL comparativamente aos controlos da mesma idade. Aferimos também a perceção de tempo dos pacientes com DCL para longos intervalos de tempo (horas, dias, meses, anos), utilizando o protocolo de juízos de passagem de tempo. Conjuntamente, estas tarefas prepararam-nos para explorar os efeitos mais latos de uma

possível alteração na perceção de tempo, nomeadamente verificar se existe uma alteração nas escolhas intertemporais.

Objetivos: Este estudo tem o objetivo de estudar a perceção de tempo em doentes com Defeito Cognitivo Ligeiro. A experiência da duração de tempo, respeitando juízos de intervalo de tempo e juízos de passagem de tempo, e as suas consequências para a decisão, usando um questionário de escolhas intertemporais, são avaliadas. Finalmente, é averiguado como os resultados obtidos se enquadram num contexto filosófico que interliga memória e tempo e feitas sugestões relativamente a trabalho futuro.

Métodos: Cinquenta e cinco pacientes com DCL e cinquenta e sete controlos saudáveis são submetidos a um protocolo experimental para a perceção de intervalos de tempo, a um questionário para a passagem subjetiva de tempo, a um questionário de escolhas intertemporais e a uma avaliação neuropsicológica.

Na tarefa de perceção de intervalos de tempo, os participantes têm de estimar e de produzir a duração de intervalos de tempos de 7 s, 32 s, 58 s, sendo inicialmente avisados que terão de estimar e produzir intervalos de tempo (paradigma prospetivo). De seguida, sem aviso prévio, é-lhes pedido que estimem o tempo que demoraram a desenhar um relógio e a duração da avaliação neuropsicológica (paradigma retrospetivo).

No questionário de passagem subjetiva de tempo, os participantes são inquiridos sobre as suas impressões subjetivas acerca a passagem de intervalos longos de tempo numa escala que abrange desde o muito depressa ao muito devagar.

No questionário de escolhas intertemporais, os participantes são sucessivamente confrontados com a escolha entre duas opções, ou optam por receber imediatamente uma pequena quantia de dinheiro ou por receber quantia maior, mas após algum tempo decorrido. A tendência para os participantes escolherem opções imediatas determina um padrão de escolha impulsivo, ao passo que a tendência para escolherem opções tardias determina um padrão de escolha auto-controlado.

Finalmente, a avaliação neuropsicológica consiste em testes de funções cognitivas, nomeadamente em testes e memória e de funções executivas e na avaliação de sintomas emocionais, nomeadamente em questionários de ansiedade e depressão.

Resultados: Os pacientes com DCL não apresentam alterações na perceção de intervalos de tempo. Contudo, referem que o tempo passa mais lentamente que os controlos. Esta experiência foi significativamente correlacionada com défices de memória, mas não com o desempenho em testes executivos ou com sintomas ansiosos e depressivos. Pacientes com DCL não têm alterações nas preferências temporais em comparação com os controlos saudáveis, não diferindo destes em termos de impulsividade.

Enquadrados num contexto filosófico, estes resultados vindos de um estudo em neurociências sugerem que Bergson e Aristóteles referir-se-iam afinal a aspetos diferentes da perceção de tempo, no primeiro caso ligado a sentimentos de passagem e tempo e, no segundo, a estimativas de intervalos de tempo. Todavia, as filosofias desenvolvidas por ambos apontam para que os diferentes aspetos de perceção de tempo tenham conexões com diferentes tipos de memória. Assim, os juízos de passagem de tempo estão sobretudo ligados a uma memória de longo prazo e os juízos de intervalo de tempo estão associados a uma memória de trabalho.

Conclusões: Défices de memória não afetam a perceção de intervalos de tempo ou preferências temporais, mas estão associados com alterações na experiência subjetiva de tempo. Seguindo as pisadas de Bergson, podemos dizer que a memória de longo prazo está associada com a experiência afetiva e qualitativa de tempo. Trabalhos futuros que investiguem a perceção de tempo em défices de memória devem examinar cuidadosamente esta dimensão em protocolos experimentais. De igual modo, futuramente será interessante considerar com maior acuidade o papel da memória de trabalho em juízos de intervalo de tempo.

Palavras-chave: Defeito Cognitivo Ligeiro, Memória, Decisões Intertemporais, Juízos de Passagem de Tempo, Juízos de Intervalos de Tempo

GENERAL INTRODUCTION

Philosophical Framework

The quest about the nature of time began early in the history of philosophy, raising important issues about mind-dependence or independence (Dyke & Bardon, 2013). Two dimensions have been generally accepted in this inquiry: objective time or physical time, which is the clock time of mathematics and physics; and subjective or psychological time, that is, time perception or the mental experience of time (Dowden, 2001). Discussions about the prevalence of one dimension over the other cross centuries. In antiquity, philosophers as Aristotle, while recognizing an objective value of time, also stated the need of a subject to perceive it. On the opposite, the emergence of Newton's physics transform time into an absolute, independent of the beings who experience it (Klein, 2003). Starting from XIX century and following the conceptual change introduced by Kant's philosophy, researchers began to look at time as something that is inside the subject. This century was marked by the industrial revolution and by the rise of psychoanalysis, turning attentions to human experience (Macey, 1994). As a consequence, time acquired a subjective value and time tended to be defined in terms of time perception. This position was overstated in the contemporary vision conveyed by McTaggart, who considered that time is completely subjective and elaborated on the notion of unreality of time (Nguyen & Corbett, 2007).

The interest to investigate the essential structures of consciousness, such as memory and attention, that enable subjective time or time perception, was brought up mainly by the school of phenomenology (Heidegger, Sartre, Husserl, Merleau-Ponty) (Hoy, 2009). Nevertheless, philosophers who stated that time is a mind-dependent phenomenon had previously highlighted the importance of mental structures for time perception. Opinions split between those who agree that the temporal experience depends on acts of attention, such as Locke, Berkeley and Hume, and those who emphasize the role of memory in the experience of time, like Aristotle, Saint Augustin, Bergson and Husserl (Zeman, 1971). Among the philosophers who established a strong link between time perception and memory, Bergson was the thinker who asserted most the intimate connection between the two, reaching the radical conclusion that time perception is indeed memory. He was not interested in the relation of time with motion as Aristotle, or in the psychological character of time dimensions as Augustin or even in deconstructing the psychological mechanisms involved in a time perception act as Husserl (Kelly, 2005). Bergson developed his philosophy when the first experimental models to measure human time perception came to light and his thoughts were, in part, a reaction to this. Indeed, Bergson's attacked the experimental time tasks relying on internal counting brought up by psychophysics. Bergson's ideas were presented in his first book "Time and Free Will". This important work had the purpose to defeat Kant's idea that freedom is out of time, and to do so the French philosopher built his argumentation into three steeps. In the first chapter, he defined time perception or the real time as the immediate data of consciousness or qualities, contrasting this view with the one conveyed by the school of psychophysics, that time perception data are quantities. Then, the French thinker related the immediate data of consciousness to memory, calling that phenomenon *durée* (duration). At last, he observed the impact of his new definition upon other areas of our life, namely decision-making, arguing that our choices are memory-time dependent (Guerlac, 2006; Massey, 2015). According to Heidegger, and as discussed in detail below, Bergson's theories about time may be envisaged as the inverse of Aristotle's theories (Heidegger, 1925-6).

The starting point of Bergson's philosophy in "Time and Free Will" is a critique of the XIX century scientific models of time perception, which he believed to prevent assessing the inner experience of the individual. However, Bergson was not an anti-scientific thinker, as he himself noted in later works. He stood for the mutual auxiliary role of science and philosophy (Gunter, 1987). As a matter of fact, both Bergson's and Aristotle's conceptions of time perception may be better understood through the current neuro-scientific models of time perception. On the other hand, their philosophic ideas may still today raise questions and provide hints that can be enlightening neuroscience progress.

Many examples of the collaboration between the domains of philosophy and neuroscience are found today, particularly in the branches of neurophilosophy, experimental philosophy and neurophenomenology. This cooperation involves the use of empirical data to clarify philosophical questions, as in the case of neurophilosophy (Churchland, 1986), testing philosophical hypothesis employing experimental procedures, like in experimental philosophy (Knobe & Nichols, 2008; Rose & Danks, 2013), or taking advantage of a philosophical background to make helpful suggestions and point out new directions, such as in neurophenomenology (Gallagher, 2003). Combining philosophical speculation with scientific experimental design contributes to open new avenues of research on neuroscience, based on the intersection of the results achieved in the experimental work and the underlying philosophical concepts. On the other hand, experimental data may probe or challenge philosophical views and arguments. The study of the relation between time and memory is just a good example of this fruitful interaction.

The perspective of Neuroscience

In the 20th century, the theme of subjective time or time perception became a subject of interest not only for philosophers, but also for psychologists and neuroscientists. Time perception was considered an intriguing and complex issue to study since it involved many variables, entailed different timescales and comprised several temporal dimensions (Wittmann, 2015). Duration, temporal perspective, simultaneity, temporal order or successiveness are among the main temporal aspects to be considered (Block, 1990; Fraisse, 1963; Friedman, 1990; Pöppel, 1997). Noteworthy, duration has been a key feature in the study of time, possibly because the experience of duration allows us to understand and become conscious of the other temporal aspects (Pöppel, 1997).

Time processes, namely duration, have a crucial impact upon our lives, influencing complex behaviour and being responsible for the adaptation to the demands of the external environment (Allman, Yin & Meck, 2014; Wittmann, 2014). Depending on the timescale considered, our actions and plans are affected by timing. Time perception begins at a scale of seconds to minutes, where interval timing unfolds our conscious experience of duration (Buhusi & Meck, 2005; Buonomano, 2007). The experience as well as the anticipation of duration influences decision-making (Allman, Yin & Meck, 2014; Buhusi & Meck, 2005; Wittmann, 2014). This is particularly evident in the case of intertemporal choices where we have to take into consideration the temporal delays of the different outcomes at stake (Wittmann & Paulus, 2008; 2009). Our subjective impressions of time passage can lead to deviations in the estimation of the time interval and guide our preferences towards immediate choices or delayed options (Tao et al., 2014; Wittmann & Paulus, 2008; 2009).

The major role that the subjective experience of time plays in our lives drove researchers to try to understand how and where time is processed in the brain. They first searched for a time sense and chronobiological explanations were proposed, that were, however, insufficient to fully account for time perception. Hence, they turned their attentions to the cognitive processes, neural mechanisms and brain areas activated during time experiences (Friedman, 1990). It appears currently that multiple neural mechanisms are involved in the experience of time, especially if we take into account the different timescales (Wiener, Matell & Coslett, 2011; Wittmann, 2013). In addition, different cognitive faculties, whose neural basis is distributed over the brain, as well as emotional and visceral feelings, can participate in the time experience (Wiener, Matell & Coslett, 2011; Wittmann, 2009; Wittmann, 2013; Wittmann & Wassenhove, 2009).

The conscious experience of duration encompasses the sense of continuity of several moments and requires a minimum of time for the subject to become aware that he/she is experiencing duration, called by James specious present (James, 1890; Wittmann, 2011; 2015). Clearly, the feeling of duration only starts from above a couple of seconds, since in a few seconds the individual just senses a moment, a "now" (Buhusi & Meck, 2005; Pöppel, 2009; Wittmann & Pöppel, 1999; Wittmann, 2009; 2011). Researchers who over the past two centuries tried to unravel the mysteries behind our conscious experience of duration, thus gave priority to experimental models focused on the experience of judging time intervals ranging from seconds to minutes (Friedman, 1990). Although the numerous experimental tasks using interval length judgments to assess the conscious experience of duration have confirmed that multiple factors are implicated in time perception, they also pointed out to attention and memory as the main cognitive processes that could explain time in mind (Block, 1992; Block & Zakay, 1997). Interestingly, a broad consensus to this regard was reached by all disciplines involved in time perception studies, including philosophy (Dyke & Bardon, 2013; Friedman, 1990; Zeman, 1971). Recently, a group of researchers have proposed that the conscious experience of duration can also be accessed through time passage judgments, related to feelings of time passage and not time interval estimations (Sucala, Scheckner & David, 2010; Wearden, 2005). In addition, experimental protocols on decision-making using intertemporal choices questionnaires have been used together with interval length judgments tasks to study the influence of the conscious experience of duration upon our choices (Wittmann & Paulus, 2008; Zauberman et al. 2009).

In order to understand the neural mechanisms involved in the human perception of time, experimental designs cover a wide range of models, like the neuroimaging/ electrophysiological studies in healthy subjects, developmental studies, and studies of patients with neurological and psychiatric disorders (Buhusi & Meck, 2005; Falter & Noreika, 2014). The study of time perception in mental disorders has a double purpose. First, it enables to scrutinize the impact that a certain impairment has on time perception, by clarifying the psychological mechanisms and brain regions that underline that temporal experience. Second, it allows an insight upon the psychological experience of these disorders, that is, the way patients perceive time and how this influences their lives (Allman & Meck, 2012). The experimental procedures mentioned above, interval length tasks, passage of time judgments protocols and intertemporal choice questionnaires, are particularly well suited to verify and understand the presence of time distortions and their consequences in models of human disease.

Experimental methods to study Subjective Duration

Subjective duration or the conscious experience of time may be assessed through interval length judgments or duration judgments, about how long an event lasts, and through passage of time judgments, related to the perceived speed of time course (Sucala, Scheckner & David, 2010; Wearden et al., 2014). Interval length judgments have been widely studied whereas passage of time judgments only recently have become a subject of interest. Studies that evaluated together these two judgments suggest that they reflect different time duration experiences (Droit-Volet & Wearden, 2015; 2016; Wearden, 2005). Interval length judgments are statements about a duration of a time interval with respect to a real measured time, while passage of time judgments are statements about how one feels an estimated time interval (Sucala, Scheckner & David, 2010; Wearden et al., 2014; Wearden, 2015). Take the following example. In *Magic Mountain*, Hans Castrop, the main character of Thomas Mann's novel, went to a sanatorium in the high mountains of Switzerland. In virtue of his health problem, he began to experience time running slower. Imagine that you question Hans Castorp about an interval length judgment before and after he enters in the health institution, asking him to estimate a duration of 3 minutes real time. Suppose he correctly answers both in the health and the sick condition, that does not mean he behaves the same way when it comes to passage of time judgments. Although he recognizes that the same amount of time has passed, he may feel the 3 minutes estimated time referential as passing slower or faster.

In spite of these differences, the two types of judgments may be influenced by similar factors. Cognitive and emotional circumstances are the basis for the experience of duration, and subjective life experiences, like routine activities or time pressure, also influence it (Friedman & Janssen, 2010; Sucala, 2011; Wearden, 2015).

Interval Length Judgments

Several models have been used to explain interval timing and the factors that influence it. Based on the school of psychophysics, which proposes that we could explain time in mind by internal counting, the internal clock models[1] became the most commonly used, especially those related to the Scalar Expectancy Theory (SET). This theory has the advantage to hypothesize that different factors could affect interval timing, but it does not argue that they are causal explanations for time perception distortions, unlike theories such as the attentional-gate model or the storage size hypothesis (Allman & Meck, 2012; Block, 1990). SET postulates the existence of an oscillatory pacemaker, which is constantly emitting pulses at the same rate and processes information along three stages. First, at the *clock stage*, the pulses enter into an accumulator when the switch is open. This arousal mechanism is affected by attention and emotions, slowing or accelerating the entrance of pulses into the accumulator. The *memory stage* follows. After the switch is closed, the pulses gated in the accumulator, which represent the current time, are stored in the working memory system for comparison with the values contained in reference memory, that is, the long-term memory for pulses accumulated in

[1] It is worth highlighting that the internal clock model is currently being challenged by competing models, like striatal-beat-frequency theory, that favours the idea of multiple timers, instead of a single one (Hinton & Meck, 2004; Matell & Meck, 2004). The discovery and investigation of different timescales in duration experience led to the conviction that time perception is a result of multiple neural mechanisms (Buhusi & Meck, 2005; Wiener, Matell & Coslett, 2011). However, in the range of seconds to minutes, there is some consensus regarding the existence of a centralized clock mechanism and consequently the internal clock may be the best model to study the different components of that particular temporal process (Wittmann & Wassenhove, 2009).

the past. Finally, in the *decisional stage*, the values present in working memory are compared with those stored in the reference memory, allowing a decision to be made on the perception of time (Allman & Meck, 2012; Droit-Volet et al., 2013; Gibbon, Church & Meck, 1984; Matell & Meck, 2000; Meck, 1984). Dysfunctions at one of these stages can originate a slower or a faster internal clock. By using an appropriate methodology, it should be possible to find the source of timing impairments.

The design of the experimental protocol must take into account the specific characteristics of the temporal task, mainly its complexity and the use or not of filled time intervals, because different neural networks that are not solely dedicated to time representation may be activated (Wittmann, 2013; Zakay, 1997). Two paradigms are generally followed (Block & Zakay, 1997; Coelho et al., 2004; Fortin & Breton, 1995; Nichelli, 1993; Nichelli, 1996; Pouthas & Perbal, 2004; Zakay & Block, 2004). In *prospective paradigm*, participants are told in advance that they will have to estimate time intervals. Thus, this paradigm focus on the experience of time in-passing or experienced duration and requires attention and short-term/working memory processing. Conversely, in *retrospective paradigm*, participants are not told in advance that they will have to estimate time intervals. Therefore, this paradigm refers to the remembered duration or the passed time and is considered to require the involvement of long-term memory. There are also several procedures to evaluate different mechanisms and cerebral areas recruited during time processes, ranging from reproduction to estimation methods (for a review see Nichelli, 1996 or Grodin, 2010). Among the distinct methods used, verbal time estimation and production tasks have the advantage that convey duration into conventional time units and, thus, establish a connection between subjective time and real clock time (Block, 1989). The judgments can be analysed in terms of accuracy, meaning the extent to which produced or estimated durations resemble real values, and in terms of precision, referring to the degree which measurements agree with one another or show variability (Nichelli, 1996). Moreover, both methods rely on the same cognitive processes (Coelho et al., 2004; Craik & Hay, 1999) and are negatively correlated (Carlson & Feinberg, 1970; Nichelli, 1996), that is, when participants are told to estimate and produce time intervals, the normal pattern is that the estimations times are above the real measured times (overestimation), and the production times are below the real measured times (underproduction). According to internal clock theory, damages in one of its components, such as in the memory stage, could affect both verbal time estimation and production (Nichelli, 1993; Nichelli, 1996).

Passage of Time Judgements

Passage of time judgments can be evaluated in real life situations or in the laboratory and span different periods of time (from minutes to years) (Wearden et al., 2014). Distinct circumstances, namely the hedonic value of the task, emotions, attention and information processing load account for variations in the subjective experience of time passage (Wearden, 2015). Similar to interval length judgments, feelings of boredom, sadness and fatigue may be at origin of a slower passage of time judgements, whereas feelings of happiness, being busy and concentration produce an acceleration of time passage (Flaherty, 1991; Watt, 1991; Wearden et al, 2014). Conversely, deficits in attention may create the impression that time is passing slower, differing from interval length judgements, where inattention will drive to longer time estimates and consequently to a faster internal clock (Sucala, Scheckner & David, 2010; Sucala, 2011). Finally, studies in laboratory have shown that when the information processing is higher, the subjective passage of time accelerates (Wearden, 2008). To the best of our knowledge, there is no study on the role of memory in everyday passage of time judgments regarding longer periods of time. Hence, we may wonder whether patients with memory impairments, where information processing is lower due to lesser information storage, would feel time passing slower.

The Experience of Duration and Intertemporal Choices

The experience of time influences decision-making. If we have to choose between taking a bus or a metro to arrive at home, we have to estimate which means of transportation is faster. A typical case where our experience of time seems to impact our choices is when we have to choose between trade-offs at different points of time. These decisions are called intertemporal choices (Soman et al., 2015).

Some individuals tend to choose lesser immediate gratifications and are typically described as impulsive, while others who are able to opt for better delayed rewards are said to be self-controlled (Kivetz & Keinan, 2006). The ideal is to achieve a balance between immediate choices and delayed choices because both self-controlled and impulsive behaviours may be dysfunctional, when carried to the extreme. A self-controlled behaviour with an excessive emphasis on future choices can lead an individual to regret having missed out the pleasures of life (Keinan & Kivetz, 2008; Wittmann & Paulus, 2009). On the other hand, an impulsive behaviour with search for immediate gratification may sacrifice the individual's well-being in the long-term (Bogg & Roberts, 2004). Impulsiveness has been related to many disorders (Wittmann et al., 2011; Wittmann, 2009) such as Attention Deficit / Hyperactivity Disorder (ADHD) (Barkley, Murphy & Bush, 2001), drug dependence (Lane et al., 2003) or border-line personality disorder (Berlin & Rolls, 2004).

Findings of timing disturbances in many diseases associated with impulsiveness led several researchers to suspect of a link between impulsiveness and deficits in temporal processing (Rubia et al., 2009; Wittmann et al., 2011). In fact, some studies showed that individuals can exhibit altered time preferences and time estimating deficits at the same time (Berlin & Rolls, 2004; Berlin, Rolls & Kischka, 2004; Wittmann & Paulus, 2008; Wittmann et al., 2011; Zauberman et al., 2009). This finding suggests that impulsive behaviour might be explained by an altered sense of time. As revealed by previous investigations, individuals who tend to overestimate time prefer smaller immediate rewards, while individuals who tend to underestimate time prefer larger delayed rewards (Tao et al., 2014). Moreover, the widespread tendency to discount future reward hyperbolically, which is considered responsible for preference reversals and planning inconsistencies (Ainslie, 2001), has been linked to the corresponding habit of mentally converting objective time duration on a logarithmic scale (Takahashi, 2005; Takahashi, Oono & Radford, 2008; Zauberman et al., 2009): the more pronounced this conversion is, the steeper the resulting delay discounting (Kim & Zauberman, 2009), thus suggesting that temporal myopia is at least partially responsible for impulsive choice behaviours. Individuals who overestimate and underproduce time intervals perceive time as being subjectively longer and associate it with higher cost, thus frequently choosing alternatives with more immediate outcomes (Wittmann & Paulus, 2008; 2009). Additionally, the connection between temporal preferences and temporal processing is also supported by neuroimaging studies in healthy subjects, which have shown that cerebral areas participating in temporal processing are similar to those activated when taking intertemporal decisions. Temporal processing is predominantly associated with the activation of the right prefrontal and striatal regions (Coull et al., 2004; Hinton & Meck, 2004) and, in the same vein, choosing with temporal delay recruits essentially prefrontal and striatal regions (McClure et al., 2004; McClure et al., 2007; Tanaka et al., 2004).

Cognitive models, namely the internal clock model, are certainly well positioned to identify how impairments in cognitive mechanisms affect time perception and alter temporal preferences. For instance, a previous research in children with ADHD suggested that attentional deficits may lead to an overestimation of time intervals and explain impulsive behaviour (Wittmann & Paulus, 2008). One of the key components of the internal clock model is memory, and since memory deficits interfere with interval length judgments (Gibbon, Church & Meck, 1984), we may wonder whether these deficits might also impinge upon temporal preferences. Previous studies suggested that the hippocampus, a brain region that is affected in memory disorders, might also play a role in controlling impulsivity (Cheung & Cardinal, 2005; McHugh et al., 2008; Sala et al., 2011; Yin & Troger, 2011), leading to an impulsive pattern of choices behaviour.

As far as we know, the relation between subjective passage of time judgements and intertemporal choices, in the perspective of underlying memory deficits, was not studied yet. Research on a population suffering from isolated memory deficits would be particularly well suited for this purpose.

Time Disorders and Memory

Disorders of temporal processing can be found in different types of pathology, compromising the life of neurological and psychiatric patients (Allman & Meck, 2012; Carrasco, Guillem & Redolat, 2000; Allman, Yin & Meck, 2014). Schizophrenia has even been called a timing disease (Friedman, 1990; Melges, 1982). The experience of time, specially tested by verbal estimation and production tasks, was found impaired in affective/mood disorders, such as depression and bipolar disease, and autism (Allman & Meck, 2012; Allman, Yin & Meck, 2014; Droit-Volet et al., 2013, Tysk, 1984; Wallace & Happé, 2008); motor disorders, such as Parkinson's and Huntington's diseases (Allman & Meck, 2012; Allman, Yin & Meck, 2014; Beste et al., 2007; Droit-Volet et al., 2013; Pastor et al., 1992); attentional disorders, such as ADHD (Allman & Meck, 2012; Pollak et al., 2009); and memory disorders, such as amnesia, Korsakoff's syndrome and Alzheimer's disease (Mimura, Kinsbourne & O'Conner, 2000; Nichelli et al., 1993; Shaw & Aggleton, 1994; William, Medwedeff & Haban, 1989).

It is essential to investigate time perception in memory disorders, inasmuch as memory is thought to be necessary for temporal experience (Graf & Grodin, 2006; Friedman, 1990; Kinsbourne & Hicks, 1990; Mimura, Kinsbourne & O'Conner, 2000; Schmiter-Edgecomber & Rueda, 2008; Zeman, 1971). Memory changes with aging (Craik, 1994), and previous studies showed alterations in the elders' experience of time duration in comparison to younger people (Carrasco, Bernal & Redolat, 2001; Coelho et al., 2004). It was hypothesized that this change in the experience of time duration might occur due to cognitive decline related to aging. In other words, the deterioration of attention and memory functions might have affected temporal processes (Coelho et al., 2004). To analyse the role of memory in the experience of duration, especially in older people, it would be helpful to find a condition entailing memory impairments but with the general cognitive function preserved, in comparison with healthy aging. We propose mild cognitive impairment (MCI) as such a condition.

The term mild cognitive impairment was coined in 1988 by Reisberg and colleagues to define a group of patients that were neither demented nor cognitively normal for aging, although the first attempts to characterize such clinical entity dated back to the XIX century, thanks to the efforts of Prichard (Prichard, 1837) and Karl (Karl, 1962). The first definition associated MCI with deficits in cognition and impairments in executive functioning, which affect complex occupational and social activities (Reisberg et al., 1988). Flicker and colleagues identified it with stage 3 of their Global Deterioration Scale (GDS) (Flicker, Ferris & Reisberg, 1991). Later, in 1999, the notion of MCI was re-conceptualized. Petersen and his colleagues considered that the GDS was a rating scale and not a diagnostic instrument. At the same time, they felt the need to pinpoint clearly a group at risk for developing Alzheimer Disease (AD). Thus, a new definition of MCI came out and the following diagnostic criteria were proposed: 1) Memory complaints documented by self-reports or by an informant; 2) Normal activities of daily living; 3) Normal general cognitive function; 4) Abnormal memory for age and education, documented by objective deficits on tests of episodic memory; 5) Not demented. According to these criteria, MCI patients exhibit a pattern of memory impairments similar to AD patients, whereas on general cognition and non-memory domains they behave more like controls. On the contrary, AD patients are more extensively impaired in non-memory cognitive domains (Petersen et al., 1999).

Since 1999, the growing interest in MCI prompted the emergence of new definitions, in line with clinical and research needs. For instance, in 2004, Winblad and co-authors, considering that Petersen criteria may exclude subjects at risk for developing dementia, proposed an extension of the concept, in order to include subjects that have deficits in domains other than memory, but that are not demented. This proposal led to a division of the MCI concept into different subtypes, amnestic mild cognitive impairment (aMCI), referring to MCI with memory impairments, and non-amnestic mild cognitive impairment (non-aMCI), assigning MCI with non-memory cognitive domains impaired (Winblad et al, 2004). The non-amnestic mild cognitive impairment type predicts other dementias beyond AD and therefore Winblad criteria may offer a better prediction of progression to dementia (Artero et al., 2006).

The criteria for the diagnosis of MCI must be careful chosen according to the purpose of the investigation. Longitudinal clinical studies showed that although patients with MCI can remain stable or return to normal over time, the vast majority will progress to dementia in the next few years. In epidemiologic studies, factors such as depression can act as confounders and account for the fact that a higher percentage of MCI cases may revert to normal (Gauthier et al., 2006). Therefore, it is crucial to apply appropriate inclusion and exclusion criteria and to select judiciously the battery of cognitive tests to be used. Importantly, many structural MRI studies have elucidated the brain areas involved in the impairments characteristic of MCI patients. Atrophy in both the medial temporal lobe, reflecting entorhinal and hippocampal volume loss, and the posterior cingulate was consistently observed (Petersen, 2001).

During consultation, MCI patients often express difficulties with time issues. However, the relation between these complaints and their memory deficits remains unclear. Studies with patients at later stages of memory decline, such AD, report impairments in temporal orientation and in time estimation abilities (Galasko et al., 1990; Nichelli et al., 1993). Time perception difficulties in MCI patients might contribute to their symptoms, since impaired time perception affects other cognitive domains, such as planning and decision-making, and may impact on activities of daily life. Thus, research on time perception in MCI patients may be helpful to implement interventions to ameliorate this condition, as well as to understand better the relation between time and memory.

Philosophy and Time-Related Disorders: Bergson and Mild Cognitive Impairment

Time studies in psychiatric and neurological human disorders have taken advantage from the support of philosophy. Philosophy has proven useful to think about concepts such as aging and dementia and to reflect upon the experimental data obtained from time studies (Christen & Churchland, 1992; Hughes, Louw & Sabat, 2006). In particular, a study on aging and time has already pointed out that chronological age or the view of time as a series of instants, like Aristotle suggested, is inadequate to appraise the aging process (Schmidtke, 1987). Bergson's thoughts may provide a better framework to understand aging, since time passage is not seen as a homogenous process, and the impact that the previous background (past and memory) may have upon the time experience is emphasised. In the same vein, Bergson may be an appropriate thinker to discuss temporal issues related to MCI. The difficulty of some memories to become present affects other domains and temporal dimensions, namely future and present. This is something we can witness in the deterioration of MCI patients towards dementia, since over time not only memory functions are impaired but also attention and planning abilities. Bergson appropriately underlines the relevance of the past, which is strongly connected with the storage of memories in mind. In contrast, for Heidegger, for instance, future is the most important and affects present and past. We are beings-to-death and what gives meaning to our lives is our life project (Heidegger, 1924). On the opposite, Sartre highlights the present dimension as the crucial one. It is the moment where we make the choices that will form our essence and where the *en-soi* (being-in-itself) and the *pour-soi* (being-for-itself) relate to each other (Sartre, 1943). In virtue of his strong emphasis on time experience associated with the past temporal dimension and with memory issues of remember and forgetting, we contend that Bergson's ideas would be particularly useful to interpret the results obtained in experimental protocols on time perception in a human model of memory disorder, thus hopefully contributing to clarify the centuries old question of the relation between time perception and memory.

Objectives

This study aims to investigate the perception of time in patients with Mild Cognitive Impairment. The experience of time duration, with respect to both interval length judgments and passage of time judgments, and the consequences for decision making, using an intertemporal choice questionnaire, will be assessed. The data obtained should bolster philosophical speculation on the relation between time perception and memory.

CHAPTER I: TIME PERCEPTION IN MILD COGNITIVE IMPAIRMENT: INTERVAL LENGTH AND SUBJECTIVE PASSAGE OF TIME

Introduction

The number of patients with cognitive complaints has been rising as a consequence of the increasing aging of the population. Clinicians have especially focused on patients diagnosed with mild cognitive impairment (MCI), because they carry a high risk for developing dementia in the ensuing few years. According to the original Mayo criteria, the presence of memory impairment in patients with preserved general cognitive function and independence in basic activities of daily living represent an increased risk of progression to Alzheimer's disease (AD; Petersen et al., 1999). Patients in the initial stages of AD often refer to losing track of dates, seasons and the passage of time (Alzheimer's Association, 2009). Difficulties in placing events in the correct temporal framework may compromise orientation and daily planning, since time perception is a crucial component of everyday decisions and goal-oriented behaviours (Buhusi & Meck, 2005; Mangels & Ivry, 2001). However, there has been scarce research on time perception in patients with MCI.

Time perception comprises at least two main subjective time experiences: *interval length judgements* and the *subjective passage of time judgements* (Block, 1990; Sucala, Scheckener & David, 2010; Wearden, 2005). Perception of interval length concern the subjective evaluation of a certain duration, and has been mainly approached using two different paradigms, *prospective* tasks (participants are told in advance that they will have to estimate a time interval) and *retrospective* protocols (participants are not told in advance that they will have to estimate a time interval), as well as two distinct methods of investigation, *verbal time estimation* (participants have to verbally estimate the duration of different intervals) and *verbal time production* (participants have to produce different interval durations). Experiencing the *subjective passage of time* involves another type of time experience that relates to the perceived speed of the time course: this is typically assessed via first-person reports on the subject's own feelings on time passage (Friedman & Janssen, 2010; Wearden, 2005).

Recent studies on time perception have often been based on the internal clock model. This model supposes that each individual has an internal clock which is moving slower or faster according to how temporal judgments about interval length approach or deviate from real measured time (Droit-Volet & Wearden, 2003; Grodin, 2010). An oscillatory pacemaker constantly emitting pulses at the same rate composes the clock, which processes information along three stages.

First, at the *clock stage*, the pulses enter into an accumulator when the switch is open. Attention plays here an important role, for instance inattention slows down the internal clock, producing a lower number of pulses. The *memory stage* follows. After the switch is closed, the pulses gated in the accumulator, which represent the current time, are stored in the working memory system for comparison with the values contained in reference memory, that is, the long-term memory for pulses accumulated in the past. Finally, in the *decisional stage*, the values present in working memory are compared with those stored in the reference memory, allowing a decision to be made on the perception of time.

The main advantage of this model is to identify the sources of individual and pathophysiological differences in time perception and relate them to neuropsychological data (Allman & Meck, 2012; Nichelli, 1993). It is important to note that, according to this internal clock model, working memory and executive functions are determinant mechanisms for time perception, due to the role of attentional shifts in determining the perceived speed of the internal clock (Henik & Yalon, 2010; Papagno, Allegra & Cardaci, 2004; Pouthas & Perbal, 2004). Remarkably, episodic memory and prospective and retrospective memory are also thought to be necessary for time perception (Graf & Grodin, 2006; Kinsbourne & Hicks, 1990; Mimura, Kinsbourne & O'Conner, 2000; Schmiter-Edgecomber & Rueda, 2008). We would then expect that a population with memory deficits, such as MCI patients, would present significant impairments in time perception. However, previous studies failed to find a clear correlation between MCI and time perception deficits.

We posit that this lack of results is due to exclusive emphasis on interval length perception, a cognitive skill that does not necessarily matters for the kind of long-term temporal projection involved in episodic and prospective memory. In studies on perception of *interval length*, there was no significant difference between MCI patients and controls in prospectively evaluating short time intervals, i.e. in between 10 and 60 s

(Rueda & Schmitter-Edgecombe, 2009). Another study evaluated self-estimation of performance time (Heinik & Ayalon, 2010): participants were asked to estimate retrospectively the actual duration of the interview (the real duration was 25 to 30 minutes). Self-estimation of performance time versus actual performance time was not impaired in MCI patients when compared to participants without cognitive impairment.

The results of these two experimental studies suggest that MCI patients have no alterations in the perception of interval length. Alternatively, methodological limitations of the chosen tasks might have hindered the detection of those alterations. First of all, it would be important to assess both the prospective paradigm and the retrospective paradigm, using the verbal time estimation as well as the verbal time production methods to estimate or produce the duration of empty time intervals, in order to evaluate more extensively the perception of the interval length. Empty time intervals were preferred in this methodology over filled intervals since non-temporal tasks would interfere with working memory and attention functions and, therefore, reduce the accuracy in temporal perception (Coelho *et al*., 2004; Fortin et al., 1993).

In contrast, the *subjective experience of time passage* in MCI patients has not been studied in the literature, to the best of our knowledge. This, we argue, constitutes a major limitation of current studies, since it is precisely the subjective experience of the passing of time that is likely to have a significant impact on memory deficits. If the perception of the passage of time is dependent upon memory (Bergson, 1889), we may speculate that patients with MCI might have a hindered perception of time passage. It is also possible that patients with MCI are less able to engage in novel activities requiring emotional or intellectual commitment, and thereby feel the time passing more slowly (Sucala *et al*., 2010).

To test this hypothesis, as well as to confirm the lack of differences in interval length judgements, in the present study we analysed time perception in MCI patients with respect to interval length and passage of time judgments on short durations (seconds, minutes), using both the prospective paradigm and the retrospective paradigm, both for verbal time estimation and for verbal time production (Coelho *et al.*, 2004). Time perception of longer intervals (hours, days, weeks) and the perceived speed of time passage in MCI were also assessed. An interesting aspect was to see whether time perception in patients with MCI would be better or worse than in controls – that is, closer to or farther from the objectively measured temporal values.

Methods

Participants:

MCI patients were recruited at a dementia outpatient clinic and a memory clinic, both in Lisbon. Controls were volunteers with no cognitive complaints from senior universities in Lisbon. The study was approved by the ethical committee of the Faculty of Medicine/ Santa Maria Hospital in Lisbon. The participants were informed of the experimental protocol and gave their written consent.

Inclusion Criteria for the MCI group

The inclusion criteria for the diagnosis of MCI were adapted from Petersen *et al.*, 1999, with an emphasis on amnestic MCI: (1) presence of memory complaints; (2) abnormal memory function, documented by the Logical Memory A below education and age adjusted values for the Portuguese population (1 SD) or who lost >3 points after delay. Logical Memory is a subtest of the *Bateria de Lisboa para Avaliação das Demências* (BLAD) (Garcia, 1984; Guerreiro, 1998), a neuropsychological battery designed to evaluate multiple cognitive domains and validated for the Portuguese population; (3) normal general cognitive function, determined by the Mini Mental State Examination (MMSE, Folstein, Folstein & McHugh, 1975) within normal values for the Portuguese population. The Portuguese version of the test, adapted from Guerreiro *et al*., 1994, was used; (4) no impairment or minimal impairment in activities of daily living determined by the Instrumental Activities of Daily Living Scale (IADL, Lawton & Brody, 1969), i.e. no more than one item from the IADL scale was abnormal. The Portuguese version, developed in the context of the LADIS project, was used (Pantoni *et al*., 2005).

Inclusion criteria for the Control group

The control participants had: (1) no memory complaints; (2) normal memory function, documented by the Logical Memory subtest of the *Bateria de Lisboa para Avaliação das Demências* (BLAD); (3) a Mini-Mental State Examination (MMSE) with normal values for the Portuguese population; (4) normal scores on the IADL scale, that is to say, no item from the IADL scale was abnormal.

Inclusion criteria for both groups

(1) Native Portuguese speakers; (2) Education ≥ 4 years; (3) Age > 45 years old;

Exclusion Criteria for both groups

(a) Dementia, according to DMS-IV-TR (American Psychiatric Association, 1994); (b) The presence of major depression according to DSM-IV-TR or serious depressive symptoms, indicated by a score >10 points on the 15-itemsGeriatric Depression Scale (GDS_{15}, Yesavage et al., 1983). The Portuguese version of the test was used, adapted from Barreto et al., 2008; (c) Neurological disorders (Parkinson's disease, stroke, brain tumour, significant head trauma or epilepsy), psychiatric conditions (such as autism or schizophrenia), or uncontrolled medical illness (hypertension, metabolic, endocrine, toxic or infectious diseases) able to interfere with cognitive performance; (d) Psychoactive medications with possible influence on cognitive performance; (e) History of alcohol or drug abuse; (f) Sensory deficits likely to interfere with assessment; (g) Participants with MMSE below education-adjusted values for the Portuguese population were excluded (<23 for equal or less than 11 years of education, <28 for more than 11 years of education);

Assessments

All the participants were submitted to the Portuguese version of the following instruments:

Neuropsychological Measures

(1) Tests that evaluate immediate memory (Digit Span forward), working memory (Digit Span backward), and verbal memory (Logical Memory). These tests are from the *Bateria de Lisboa para Avaliação das Demências* (BLAD) (Garcia, 1984; Guerreiro, 1998).

(2) Stroop test (STROOP, MacLeod, 1991). The Stroop test assesses executive functions, namely selective attention. The Portuguese version of the test, adapted from Castro *et al*., 2000, was used.

(3) Trail Making Test (TMT, Reitan, 1958). The TMT evaluates executive functions, namely attention switching, planning and internal ordering. The Portuguese version of the test, adapted from Fernandez & Marcopulos, 2008, was used.

(4) Subjective Memory Complaints (SMC, Schmand et al., 1996). The SMC is a questionnaire that assesses memory complaints. The Portuguese version of the test, adapted from Ginó *et al*., 2008, was used.

(5) Prospective and Retrospective Memory Questionnaire (PRMQ, Smith et al., 2000). This is a tool to measure self-reports of prospective and retrospective memory. A Portuguese version was used (based on Sara da Câmara's master thesis, unpublished).

Emotional Status Measures

(1) State-Trait Anxiety Inventory (STAI, Spielberger et al., 1983). The STAI is a questionnaire that evaluates the trait and the state of anxiety. The Portuguese version of the test, adapted from Silva, 2006, was used.

(2) The Geriatric Depression Scale (GDS_{15}). The GDS is a questionnaire that evaluates presence and severity of depression.

Experimental Measures of Time Perception

To evaluate time perception, all participants were asked to complete the following tasks:

(1) An experimental protocol for time perception on interval length (Coelho *et al*., 2004). In this test, participants first have to prospectively *estimate* empty intervals signalled by auditory beeps (of 7 s, 32 s and 58 s duration); then participants have to prospectively *produce* empty intervals signalled by auditory beeps (again, of 7 s, 32 s and 58 s duration). For each task, every duration was repeated 3 times in a pseudorandom order, so that for both estimation and production tasks 9 trials were performed. Participants were told to start the internal counting of seconds after they heard the first beep and to stop counting when they heard the second beep (in case of the estimation task) or to tell the examiner when they had reached the target duration (in case of the production task). They were specifically instructed not to count aloud nor to perform any digital counting, or use any body rhythm to help in the estimation. In addition, participants were asked, retrospectively, to estimate the time elapsed while they were drawing a clock and during the neuropsychological evaluation. Participants are said to have a faster internal clock if

they overestimate and underproduce time intervals, that is, their estimations are above actual duration while their productions are below it. On the contrary, participants are said to have a slower internal clock if they underestimate and overproduce time intervals.

(2) A questionnaire for the subjective passage of time (Friedman & Janssen, 2010). This tool assesses the subjective impressions of longer time intervals, that is, whether participants experience time as passing slowly or quickly. The test consists of two parts. The first part has 6 questions concerning how participants experience the speed at which time seems to pass (these questions are included in the caption of Fig. 1): each item is to be rated on a five-point scale, ranging from very slow (-2) to very fast (+2). Two questions ask about our time experience in the present, the first concerning our typical experience of time ('How long does time usually pass for you?') and the second referring to a specific time perception ('How long do you expect the next hour to pass?'). The other four questions cover the perception of the past, focusing on various time intervals (last week, last month, last year and the past 10 years). The global perceived speed of time is measured as a composite speed-of-time score, which is the sum of the six questionnaire items (Friedman & Janssen, 2010). The second part includes 11 statements about the subject's experience of time (see the leftmost column of Table 3), which the participants have to rate on a seven-point scale ranging from 'strongly disagree' (-3) to 'strongly agree' (+3). The statements of the subjective experience of time were conceived to evaluate the impact of subjective impressions of life experience on the subjective feelings of time passage, focusing on: (a) the effects of recent life changes (items 1-4), since it is thought that more activity and more life experiences would give the impression that time is moving at a fast pace; (b) forward telescoping (items 5-7), i.e. the temporal displacement of a distant event could make it look more recent than it actually was, thus conveying the impression that the time is passing quickly; and (c) the amount of pressure and rushing one experiences in life (items 8-11), since feelings like being always busy or never having enough time to get things done usually sustain the sensation that time is fleeting.

Statistical Analysis

Sample size was estimated from a power analysis using the Power and Precision (v.4; BioStat; Englewood, NJ) software. For previous sample statistical estimates required for sample size calculation, preliminary data from 20 participants (10 MCI and 10 controls) was used. The values obtained for estimation of time (7 s) were 17.1±6.3 s in MCI patients and 13.7±3.5 s in controls. With such estimates, to detect a significant difference between MCI and controls, assuming a power = 90%, α= 0.05 and 2-tails Student's t-test, 100 participants (50 MCI and 50 controls) would be required.

Demographic, clinical and neuropsychological data were compared between the 2 groups, MCI and controls, with the Student's *t*-test for numerical variables and χ^2 for categorical variables.

Analysis on time perception using the prospective paradigm and short intervals was performed with a mixed effects repeated measures ANOVA. Patients with MCI and controls were used to evaluate between-subjects effects, while time (7 s, 32 s, 58 s) and order of presentation (1^{st}, 2^{nd}, 3^{rd}) were used to evaluate within-subjects effects. When significant effects were detected with the ANOVA, Student's t-tests were performed with Bonferroni corrections, to identify the group differences. Effect sizes were estimated by the partial eta squared (η^2_P) calculated by SPSS. Differences in the retrospective paradigm on long intervals between the 2 groups were evaluated with the Student's *t*-test. The differences in the perceived speed of time between the two groups were assessed using a composite speed-of-time score (Friedman & Janssen, 2010). Differences in individual items scores were additionally explored with the same test. The scores of the statements about the subjective experience of time were also compared using the Student's *t*-test. The correlational analysis between neuropsychological variables and the composite speed-of-time scale score was performed with the Pearson's correlation.

Statistical analyses were performed using SPSS for Windows (SPSS 19; SPSS Inc., Chicago, Ill). Effects with *P* values <0.05 were considered statistically significant.

Results

One hundred and twelve participants, 57 controls and 55 MCI patients, were submitted to neuropsychological evaluation, an experimental protocol for time perception on both short intervals and long intervals and a questionnaire on subjective passage of time. There were no statistically significant differences in age, education, gender and activity/retirement status between the two groups (Table 1).

Neuropsychological characteristics

As expected, the MCI participants had lower MMSE scores, worse performances in cognitive tests, namely memory (Logical Memory, Digit Span) and executive functions tests (Trail A and B, Stroop test), and presented more subjective memory complaints (SMC, PMRQ) as well as anxiety (STAI) and depressive (GDS) symptoms than controls (Table 1).

Table 1. Demographic and Neuropsychological Characterization

	MCI (n=55)	CONTROL (n=57)	*P* Value
AGE, years, mean (SD)	70.9 (8.9)	67.6 (8.5)	0.05[a]
EDUCATION, years, mean (SD)	10.9 (4.4)	11.1 (4.5)	0.74[a]
GENDER, female/male, n	36/19	35/22	0.66[b]
ACTIVITY, active/retired, n	8/47	7/50	0.73[b]
MINI-MENTAL STATE EXAMINATION, mean (SD)	27.2 (2.2)	29.1 (1.1)	**<0.01**[a]
LOGICAL MEMORY A (immediate recall), mean (SD)	7.1 (3.3)	15.0 (4.1)	**<0.01**[a]
LOGICAL MEMORY A (delayed recall), mean (SD)	5.5 (3.7)	15.1 (4.4)	**<0.01**[a]
DIGIT SPAN FORWARD, mean (SD)	5.5 (0.7)	5.8 (1.2)	0.14[a]
DIGIT SPAN BACKWARD, mean (SD)	3.9 (1.1)	4.4 (1.0)	**0.01**[a]
STROOP TEST (interference), mean (SD)	22.0 (7.5)	30.4 (9.2)	**<0.01**[a]
TRAIL MAKING TEST A, seconds, mean (SD)	79.0 (37.6)	51.0 (21.3)	**<0.01**[a]
TRAIL MAKING TEST B, seconds, mean (SD)	191.1 (54.7)	139.9 (57.9)	**<0.01**[a]
SUBJECTIVE MEMORY COMPLAINTS, mean (SD)	9.6 (3.6)	5.5 (3.0)	**<0.01**[a]
PMRQ (prospective memory), mean (SD)	22.7 (5.9)	17.5 (3.8)	**<0.01**[a]
PMRQ (retrospective memory), mean (SD)	22.4 (4.8)	18.1 (4.3)	**<0.01**[a]
STATE TRAIT ANXIETY INVENTORY (trace), mean (SD)	39.9 (9.8)	32.5 (9.0)	**<0.01**[a]
GERIATRIC DEPRESSION SCALE, mean (SD)	4.2 (2.4)	2.2 (1.7)	**<0.01**[a]

Abbreviations: MCI, mild cognitive impairment; SD, standard deviation; PMRQ, prospective and retrospective memory questionnaire.

Statistically significant values are shown in bold.

[a] Independent samples Student's t tests.

[b] Pearson chi-square test.

Time perception on interval length

In the *prospective paradigm on short intervals*, the time estimates were above the actual times, and the time productions were under the actual times, for the 3 times considered (7 s, 32 s, 58 s), in both MCI patients and controls, as widely known from previous studies (Table 2). There were no significant differences between MCI patients and controls on *time estimate* (repeated measures ANOVA, F(1,110)=0.138, p=0.711, η^2_p=0.0013). Furthermore, no interactions between the diagnostic group and the time (7 s, 32 s, 58 s; repeated measures ANOVA, F(2,220)=0.072, p=0.930, η^2_p=0.0006) and the diagnostic group and the order of presentation (1st, 2nd, 3rd; repeated measures ANOVA, F(2,220)=0.971, p=0.380, η^2_p=0.0087) were found on average time estimates. There were also no significant differences between MCI patients and controls on *time production* (repeated measures ANOVA, $F(1,110)=0.043$, $p=0.837$, $\eta^2_p=0.0003$). No interactions between the diagnostic group and the time (7 s, 32 s, 58 s; repeated measures ANOVA, $F(2,220)=0.021$, $p=0.980$, $\eta^2_p=0.0001$) and the diagnostic group and the order of presentation (1st, 2nd, 3rd; repeated measures ANOVA, $F(2,220)=1.190$, $p=0.306$, $\eta^2_p=0.0107$) were found on average time production.

Regarding the retrospective paradigm on long intervals, there were no significant differences in the estimates of the time required to draw the clock and the duration of the interview between MCI patients and controls (Table 2).

Table 2. Time Perception on Interval Length

		MCI mean ± SD	CONTROL mean ± SD	P Value
PROSPECTIVE PARADIGM (SHORT INTERVALS)				
Time Estimation	7 s	14.4 ± 5.0	14.5 ± 5.2	0.71[a]
		14.6 ± 6.1	15.3 ± 7.1	
		14.5 ± 5.9	15.2 ± 6.7	
	32 s	51.2 ± 17.5	54.2 ± 17.8	
		54.5 ± 19.8	56.2 ± 21.0	
		54.7 ± 18.3	55.1 ± 19.7	
	58 s	90.4 ± 29.3	93.7 ± 31.4	
		91.5 ± 31.3	92.4 ± 33.5	
		93.2 ± 31.6	93.8 ± 34.2	
Time Production	7 s	4.8 ± 2.2	4.5 ± 2.3	0.84[a]
		5.0 ± 2.9	4.9 ± 2.3	
		5.1 ± 2.9	5.0 ± 2.8	
	32 s	19.9 ± 9.5	18.7 ± 9.4	
		20.3 ± 9.6	20.2 ± 10.1	
		19.9 ± 10.8	20.0 ± 10.6	
	58 s	37.3 ± 16.1	36.4 ± 16.7	
		37.9 ± 17.8	37.3 ± 18.2	
		37.2 ± 19.1	36.9 ± 18.1	
RETROSPECTIVE PARADIGM (LONG INTERVALS)				
Time to draw a clock	s	-23.9[b] ± 84.1	-4.6[b] ± 58.4	0.16[c]
Time of the interview	s	12.8[b] ± 591.9	-74.7[b] ± 549.6	0.42[c]

Abbreviations: MCI, mild cognitive impairment; SD, standard deviation.
For each time, the three values concern the first, second and third presentation of the same interval length.
[a] An analysis of repeated measures showed no significant statistically differences ($p<0.05$) between the Control group and the MCI group in prospective time.
[b] The values concern the difference between real time and time estimation. Large standard deviations stem from the variability of time estimates as well as high variability of the real time, that is, participants took rather different intervals to draw a clock or had variable interview times.
[c] Independent samples Student's t-tests.

Perception on subjective passage of time

Regarding the perceived speed of time passage, the composite speed-of-time scale score was significantly lower in MCI patients (0.58 ± 0.9) as compared to controls (0.73 ± 0.8; t(670)=-2.341, p=0.02, Student's t test), meaning that the MCI patients reported the time to be passing slower. The individual scores for the 6 time questions are shown in Fig. 1. In all the questions, except question 2 that relates to the anticipated speed of time in the next hour, the MCI patients reported the time to be passing slower, and QTI3 (*How fast did the last week pass for you?*, t(110)=-2.252, p=0.03, Student's t test), and QTI4 (*How fast did the last month pass for you?*, t(110)=-2.063, p=0.04, Student's t test) differed significantly between the two groups.

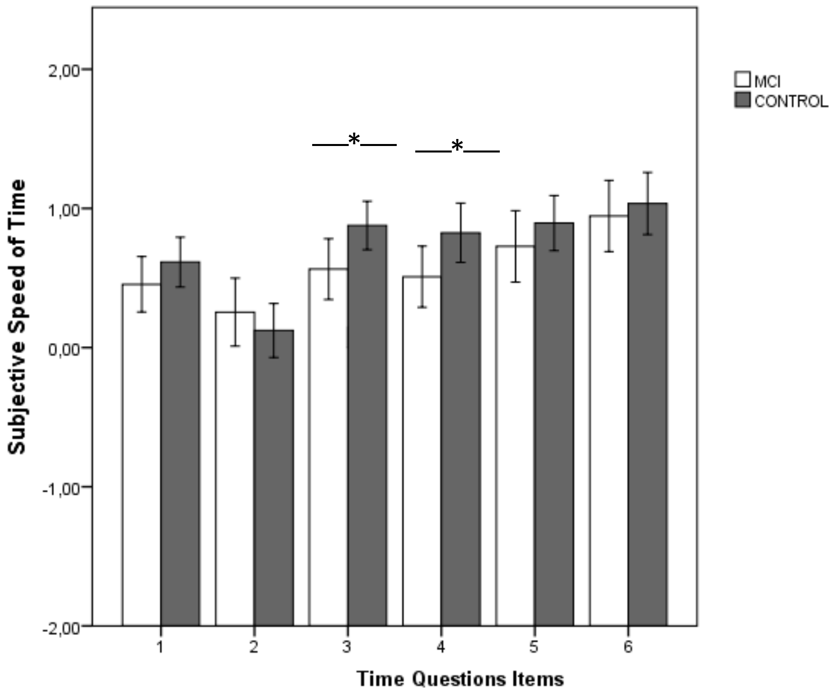

Figure 1. Perceived Speed of Time

Abbreviation: MCI, mild cognitive impairment.
The ratings of the perceived speed of Time Questionnaire are shown (Mean ± S.E.; Items: 1. How fast does time usually pass for you? 2. How fast do you expect the next hour to pass? 3. How fast did the previous week pass for you? 4. How fast did the previous month pass for you? 5. How fast did the previous year pass for you? 6. How fast did the previous 10 years pass for you?). Participants rated the statements on a five-point scale that ranged from 'very slowly? [-2] to 'very fast' [2].
*Statistically significant; Independent samples Student's t-tests.

An exploratory analysis was performed on the statements about the subjective experience of time. No differences were found between MCI patients and controls except on item 2 (*In the past several years my life has been quite a routine*), where MCI patients described their life as being more like a routine (Table 3).

Table 3. Statements about the Subjective Experience of Time

	MCI mean ± SD	CONTROL mean ± SD	*P* Value [a]
1. The past two years have been a time filled with many new experiences	-0.06 ± 1.62	0.46 ± 1.34	0.07
2. In the past several years my life has been quite a routine	0.54 ± 1.57	-0.16 ± 1.57	**0.02**
3. When I think back over the past two years, few notable events came to my mind	0.07 ± 1.72	-0.11 ± 1.67	0.58
4. There have been few notable changes in my life in the past year	0.67 ± 1.72	0.58 ± 1.66	0.79
5. When I try to remember the date of some event, I often come up with a time that is not as long as the true time	0.19 ± 1.85	0.74 ± 1.32	0.07
6. When I think that something was just a few years ago, it often turns out that it happened long before that	0.78 ± 1.63	0.46 ± 1.67	0.31
7. I often find that things occurred much longer ago than I thought	0.94 ± 1.43	0.49 ± 1.54	0.11
8. There is often not enough time to do everything I want or need to do	0.98 ± 1.74	1.18 ± 1.50	0.53
9. I frequently have to rush to make sure everything gets done	0.72 ± 1.76	0.88 ± 1.56	0.62
10. I usually have plenty of time for all things I want to accomplish in a day	0.20 ± 1.96	0.26 ± 1.67	0.86
11. These days I am not very busy	0.43 ± 2.00	0.09 ± 1.88	0.36

Abbreviations: MCI, mild cognitive impairment; SD, standard deviation.
Participants rated the statements on a seven-point scale that ranged from 'strongly disagree' [-3] to 'strongly agree' [3].
[a] Independent samples Student's t-tests.
Statistically significant values are shown in bold.

Perceived speed of time and cognition

Since significant differences in the perceived speed of time were found between the MCI patients and control participants, it would be important to know whether the perceived speed of time could be related to performance in neuropsychological domains, as well as anxiety and depression symptoms. In control participants, no correlations were found between the speed-of-time scale score and performances in cognitive tests, subjective memory, depressive or anxiety complaints (Table 4). In contrast, in MCI patients there was a positive correlation between the speed-of-time scale score and performance on Logical Memory A (both immediate and with delay), that is, patients with more severe memory deficits felt that time was passing more slowly (Table 4). There was also a positive correlation between the speed-of-time scale score and the SMC score, that is, patients with less cognitive complaints perceived time as being slower (Table 4).

It is important to add that no statistically significant correlation was detected in MCI patients between SMC score and Logical Memory A (both immediate and with delay), meaning that patients with more cognitive deficits were not those who necessarily had more cognitive complaints. No statistically significant correlations were found in MCI patients between the speed-of-time scale score and performances in executive tests, nor with depressive or anxiety complaints (Table 4).

Interestingly, item 2 of the statements about the subjective experience of time was also negatively and significantly correlated with Logical Memory A, both immediate (r=-0.31, p=0.02) and with delay (r=-0.44, p<0.01): that is, in MCI patients, the more severe memory deficits were, the more life felt like a routine.

Table 4. Correlations between Composite Speed of Time-Scale Score and Neuropsychological Variables

		QTavg	
LOGICAL MEMORY A (immediate recall)	MCI	**r=0.45**	**p=<0.01**
	CONTROL	r=0.05	p=0.74
LOGICAL MEMORY A (delayed recall)	MCI	**r=0.44**	**p=<0.01**
	CONTROL	r=0.04	p=0.78
TRAIL MAKING TEST B	MCI	r=-0.27	p=0.05
	CONTROL	r=0.10	p=0.46
GERIATRIC DEPRESSION SCALE	MCI	r=0.22	p=0.11
	CONTROL	r=0.14	p=0.30
STATE TRAIT ANXIETY INVENTORY (trace)	MCI	r=0.16	p=0.32
	CONTROL	r=0.12	p=0.37
SUBJECTIVE MEMORY COMPLAINTS	MCI	**r=0.39**	**p=<0.01**
	CONTROL	r=0.16	p=0.24
PMRQ (prospective memory)	MCI	r=0.15	p=0.27
	CONTROL	r=0.03	p=0.82
PMRQ (retrospective memory)	MCI	r=-0.07	p=0.63
	CONTROL	r=-0.02	p=0.89

Abbreviations: MCI, mild cognitive impairment; QTavg, composite speed of time-scale score; r, Pearson's correlation; PMRQ, prospective and retrospective memory questionnaire.

Statistically significant values are shown in bold.

Discussion

The main finding of this study is that MCI patients have alterations in the perception of the subjective passage of time, that is, they experience time as if it is passing more slowly, compared to healthy controls.

Remarkably, an abnormal internal clock was not the basis for these alterations in the perception of the subjective passage of time, since perception of the interval lengths was not different in MCI patients as compared to controls. These findings replicate a previous study, that used a prospectively time estimation paradigm, where participants were told in advance to estimate short time intervals (10 s, 25 s, 45 s, 60 s), and did not find changes in estimation of the interval length in MCI patients (Rueda & Schmitter-Edgecombe, 2009). Another study asked participants to retrospectively estimate a longer time interval, the duration of an interview (administration 25 to 30 minutes) (Heinik & Ayalon, 2010), and again did not find changes in MCI patients – although it is worth noticing that controls in this study were psycho-geriatric referrals with cognitive complaints, not healthy participants.

The present study has the advantage to propose an extensive and detailed analysis of interval length perception, in well-characterized MCI patients and healthy controls. We used both the prospective paradigm and the retrospective paradigm and the methods of verbal estimation and production of time intervals. No differences in prospective (7 s, 32 s, 58 s) and retrospective (time to draw a clock, time of the interview) time estimates were found in MCI patients. No differences in prospective time intervals production (7 s, 32 s, 58 s) were detected either. As mentioned, each duration in the prospective paradigm (7 s, 32 s, 58 s) was repeated three times (1^{st}, 2^{nd}, 3^{rd}) in a pseudorandom order, both in time estimation and in time production. Again, MCI patients did not show any drift along the different periods of time, or in the order of presentation, either in time estimation or in time production, as compared to control participants.

It is interesting to note that normal subjects, in the prospective paradigm on short intervals, tend to make time estimates that are above the actual times, and produce time intervals that are under the actual times (Carrasco, Bernal & Redolat, 2001; Coelho *et al.*, 2004). This finding was replicated in the present study. Usually, older adults are said to have faster internal clocks than younger adults, since they overestimate time intervals (Coelho et *al.*, 2004; Fraisse, 1963). Regarding the age effect, it is fair to say that MCI patients do not tend either to exaggerate, or to correct, the deviations normally observed with respect to objective durations. This suggests that their internal clock is consistent with normal aging.

The subjective passage of time, as far as we know, had not been previously investigated in MCI patients. Doing so in the current study allowed to discover that MCI patients, in spite of their "healthy" internal clock, experience time as passing slower than controls, as shown by a significantly lower speed-of-time scale score, and had generally lower individual scores for the items related to the past. In this respect, MCI differs from normal aging, since old adults report the time to pass more quickly, rather than more slowly, when compared to young adults (Friedman & Janssen, 2010; Wittmann & Lehnhoff, 2005).

Results on statements about the subjective experience of time also revealed that MCI patients felt the time passing more like a routine than controls (item 2). This may reflect the forced abandonment of some complex activities of daily living that MCI experience (Pedrosa, 2010). From the present data, the overall level of personal activity/engagement did not affect differently MCI patients and controls, as far as subjective time perception was concerned. The level of personal activity is known to influence time perception, as people less active tend to feel as if the time is passing more slowly (Fraisse, 1963). Thus, if MCI participants were less active due to their condition, this may had influenced their perception of time; however, if controls were also engaged in less activity, e.g. due to normal aging, they might report time passage the same way as MCI patients did. Interestingly, other aspects of the subject's experience of time, like forward telescoping (item 5-7) and life pressures (item 8-11), did not reveal differences between MCI patients and controls.

Since the internal clock was not found to be impaired in MCI patients, it would be important to look for other reasons that could explain the changes that MCI patients showed in the perceived speed of time. Previous studies emphasised the importance of memory and executive functions for time perception (Heinik & Ayalon, 2010; Papagno, Allegra & Cardaci, 2004), as well as emotional factors, such as depression and anxiety (Nichelli, 1993). We found that the speed-of-time scale score was correlated with memory tests in MCI patients, that is, patients with more severe memory deficits felt that time was passing more slowly.

The influence of memory deficits on the distortion of perceived speed of time seems specific, since (i) it was only observed in MCI patients, not in healthy controls, and (ii) speed-of-time scores correlated with memory results but not with performance in executive tests or with complaints of depression or anxiety, even if MCI patients presented abnormalities on all these measures. It is interesting to add that patients with poorer memory were also those who felt the time passing more like a routine, confirming that memory deficits are associated with alterations in the subjective experience of time. Remarkably, patients with less severe memory complaints were also those who felt time as passing most slowly. The fact that memory complaints did not correlate with memory deficits suggests that subjective memory complaints may not accurately reflect memory deficits in patients with cognitive impairment (see, for instance, Silva *et al*., 2014).

The relationship between memory deficits and the distortion of perceived speed of time certainly reinforces the concept, advanced by previous authors (Graf & Grodin, 2006; Kinsbourne & Hicks, 1990; Mimura, Kinsbourne & O'Conner, 2000; Schmitter-Edgecombe & Rueda, 2008), that memory is necessary to time perception. The idea of a connection between time perception and memory is not a modern one. It can be traced back to Aristotle, according to whom memory is what allows us to place events in time and to count them (Ricoeur, 2004). In fact, ancient philosophers like Aristotle and Saint Augustin argued that our sense of time passage is due to memory operations, although they emphasized the thought that we become acquainted of that passage by measuring time intervals, an idea that still prevails in current time studies.

Later, in the XIX century, philosophers and psychologists (Guyau, 1890; James, 1890) studied human temporal distortions and related them with memory changes (Guyau, 1890). However, these studies focused on the ability to count time intervals and on the quantitative aspect of time perception. Bergson was the first to drive attention towards the qualitative aspect of time perception and its association with memory (Guerlac, 2006). Indeed, Bergson famously expressed the radical thought that time *is* memory, a succession of qualitative states that interpenetrate and mix together (Bergson, 1889). The relevance of memory for time perception is certainly recognised by contemporary researchers, who have also called the attention to non-cognitive processes, namely qualitative sensations expressed by emotional and visceral states, that are not necessarily part of the core timekeeping system, but contribute to our self-experience and the subjective judgements of time passage (Wittmann, 2009).

In conclusion, MCI patients experience time as passing more slowly than controls. Since time perception is an essential component of everyday goal oriented behaviours, this altered experience of time may contribute to some of the symptoms that patients with MCI report, especially memory deficits and difficulties in activities of daily life.

CHAPTHER II: DELAY DISCOUNTING IN MILD COGNITIVE IMPAIRMENT

Introduction

Critical domains of our lives, such as finance and healthcare, are decision-making dependent. Many choices in our lives are intertemporal in nature, since they involve outcomes that occur at different points in time, and intertemporal preferences largely influence decision-making (Soman et al., 2005). We may prefer to buy a car now or to make a long-term investment in a health insurance; to have pleasure eating a chocolate now or to stick to a diet in order to be healthier in the long run. Thus, an immediate choice may have positive short-term consequences but negative long-term results. One way to assess intertemporal preferences is through a delay choice questionnaire (sometimes also referred to as intertemporal choice task or delay discounting task; for discussion, see Soman et al., 2005; Addessi et al., 2013). The delay choice questionnaire evaluates preferences between smaller, immediate rewards and larger, delayed rewards (e.g., “Would you rather prefer 20€ now or 150€ in 50 days?”), reflecting the level of individual impulsiveness, as the subject moves away or towards short-term interests. The value which we assign to immediate options or to delayed outcomes has different consequences upon our lives. Temporal discounting, the tendency to prefer immediate rewards over delayed but larger rewards, is linked to sub-optimal decision-making in finance and health (Bidewell, Griffin & Hesketh, 2006; Daugherty & Brase, 2010; James et al., 2015; Lindbergh et al., 2014a).[2]

Intertemporal preferences are influenced by emotional factors, like anxiety (Ludwig et al., 2015; Rounds, Beck & Grant, 2007) and depression (Pulcu et al., 2014; Takahashi et al., 2008), cognitive abilities, namely executive functions (Weatherly & Ferraro, 2011) and

[2] It must be noted at this point that delay discounting captures just one facet of the decision-making process, albeit a crucial one. Other paradigms evaluate decision-making dealing with probabilities, under a context of risk or ambiguity. Decisions under risk usually use a probability discounting paradigm (e.g., “Would you rather prefer 60€ guaranteed or a 50% chance of receiving 100€?) (Shead & Hodgins, 2009), whereas decisions under ambiguity present tasks where information is missing, such as the Iowa Gambling task (IGT) (Bechara, Damasio, Damasio & Anderson, 1994). Although decisions involving temporal delay and decisions involving probabilities may exhibit similarities, like the tendency of impulsive individuals to take more risks (Richards, Zhang, Mitchell, de Wit, 1999), they seem to rely on different cognitive processes (Weber & Huettel, 2008).

the ageing process itself (Green, Fry, & Myerson, 1994; Halfmann, Hedgcock, Denburg., 2013; Harrison, Morten, & Williams, 2002; Read & Read, 2004). To study individual preferences in aging is of crucial importance, since older people have to face important decisions in health and finance at the end of their lives (James et al., 2015; Mather, 2006; Sproten et al., 2010). Serious health conditions in aging, such as dementia, could also contribute to alter intertemporal preferences and compromise decision-making (Lindbergh et al., 2014a). Nowadays, a great deal of attention is paid to a group of patients that are at risk of developing dementia, mainly Alzheimer's disease (AD), in the ensuing few years, a condition called Mild Cognitive Impairment (MCI). When evaluated, patients with MCI present abnormal memory function, below the expected for age and education, but they exhibit normal general cognitive function and perform normal daily activities (Petersen et al., 1999; Petersen, 2004). According to this concept, patients with MCI are able to answer consistently to questions regarding everyday care preferences and make appropriate choices (Feinberg & Whitlatch, 2001).

However, it is recognized that more complex activities, like balancing the cheque book, or keeping appointments and meetings, may be impaired in MCI patients (Pedrosa et al., 2010). Mild cognitive impairment is associated with poorer decision-making, particularly in complex life domains (Han et al., 2015) and when facing choices involving uncertainties (Zamarian, Weiss, & Delazer, 2010). This was mainly studied in the financial domain, where MCI patients exhibit impaired and declining financial skills and abilities (Triebel et al., 2009; Lui et al., 2013). Patients with MCI have to face important decisions that may involve costs and benefits across time, as planning retirement (Bidewell, Griffin & Hesketh, 2004), which are dependent upon intertemporal preference choices.

Previous studies using delay discounting questionnaires in older people with cognitive impairment provided rather variable results. A cross sectional study in 64 community older adults showed that functional decline, indicated by a decrease in the instrumental activities of daily life (IADL) scale score, was associated with inconsistency in delay discounting answers (Lindbergh et al., 2014b), that is, choice consistency could serve as a marker for functional decline, likely due to neurocognitive deterioration. In this research, participants with dementia or with a score ≤20 on the Mini-Mental State Examination (MMSE) were excluded. Noteworthy, by these criteria, cognitively normal subjects, as well as subjects with mild cognitive impairment, might have been included. A longitudinal study examined discounting preferences in 455 community older adults (James et al., 2015). Subjects who met criteria for dementia or MCI based on evaluation of a clinician, a neuropsychologist or a computer scoring of neurobehavioral tests, were excluded at the baseline. In this study, the criteria used for the diagnosis of MCI were not specified. A higher delay discounting rate at the baseline was associated with cognitive decline in the 3 years follow-up, meaning that delay discounting could potentially identify cognitive decline early in the neurodegenerative process. Another study specifically examined delay discounting in patients with well-defined criteria for MCI (Albert et al., 2011), recruiting 25 patients with MCI and 39 healthy controls who were submitted to 27-item and 80-item delay discounting questionnaires (Lindbergh et al., 2014a). Patients with MCI tended to prefer immediate choices at small reward magnitude, but not at medium, large and extra-large reward magnitudes, showing an increasing impulsiveness with decreasing reward magnitude. There were no significant differences between the two groups in delay discounting response consistency.

Regarding more serious cognitive impairment, it might be expected that AD patients would discount future rewards to a greater extent. Notwithstanding, contradictory findings were reported. A study that compared mild to moderate AD patients with behavioural-variant frontotemporal dementia patients and healthy older adults on delay discounting found that patients with AD, in contrast to behavioural-variant frontotemporal dementia patients, had similar delay discounting preferences as healthy controls (Bertoux et al., 2015). Another longitudinal study recruited patients with mild AD and MCI, and detected an increase in delay discounting rates at the 2-years follow-up in patients with mild AD as compared to patients with MCI (Thoma, Maercker & Forstmeier, 2016).

Since delay discounting can be measured in various ways (for discussion, see Soman et al., 2005; Madden & Johnson, 2010; Addessi et al., 2013; Paglieri, 2013), one might naturally suspect that such varied results are due, at least partially, to different measures being used across studies. By and large, this was not the case: most studies used some version of the questionnaire-based delay choice task adopted also in the present study. The reason why delay choice questionnaires are preferred in studying delay discounting in MCI patients is twofold: firstly, the task is easy to administer and understand, and it takes relatively little time to complete (which is crucial, in experimental designs involving multiple tasks on ageing participants); secondly, the task allows to explore the delay length (medium-long delays) that is most likely to be of significance in MCI patients, in light of their memory deficits; thirdly, delay choice questionnaires do not only measure delay discounting, but also the level of consistency of each participant's choices, which is an important factor to assess in MCI patients. In contrast, other methods of assessing delay discounting are either too long or too hard to administer (e.g., variable delay and variable amount protocols), measure delay tolerance only on short delays (e.g., delay maintenance paradigms), fail to provide data on choice consistency, or a combination of the above limitations. Thus questionnaire-based delay choice tasks remain the preferred methodology for investigating intertemporal preferences in MCI patients.

Taking into account methodological differences and the variable results obtained in previous studies, our experiment aims to reappraise the issue of intertemporal preferences and delay discounting in older people with cognitive decline using an appropriately sized sample and a well-defined group of amnestic MCI patients. The hypothesis is that, to the extent that this particular delay choice task may involve memory capabilities, patients with MCI should present greater and more inconsistent temporal discounting as compared to healthy controls. Conversely, a failure to observe a difference with the control group would indicate that the type of economic choices used in the questionnaire do not largely require intact memory functions.

Methods

Participants:

Patients with MCI were recruited at a dementia outpatient clinic and a memory clinic, both in Lisbon. Controls were volunteers with no cognitive complaints from senior universities in Lisbon. The study was approved by the ethics committee of Faculty of Medicine/ Santa Maria Hospital in Lisbon. The participants were informed of the experimental protocol and gave their written consent.

Inclusion Criteria for the MCI group

The inclusion criteria for diagnosis MCI were adapted from Petersen *et al*, 1999, which correspond to amnestic MCI: (1) presence of memory complaints; (2) abnormal memory function, below the expected for age and education, documented by the Logical Memory subtest of the *Bateria de Lisboa para Avaliação das Demências* (BLAD, see below); (3) normal general cognitive function, determined by the Mini Mental State Examination (MMSE, see below) within normal values for Portuguese population; (4) no or a minimal impairment in activities of daily living determined by the Instrumental Activities of Daily Living Scale (IADL, see below), that is to say, no more than one item from the IADL scale was altered.

Inclusion criteria for the Control group

(1) present no memory complaints; (2) have normal memory function, documented by the Logical Memory subtest of BLAD; (3) have a MMSE with normal values for the Portuguese population; (4) have normal IADL scale, that is to say, no item from the IADL scale was altered.

Inclusion criteria for both groups

(1) Native Portuguese speakers; (2) Education ≥ 4 years; (3) Age > 45 years old.

Exclusion Criteria for both groups

(1) Dementia, according to DMS-IV-TR (American Psychiatric Association, 1994); (2) Presence of major depression according to DSM-IV-TR or serious depressive symptoms, indicated by a score >10 points on the 15-items Geriatric Depression Scale (GDS_{15}, see below); (3) Neurological disorders (Parkinson's disease, stroke, brain tumour, significant head trauma or epilepsy), psychiatric conditions (such as autism, schizophrenia), or uncontrolled medical illness (hypertension, metabolic, endocrine, toxic or infectious diseases) able to interfere with cognition; (4) Psychoactive medications with possible influence on cognition; (5) History of alcohol or drug abuse; (6) Sensory deficits likely to interfere with assessment.

Procedures

All the participants were submitted to the Portuguese versions of the following instruments:

(1) Mini-Mental State Examination (MMSE, Folstein, Folstein & McHugh, 1975). This test is used for evaluation of the mental state and screening of dementia. The Portuguese

version of the test adapted from Guerreiro *et al*., 1994, was used. Participants with MMSE below education-adjusted values for the Portuguese population were excluded (<23 for equal or less than 11 years of education, <28 for more than 11 years of education)

(2) Logical Memory A, this test evaluates verbal memory and is from *Bateria de Lisboa para Avaliação das Demências* (BLAD) (Garcia, 1984; Guerreiro, 1998), a neuropsychological battery designed to evaluate multiple cognitive domains and validated for the Portuguese population. Participants with Logical Memory A (immediate or delayed recall) below education and age adjusted values for the Portuguese population (1 SD) were considered impaired. A cut-off value of 1 SD was adopted considering that the use of the cut-off value of 1.5 SD (Petersen *et al*., 1999) could exclude subjects that from a clinical point of view suffered from MCI (Palmer, Frantiglioni & Windblad, 2003; Winblad et al., 2004).

(3) Trail Making Test (TMT, Reitan, 1958). The TMT is a tool that evaluates executive functions, namely attention switching, planning and internal ordering. It consists of two parts. In part A, the subject is instructed to connect a set of 25 numbers as fast as possible while still maintaining accuracy. In part B, the subject is instructed to connect numbers sequentially with letters. Scoring is expressed in terms of the time in seconds for Part A and Part B of the test. The Portuguese version of the test adapted from Fernandez & Marcopulos, 2008, was used.

(4) Subjective Memory Complaints (SMC, Schmand et al., 1996). The SMC is a questionnaire that assesses memory complaints. The Portuguese version of the test, adapted from Ginó *et al*., 2008, was used.

(5) State-Trait Anxiety Inventory (STAI, Spielberger et al., 1983). The STAI is a questionnaire that evaluates the trait and the state of anxiety, comprising 40 items, 20 about the trait of anxiety and 20 about the state of anxiety. The maximum score is 80 points and the minimum score is 20. The Portuguese version adapted from Silva, 2006, was used.

(6) The Geriatric Depression Scale (GDS_{15}, Yesavage & Brink, 1983). The GDS is a questionnaire that evaluates the existence and the degree of depression symptomatology. The maximum score is 15 and a score >10 is considered to reflect serious depressive symptoms. The Portuguese version adapted from Barreto et al., 2008, was used.

(7) Instrumental Activities of Daily Living Scale (IADL, Lawton & Brody, 1969). The IADL is a tool that evaluates daily self-care activities. The Portuguese version, done in the context of LADIS project, was used (Pantoni *et al*., 2005).

To evaluate their temporal preferences, all participants were submitted to the following instrument:

(1) A 24 items intertemporal choice questionnaire, which is a shortened version of the 48 items used in Paglieri et al. (2013) and based on the method developed by Kirby & Marakovic (1996). The participants are asked to choose between a smaller prize available immediately and a larger reward available only after a certain delay (e.g. “Do you prefer to receive immediately 121€ or wait 38 days to receive 190€?”; “Do you prefer to wait 64 days to receive 25€ or to receive immediately 21€?”). The purpose of the test is to assess the level of delay discounting of each individual. Three parameters were used to evaluate delay discounting behaviour. The hyperbolic discounting function assumes that people tend to prefer sooner rewards to later rewards, but that their discount rate, k, is not constant across the delays. The Mazur’s formula for hyperbolic discounting, $V=A/(1+kD)$, where V is the discounted value of the delayed reward, A is the amount of the delayed reward, D is the delay measure and k is the discount rate parameter, predicts that discount rates decline when delay increases. Higher values of k represent a greater discounting of delayed rewards (Kirby & Marakovic, 1996; Green et al., 1996). Another parameter is the percentage of choices for the larger and later reward, %LL, which is inversely related to k. The higher the discount rate, the more future rewards are devaluated, and thus the lower the percentage of choices for delayed rewards. The %LL is a more direct measure than k, but also coarser, since it is not sensitive to choice inconsistencies within the same magnitude range. Finally, response consistency, Acc, measures how many actual choices of each participant are consistent with the discount rate estimated for that participant.

Statistical Analysis

Sample size was estimated from a power analysis using the Power and Precision software (v.4; BioStat; Englewood, NJ). Values of k for older adults (upper income) taken from a previous work (Green *et al*., 1996) were used. To detect a 25% change in the discounting *k* parameter, 100 participants (50 MCI and 50 controls) would be required, assuming a power = 90%, α= 0.05 and 2-tails Student's *t*-test.

Demographic, clinical and neuropsychological data were compared between the 2 groups, MCI and controls, with the Student's *t*-test for numerical variables and χ^2 for categorical variables. The delay discounting questionnaire was analysed using the 3 parameters, *k*, %LL and ACC, for the 3 magnitudes (small, medium and large), with repeated measures ANOVA. Patients with MCI and controls were considered to represent between-subject effects, while reward size (small, medium, large magnitudes) was used to evaluate within-subject effects. Effect sizes were estimated by the partial eta squared (η^2_p). This analysis was repeated entering age, education gender, MMSE scores, anxiety and depression as covariates.

Statistical analyses were performed using SPSS for Windows (SPSS 19; SPSS Inc., Chicago, Ill). Effects with *P* values <0.05 were considered statistically significant.

Results

One hundred and twelve participants, 57 controls and 55 MCI patients, were submitted to neuropsychological evaluation and the delay discounting questionnaire. There were no statistically significant differences in age, education and gender between the two groups (Table 1).

Neuropsychological characteristics

The MCI participants had lower MMSE, worse performances in cognitive tests, namely memory (Logical Memory A) and executive functions tests (Trail A and B), and presented more subjective memory complaints (SMC) as well as anxiety (STAI) and depressive (GDS) symptoms than controls (Table 1).

Table 1. Demographic and Neuropsychological Characterization

	MCI (n=55)	CONTROL (n=57)	*P* Value
AGE, years, mean (SD)	70.9 (8.9)	67.6 (8.5)	0.05[a]
EDUCATION, years, mean (SD)	10.9 (4.4)	11.1 (4.5)	0.74[a]
GENDER, female/male, n	36/19	35/22	0.66[b]
MINI-MENTAL STATE EXAMINATION, mean (SD)	27.2 (2.2)	29.1 (1.1)	**<0.01**[a]
LOGICAL MEMORY A (immediate recall), mean (SD)	7.1 (3.3)	15.0 (4.1)	**<0.01**[a]
LOGICAL MEMORY A (delayed recall), mean (SD)	5.5 (3.7)	15.1 (4.4)	**<0.01**[a]
TRAIL MAKING TEST A, seconds, mean (SD)	79.0 (37.6)	51.0 (21.3)	**<0.01**[a]
TRAIL MAKING TEST B, seconds, mean (SD)	191.1 (54.7)	139.9 (57.9)	**<0.01**[a]
SUBJECTIVE MEMORY COMPLAINTS, mean (SD)	9.6 (3.6)	5.5 (3.0)	**<0.01**[a]
STATE TRAIT ANXIETY INVENTORY (trace), mean (SD)	39.9 (9.8)	32.5 (9.0)	**<0.01**[a]
GERIATRIC DEPRESSION SCALE, mean (SD)	4.2 (2.4)	2.2 (1.7)	**<0.01**[a]

Abbreviations: MCI, mild cognitive impairment; SD, standard deviation.
Statistically significant values are shown in bold.
[a] Independent samples Student's *t* test.
[b] Pearson χ^2 test.

Delay discounting questionnaire

No significant differences were found in the delay discounting questionnaire between MCI patients and controls for the 3 reward sizes (small, medium and large) (Table 2; Figure 1), considering both the hyperbolic discounting *k* parameter (repeated measures ANOVA, F(1, 110)=1.210, p=0.274, η^2_p=0.0119), and the percentage of choices for the larger and later rewards, %LL parameter (repeated measures ANOVA, F(1, 110)=0.390, p=0.530, η^2_p=0.0035). As expected, a significant difference in reward size was detected reflecting the discounting phenomenon, both in *k* (repeated measures ANOVA, F(2, 220)=45.502, p=<0.001, η^2_p=0.293) and in %LL (repeated measures ANOVA, F(2, 220)=63.347, p=<0.01, η^2_p=0.3654). Importantly, no interaction between the diagnostic condition and the reward size was found, both for *k* (repeated measures ANOVA, F(2, 220)=0.056, p=0.945, η^2_p=0.001) and for %LL (repeated measures ANOVA, F(2, 220)=0.273, p=0.761, η^2_p=0.0025).

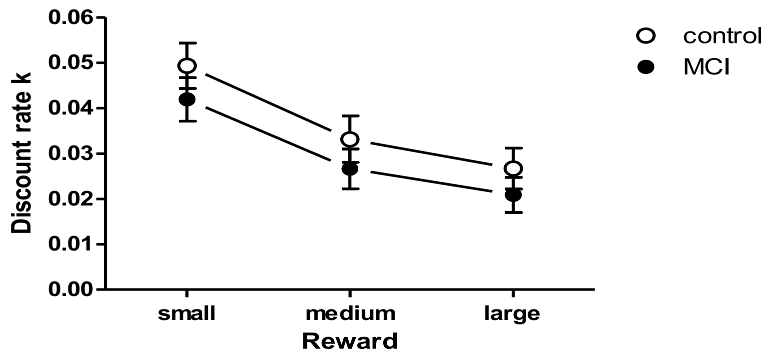

Figure 1. – Estimates of the k parameter for both MCI and Control groups in the hyperbolic discounting function as a function of reward magnitude (small, medium and large).

Regarding response consistency, the Acc parameter, there were no significant differences (repeated measures ANOVA, $F(1, 110)=2.148$, $p=0.146$, $\eta^2_p=0.0192$) between MCI patients and controls for the 3 reward sizes (small, medium and large). There were also no significant differences in reward size (repeated measures ANOVA, $F(2, 220)=1.283$, $p=0.279$, $\eta^2_p=0.0115$) and no interaction between the diagnostic condition and the reward size (repeated measures ANOVA, $F(2, 220)=0.745$, $p=0.476$, $\eta^2_p=0.0067$).

The analysis on delay discounting performance using k, LL, Acc parameters was repeated with a mixed effects repeated measures ANOVA accounting for age, education, gender, MMSE scores, anxiety and depression as covariates. The main effects under study did not change.

Table 2. Parameters of delay discounting

		MCI mean ± SD	CONTROL mean ± SD	*P* Value
K	Small	0.042 ± 0.035	0.049 ± 0.038	0.274[a]
	Medium	0.027 ± 0.032	0.033 ± 0.039	
	Large	0.021 ± 0.029	0.027 ± 0.034	
%LL	Small	34.3 ± 27.7	29.8 ± 27	0.530[a]
	Medium	49.8 ± 27.8	46.8 ± 31.7	
	Large	53.4 ± 27.3	51.8 ± 29.5	
Acc	Small	87.04 ± 13.2	87.9 ± 16.4	0.146[a]
	Medium	87.3 ± 18.9	92.3 ± 13.3	
	Large	85.00 ± 20.04	89.3 ± 16.3	

Abbreviations: MCI, mild cognitive impairment; SD, standard deviation; *k*, discount rate; *%LL*, percentage for later and delayed rewards; *Acc*, response consistency

[a] Repeated measures ANOVA showed no statistically significant differences (p<0.05) between MCI patients and controls, and no interaction between the diagnostic condition and the reward size.

Discussion

The main finding of this study is that patients with MCI have no alterations in intertemporal preferences, namely delay discounting rate and consistency, as compared to healthy controls, when tested using a delay choice questionnaire with monetary rewards.

Certainly, patients with MCI may make sub-optimal decisions particularly in complex situations (Han et al., 2015; Pertl et al., 2015). But it has been controversial whether patients with MCI display deficits in intertemporal preference choices and delay discounting that could hinder their decisions. The conflicting results found in previous studies may be due to methodological differences, particularly regarding the criteria for cognitive impairment, as well as to different study designs. Older people with cognitive impairment were reported to have higher delay discounting or more inconsistent discounting answers, but the impaired participants were defined as having some degree of functional decline (Lindbergh et al., 2014b), or presented deficits in a test that simulates real-life decisions (Halfmann, Hedgcock & Denburg, 2013). We contend that participants must have well defined and widely accepted diagnostic criteria for cognitive impairment. A previous study that recruited participants fulfilling criteria for MCI (Lindbergh et al., 2014a) showed that these had higher delay discounting, that is, tended to prefer the immediate outcomes, but only for small reward magnitudes, and were not affected in delay discounting response consistency. However, that study presented some methodological limitations that might have biased the results, namely the sample size was small, and there was a significant unbalance in variables, such as gender and age, that might influence delay discounting, between MCI patients and controls. The study design could also explain variable results found in previous studies. For instance, some studies cross-sectionally compared patients with cognitive decline with healthy controls (Bertoux et al., 2015; Lindbergh et al., 2014b; Lindbergh et al., 2014a), whereas others followed longitudinally subjects with various degrees of cognitive impairment (James et al., 2015; Thoma, Maercker & Forstmeier, 2016).

In the present study, using well defined and widely recognized criteria for diagnosing MCI, patients with MCI had no alterations in delay discounting preferences, namely delay discount rate and consistency, as compared to matched healthy controls. It could be argued that a small difference in delay discounting in MCI patients would not be detected, which is true, as pointed out by the previous sample size calculation. However, looking at the results, and particularly at Figure 1, the tendency, if any, is for the MCI patients to have a *lower* delay discounting across all the magnitudes, just the opposite that has been invoked to explain suboptimal decision-making (Bidewell, Griffin & Hesketh, 2006; Daugherty & Brase, 2010; James et al., 2015; Lindbergh et al., 2014a). Furthermore, if patients with MCI showed deficits in delay discounting, previous studies would have presumably revealed even more exacerbated deficits at later stages of cognitive decline, that is, Alzheimer's disease. This was not indisputably the case. Patients with Alzheimer's disease displayed no alterations in delay discounting preferences compared to healthy controls (Bertoux et al., 2015), although in a longitudinal study an increase in delay discounting compared to patients with MCI was found (Thoma, Maercker & Forstmeier, 2016).

It is important to recognize that the aging process itself may influence intertemporal preferences. Several studies showed a decrease of delay discounting over the life span (Harrison, Morten & Williams, 2002; Green, Fry & Myerson, 1994), indicated that middle age people discount less than both young and old people (Read & Read, 2004), or found differences between middle age and old people that depended on whether rewards or losses were considered (Halfmann, Hedgcock & Denburg, 2013). Notably, these studies did not take into account important factors, such as income or wealth, related to the age of the participants, that may influence intertemporal preferences (Green et al., 1996). Other studies that controlled for relevant socio-economic variables, such as household income, did not find differences in delay discounting choices between young and old people (Green et al., 1996; Roalf et al., 2011). The present study has the limitation that socio-economic status was not formally assessed, nevertheless we checked that education, that might be considered a proxy of socio-economic status, did not influence the results. A further interesting question is to what extent the awareness of having a disease, in this case MCI, that will probably progress in the future, might influence intertemporal preferences.

The relevance of memory capabilities for intertemporal preferences has long been debated. The French philosopher Bergson, for instance, emphasised the importance of memory for our choices (Bergson, 1889). Since the hippocampus and related medial temporal lobe regions are involved not only in recalling past episodes but also in mental time travelling, it was proposed that these brain structures could influence intertemporal choices by endorsing the capacity to imagine future outcomes (Lebreton et al., 2013). However, a case report of episodic amnesia caused by bilateral hippocampal damage pointed out that the patient, in spite of marked episodic memory deficits, was not affected in a delay discounting questionnaire (Kwan et al., 2012); the same result was later confirmed with a larger sample of amnesic individuals with hippocampal damage and associated impairments in episodic memory and future imagining (Kwan et al., 2013). The present study also showed that patients with amnestic MCI, who typically have hippocampal atrophy (Nunes et al., 2010), exhibited marked deficits in episodic memory, but could nevertheless perform the delayed discounting task similarly to controls. Recent studies, based on functional imaging, have highlighted the brain regions involved in temporal discounting. The brain networks activated during intertemporal choices are associated with executive-control areas, namely the dorsal prefrontal cortex and posterior parietal cortex, as well as brain reward areas, namely the ventral striatum and ventromedial prefrontal cortex (Kim, Sung, McClure, 2012; McClure et al., 2004), and not so the episodic memory related medial temporal lobe regions.

In conclusion, patients with MCI perform similarly to healthy controls in a delay discounting task, suggesting that episodic memory deficits do not notably affect intertemporal preferences. An intriguing speculation for future studies concerns the type of outcomes presented to participants, insofar as the type of choice in the present temporal discounting paradigm involves a rather simple trade-off between amount and delay, and can be handled using relatively simple similarity-based heuristics (Rubinstein, 2003). It would be interesting to test choices that require imagining oneself in the future, and ascertain how patients with MCI would deal with this type of prospective imagination.

CHAPTER III – A CASE OF PHILOSOPHICAL EXPERIMENTATION UPON MILD COGNITIVE IMPAIRMENT'S TIME PERCEPTION. TESTING BERGSON AND ARISTOTLE ON TIME AND MEMORY

What I wanted is a philosophy which would submit to the control of science and which in turn could enable science to progress. A truly intuitive philosophy would realize the union so greatly desired of metaphysics and science.

[Bergson 1934]

Introduction

According to Bergson, for the sake of knowledge progression, science and philosophy are able to test one another or, in other words, of mutual verification. Although different in object and method (science cares about the study of the brain using scientific methodology and philosophy investigates mind through philosophical intuition), they share in common the human experience. For instance, when investigating time perception, scientists may wonder about the neuropsychological functions or brain structures involved in the experience of time whereas philosophers may question how time appears to human mind. In the best-case scenario, for Bergson, the results of scientific research should match with philosophical intuitions, otherwise rectification is needed in science, in philosophy or in both, because scientific procedures or philosophical reasoning may be mistaken (Bergson, 1934; Gunther, 1987). This proposal resembles the contemporary movements of intersection between philosophy and neuroscience, more specifically, neurophenomenology, which profits from philosophical ideas to point out new directions to science (Gallagher, 2003); experimental philosophy (taken in a broader sense[5]), which employs experimental procedures to test philosophical hypotheses (Rose

[5] According to Rose and Danks, we must distinguish between a narrower sense and a broader sense of experimental philosophy. The broader sense deals with more than investigating people's intuitions underlying philosophical topics, that is, the way we usually think. It concerns the testing of ideas through experimental tasks. The two thinkers give the example of Helmholtz, whose experiments on perception were explicitly intended to test many of Kant's claims about the nature and the origin of categories. Therefore, they concluded that experimental philosophy broadly understood is "an instance of a long

& Danks, 2013); and particularly neurophilosophy, where the empirical data is used to enlighten philosophical questions (Churchland, 1986). Notwithstanding, Bergson does not advocate a reductionist perspective as the neurophilosopher Patricia Churchland, since he argues that the two knowledge domains complement each other and that philosophy penetrates in realms not accessible by science (Bergson, 1934). Unlike Churchland, for Bergson, mind concepts as duration can be neither fully explained by science nor represented into brain or cerebral processes.

Recently, it was investigated time perception and its consequences in patients with mild cognitive impairment (MCI) using an interval length task, a passage of time judgments protocol and an intertemporal choice questionnaire (Coelho et al., 2016a; Coelho et al., 2016b). Mild cognitive impairment patients suffer from memory deficits but have their general cognitive function preserved (Petersen et al., 1999). Therefore, it is a group of particular interest to examine the relation between temporal experience and memory. Memory has long ago been connected with time perception in the philosophical realm (Bardon, 2013), but also in science several studies associated time perception with short-term and long-term memory (Graf & Grodin, 2006; Kinsbourne & Hicks, 1990; Mimura, Kinsbourne & O'Conner, 2000; Schmitter-Edgecombe & Rueda, 2008).

Recently, by employing the interval length judgments task previously mentioned, it was evaluated time estimation and time production abilities in patients with MCI (Coelho et al., 2016a) based on the hypothesis that their internal clock is damaged. The internal clock hypothesis was conceived by science to explain the factors that influence time perception (Grodin, 2010). It assumes the presence of an oscillatory pacemaker that is constantly emitting pulses and processes information along three stages. When asked to estimate time intervals, a person should count the pulses and save them into an accumulator for later comparison with the memory of pulses counted in the past. As the internal clock model includes a memory (both short-term and long-term) stage in its mechanism, memory impairments could corrupt the internal clock functioning, thus affecting time estimate and production. Patients with MCI were also submitted, for the first time, to an experimental protocol on passage of time judgments (Coelho et al.,

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tradition of philosophical naturalism conjoined with an active research in cognitive science" (Rose & Danks, 2013).

2016a), supposing that this experiment will capture long-term memory awareness. Results showed that patients with MCI were not affected in time estimation and time production abilities, however they differed from healthy aged subjects on passage of time judgments, and this alteration was associated to long-term memory deficits and feelings of routine. Finally, it was verified that patients with MCI did normal intertemporal choices (Coelho et al., 2016b), suggesting that the conscious experience of time duration is not involved in this type of decision-making process.

Taking advantage from Bergson's opinions of how science and philosophy should interact, we propose to analyse if and how Bergson's ideas match the experimental design used and the main results obtained. We intend to profit also from his philosophical intuitions to enlighten the results obtained in the experimental protocol and also to advance helpful suggestions regarding further scientific research on the field. Essentially, three sections of his major work *Time and Free Will* are the ones to be taken into account. This work opens scissions, dividing the worlds of science and philosophy, not to diminish the role of science but to show what science lost without the help of philosophy. Later works, mainly *Matter and Memory*, overcame those divisions, by showing an interaction between both domains.

In section I and II of *Time and Free Will*, Bergson presents his conception of time perception and in section III he relates it to free choices. Since the ideas presented in the first two sections are the foundations of his construction, we thought it would be profitable to contrast his thoughts with an opposite vision and to map that distinction onto two experimental paradigms that we used to investigate time perception. As Heidegger sustained, Bergson's thoughts may be considered the opposite of Aristotle thinking (Heidegger, 1925-6). Heidegger sees that for the Aristotle and Bergson the time experience arises from the feeling of the succession of our ideas. For both thinkers, memory is an essential component of time experience. However, we can classify that succession as quantitative, like Aristotle, or as qualitative, like Bergson (Massey, 2015). Both argued that time perception depends on memory and built their definitions of time in close connexion with time perception. Notwithstanding, to Aristotle time perception is a question of counting instants whereas to Bergson it is a matter of feelings.

As we shall demonstrate in the next following sections, the two experiments performed might be inspired in two different conceptions of time perception, which are, in the first case, Aristotelian and, in the second case, Bergsonian. In the first section, we will present Aristotle's ideas about time perception and relate them to the interval length judgments task. In the second section, we will portray Bergson's ideas about time perception and its broader consequences and relate them to the passage of time judgments protocol and the intertemporal choice questionnaire. In the third section, we will try to refute some possible objections that could arise from that association of Bergson's ideas with the time perception. At last, we will point out how Bergson's ideas match the experimental evidence obtained in our experimental studies, as well as the contributions that Bergson's intuitions could give to this scientific work, in comparison to Aristotle's ideas.

Aristotle on Time

By trying to answer the question "What is time?" in *Physics* IV.10-14, Aristotle often mixes the definition of time with the perception of time. The Stagirite states that time is the "number of movement (or change) in respect to the before and after" (Aristotle, *Physics*, IV.xi, 220a) and although this statement seems independent from subjects with intellective souls, Aristotle will clarify that time is mind-dependent. Ricoeur highlighted hat Aristotle does not make any reference to the soul in his time definition, but at the stages of the definition he mentions the mind operations of perception, discrimination and comparison (Ricoeur, 1985). This means that time cannot exist in the absence of beings who perceive it. The faculty responsible for time perception is memory as Aristotle points out in his little treatise *Memory and Reminiscence* (Aristotle, *Memory and Reminiscence*, 449a-453b). We know that time has passed thanks to memory operations. In each step of his time definition, Aristotle mentions the role of memory implicitly (Ricoeur, 1985; 2004).

Aristotle argumentation to define time develops itself in three stages (for a comment on Aristotle thoughts about time see Coope, 2005; Hussey, 1983; Reis, 2007; Ricoeur, 1985; 2004; Soares, 2013). Following his predecessors, he starts by connecting time with movement or change. Plato stated that the succession of days and nights, months and years, which are the product of stars regular and cyclic movements that we observe when we look up the skies, is time. Unlike Plato, that found time in cosmos, Aristotle will discover time inside consciousness. Indeed, he declares that we perceive movement or change and time at the same time. Notwithstanding, that change or movement can be out of the subject or inside the subject, like a mental experience. “Even if were dark and we were conscious of no bodily sensations, but something were ‘going on’ in our minds, we should, from that very experience, recognize the passage of time” (Aristotle, *Physics*, IV, XI, 219a). However, movement or change is not identical to time because a change can be said to be slower or faster but not time. We say ‘faster’ when we see more change in lesser time, but time cannot measure itself. Besides that, time is equal everywhere and in everything, is not attached to any particular change. Thus, time is something of a movement. And time is something of a movement because it follows movement. Take the example above: you are in the dark, with no body feelings and a thought crosses your mind. You imagine little lambs jumping a fence. Something is ‘going on’ in your mind, you start by seeing the first lamb jumping the fence and finish by seeing the last lamb jumping that fence. You notice that time has elapsed when you follow the little lambs jumping the fence. A change is always associated with the thing that undergoes change. In this case, we perceive change when we accompany the thing-in-motion, the little lamb, moving from inside the fence to the outside the fence. This movement or change implies a travelled distance or as Aristotle called it, a magnitude (spatially extended). Therefore, the Stagirite says that movement follows magnitude, as well as time follows movement. As magnitude is continuous, so movement and time are. Additionally, the faculty that recognizes movement and magnitude is memory.

In the second part of his argumentation, Aristotle introduces the before and after relationship. To have a notion that some time has elapsed we have to distinguish two moments as different from each other and perceive a change between them. When we distinguish two moments, we divide something continuous and that continuity is not time, since time cannot measure itself, but change. As change follows magnitude, we divide change when we divide magnitude. Thinking about the little lamb, you see the movement of him jumping the fence and you know he travelled a distance from inside the fence to outside the fence. So you can mark the magnitude into two places, for instance, place one – the little lamb inside the fence -, place two – the little lamb outside the fence; and, thus, divide change. By correspondence, you can also mark two instants. The first instant, when you see ‘now’ the little lamb inside the fence and the second instant, when you see ‘now’ the little lamb outside the fence. If you recognize two instants as different (because firstly you recognize two places as different), you put them in an order. One instant succeeds the other, and that succession is what we call the before and after relationship. Of course, that relationship is only possible because memory saves the first instant in mind and adds it to the second instant, building an ordered succession of instants.

Nevertheless, how can we reconcile the vision that time is continuous and cannot be interrupted with the fact that we create parts in change by dividing it? The answer is that we can divide change without actually creating parts in it, if we divide it potentially. A potential division is a point where a change *can be* interrupted and *is* not, in fact, interrupted. It is the subject's activity that arbitrarily creates those potential divisions. It means that it is up to us to decide when we mark a 'now' or not. We create series of 'nows' or potential divisions by counting them.

Finally, we reach the last part of Aristotle's argumentation: time is a kind of a number, 'a number of movement'. By saying that time is a number, Aristotle means a countable number (the thing we attribute a number to), not the number by which we count (1, 2, 3). If we see ten little lambs jumping the fence, we mark an instant by each lamb jumping the fence. The succession of those lambs we marked as instants is time. However, the Greek philosopher admitted that in order to something be countable there must exist beings who can count. Analysing our time perception, we may say that ten instants have passed, corresponding each unit (the number by which we count, like 1) to a jumping lamb (a countable number). Our counting activity, the number by which we count, is needed to time perception. Then we determine quantitatively the movement we experienced. Although he tries to separate the definition of time from the perception of time he is unable to do it. Moreover, the perception of a first, a second and a third instant, as a perception of time, occurs thanks to memory, that saves the instants.

Aristotle's positions concerning time perception might be considered akin to the internal clock model and enlighten the interval length judgments task in the experimental protocol. This task, based on the presumption that we have an internal clock, implies that the subjects count time intervals and emit judgments about time passage, pointing a precise duration, quantitatively. In the same vein, we make also use of our memory skills to save the counted instants in our mind and to add them to the previous instant, producing a final answer. This cognitive process would in modern terms be said to depend upon working memory resources (Cowan, 2009). As requested by Aristotle's philosophy, memory and counting activity are features of time perception. Furthermore, Aristotle's model assumes that time perception is expressed in terms of quantities, considering interval length judgments, which was precisely the object of study in the experimental protocol.

Bergson on Time

Bergson does not separate time and time perception. For the French philosopher, the real time is indeed time perception and the real time is memory. He condemns our tries to represent something interior, time consciousness, by means of the exterior, the mathematical and physical time of science. This was the error of Kant's philosophy. By denouncing Kant's failures, Bergson designs a new model of consciousness, where he attributes three features to the immediate data of consciousness, and consequently, to time perception. Our inner time data are first qualities, secondly they are duration and thirdly they are freedom (Guerlac, 2006).

The interest in time studies dominated the end of the 19^{th} century. There was a belief brought up to the surface by the school of psychophysics and Fechner's followers that we could measure time sensations and transform them into quantities. According to Bergson, psychophysics falls down into a vicious circle because it departs from a wrong postulate, the equivalence between quality and quantity (for comments on Bergson and psychophysics see Guerlac, 2006 and Reis, 2015). By quantity, we mean how much, and we are talking about a degree, whereas by quality we mean how things feel to us, and this is a difference in kind, as the nuances of a colour. Bergson argued, in the first chapter of *Time and Free Will*, that the intensity of states of consciousness cannot be expressed in terms of quantities. The states of consciousness are divided into three branches, the feelings, the sensations and the efforts. Take the example of a sensation, the sensation of pain, which can vary in intensity from a state to another. We can feel more or less pain, from a moment to another. Imagine that you are ill, and your doctor asks you in scale from 1 to 10 how bad is your pain? You answer 8. When you give such an answer, you are merely objectifying your subjective states of consciousness. In reality, you went from certain body state that gave you specific corporal feelings to another body state that makes you feel different. However, the number does not depict the series of corporal changes that you have been through. What psychophysics does is to compare those stages that interpenetrate and mix together and attribute them a number. That is how qualities become quantities. The psychophysics mistake is having noticed a growing of a sensation relate it to a numerical sequence. If my pain today is worse than yesterday, I may say that I am experiencing the double of pain, but, in fact, I am treating two mind states as they were numerical quantities. Nevertheless, qualities cannot be measured because they are not quantities.

If time is a quality and not a quantity, what would Bergson say about Aristotle's definition of time perception? What happens when we are counting instants? Bergson argued, in the second chapter, that when we count time intervals, we are only spatializing time. To count little lambs jumping a fence is solely to insert units into an imagined space, to put each little lamb occupying a different position in space. Our intelligence is representing the experience with the aid of a number, which repeats itself. Then, we are thinking of time in terms of space, a homogenous milieu. This operation does not convey the real experience of time. The real time is not the time conceived by science. It is a succession of qualitative states that never repeat. The French philosopher named this heterogeneity duration and he would later identify it with memory (Bergson, 1889; Guerlac, 2006).

The concept of duration is better perceived if we take a look at *Matter and Memory* (Bergson, 1896; for a comment on Bergson's works *Time and Free Will* and *Matter and Memory* see Guerlac, 2006). Our mind is composed of images that we perceived and framed with the help of memory. Memory always accompanies perception. These images are stored as memory-images. Two fictions picture our mind: pure perception (pure matter or body) and pure memory (spirit or mind). Memory moves between the two realms, moving away or approaching the brain[6]. The present is a dimension that almost does not exist. Two directions compose the psychological experience of the present. One dilates towards the past, where recollections are recorded in our memory. The other contracts towards the future, where memory-images are selected to perform an action. The movements of selection and recollections are a multiplicity of qualitative states that

[6] Bergson conceives several types of memory, mainly pure memory (akin to episodic memory nowadays) and habit memory (equivalent to working memory today) (for a revision see Teixeira, 2012). He alludes to the image of an inverted cone to illustrate the idea that there are several plans or levels of consciousness or memory. In the top of the cone, we find pure memory (mind). In the end, we find pure perception (brain). Pure memory is never destroyed. When we face brain lesions, we observe the difficulty of memories to become present, to be actualized, but this is only the failure in the process of recognition (Deleuze, 1966).

never repeat. They are duration and so duration is memory (for comments on Bergson's time and memory see Bernet, 2005; Perri, 2014; Tucker, 2012).

Real time does not match with clock time. Bergson does not advocate a linear model of time. Time does not follow a sequence, past, present and future. Instead, these three dimensions mix together. When we notice that a time interval has elapsed, we do not mark two instants and order them. On the contrary, we feel that passage. Taking the example mentioned before: the sensation of time passage when you imagine little lambs jumping the fence. If someone asks you how much time has elapsed and you answer 30 seconds, you are answering according to the clock time but not according to the real time. To report the real time, we have to touch the individual's inner self to answer about the subjective feelings of time passage. At the same time, we notice that time intervals had elapsed, and we have subjective feelings that time has run slower or faster. The process that leads to such an answer is not linear. Picking the example of little lambs jumping the fence, when you noticed a time elapsed during that observation you stored that present feeling in your memory. After that, memories of past feelings came to your mind (from pure memory), for example about other times when you imagined little lambs jumping the fence and felt that passage, and you have to enter a process of selection of these memory-images to discover which memory-images feelings resemble better the recent memory-image feeling recollected. Only then can you produce a judgment of time passage.

Bergson's positions regarding time perception hopefully enlighten and clarify the findings obtained with the questionnaire about the subjective passage of time in the experimental protocol. Participants had to answer 6 questions concerning the experience of the speed of time and rate them within a five-point rating scale, ranging from very slow (-2) to very fast (+2). Contrary to the previous task on interval length judgments, this experiment is highly subjective, since the subject reports his subjective feelings about time passage. He does not measure his time sensations. However, the results of the experiment are analysed from an objective point of view, and the conclusions are achieved not from the first person perspective but from the third person perspective. Despite this, subjective passage of time judgments concern feelings about time passage and, as Bergson proposes, express time perception in terms of qualities.

The results obtained with the first task on interval length judgments substantially differ from the results of the second task on the subjective passage of time judgments, when at the first sight we would expect them to be coincident. The reason might be because in the latter experimental protocol the level of subjectivity is deepened. In other words, we stay closer to the inner experience of the individual, to the immediate data of consciousness. In fact, the participant talks to us from the first person point of view. On the contrary, expressing our inner experience by a mathematical symbol is to keep us away from the feelings about time. Just remember Thomas Nagel's famous article "What is like to be like a bat" (Nagel, 1974). Even if we held the whole scientific knowledge about the nervous system of a bat, we would never know what is to be like a bat, to have bat experiences or feelings, unless we were bats. In the task on the subjective passage of time judgments, we specifically addressed our inquiry to the inner feelings of the individual.

In view of the above, we reach finally the last chapter of *Time and Free Will*, where Bergson is ready to present his main objection against Kant. Having proved that consciousness is quality and duration, he proceeded to demonstrate that free acts are the product of the organization of memory states. There are the operations of memory that turn our free acts possible. How does this happen? By anticipating the future, our mind has available memory-images from past experiences that can be selected in order to perform an action. There is a zone of indeterminacy that enables our voluntary action. Take the following example. Imagine that you are going to buy bananas. Before you do anything, your mind retrieves memory-images of you buying bananas (in the past) and progressively eliminates those that do not matter to you (expensive stores, and so on) until it reaches the ideal one. The channel of your memories goes progressively shrinking towards the future. The hesitation is a time factor, designed by the survival of the past into the present, that enables free acts. Free actions cannot be seen as the result of abstract choices. If we do so we are placing freedom outside time. That was Kant's mistake. In other words, having connected time with memory, Bergson wants to evaluate the influence of *durée* (time-memory) upon freedom, a realm where we have to make choices. In a similar vein, it was experimentally evaluated the influence of memory on a case of decision-making, namely a delay-discounting task, using an intertemporal choices questionnaire. In this task, participants were presented a list of questions, where they had to systematically choose between an immediate monetary reward and a larger but delayed monetary reward. Nonetheless, results obtained showed no significant differences between MCI group and control group regarding temporal preferences, that is, the trend of choices of MCI patients is similar to the healthy aged-matched controls.

Bergson against Bergson

Despite Bergson's considerations about the role of science and philosophy, if we take a closer look at our assumptions about the linkage between subjective passage of time judgments and Bergson's philosophy, two questions, at least, may arise. In first place, although we asked for the feelings of time passage, we were conducting a quantitative analysis and using a scientific methodology to reach scientific conclusions. So does not Bergson state that scientific method cannot give us access to the inner experience? This problem can be solved if we think what Bergson referred in *Matter and Memory* regarding the existence of rhythms of duration:

> In reality, there is not one unique rhythm of duration; one can imagine many different rhythms, which, slower or faster, would measure the degree of tension or relaxation of consciousness, and, in that way, would fix their respective places in the series of beings. This representation of durations of unequal elasticity is perhaps painful for our minds to entertain, because our minds have contracted the useful habit of substituting a homogeneous and independent time for the real duration experienced by consciousness.
>
> [Bergson 1896]

When we talk about rhythms of duration, memory is called into play. It is the role of memory to prolong the past into the present, selecting memory-images to perform and action, or to turn perceptions into memories, going from the present to the past. Thanks to memory, the three dimensions of time, present, past and future interpenetrate and mix in a single way. However, as we can see in the quotation above, Bergson refers that "different rhythms would fix their places in the series of beings", showing us the ontological dimension of the rhythms of duration. Indeed, in this quotation, Bergson allows us to look at patterns of behaviour. In spite of being focused on the inner experience of the individual, *Time and Free Will* opens the gates to *Matter and Memory* when he tells us what is conscious and what is not. A look from the third person's view is introduced and deepened in *Matter and Memory* when subjectivity and objectivity, mind and brain, are reconciled. Indeed, if we have brain injuries, difficulties in memory-images to be actualized become apparent and as memory is duration we will have another rhythm of duration. According to Bergson's ideas, we can classify groups of beings by their rhythms of duration. Like John Searle has pointed out, the first's person point of view is impossible to be achieved by the third's person point of view (Searle, 1994). Nevertheless, Bergson put objectivity close to subjectivity when he saw how brain and mind could interact. The task on subjective passage of time judgments actually enables two experiences, the experience of a first person when the participant rates his own experience of time passage and the experience of a third person, when we observe patterns of behaviour in the participant's global responses, which are a reflex of the process of his own memories.

In second place, closely connected to the first problem, we may wonder about the importance of the subjective passage of time judgments to science. Science occupies itself with the objective, the immobile, the external world and the external self, the functioning of the body, and does not pay attention to the soul business or the subjective states of mind. The answer to this problem may come from the Bergson's separation between an external self and an internal self. Bergson distinguishes between an external or social self, identified with our adaptations to the external world and known by science and an internal self, related to the inner states of consciousness and the uniqueness of our experience and beyond the reach of science. Although inner self is far from the realm of science, we may come close to an understanding of it if we query for the affective experiences of an individual. The experimental protocol allowed us to investigate the impact of memory changes upon the affective experience of time awareness in patients with MCI, by questioning feelings of time passage and assessing subjective life experiences like routine. In fact, as recent research has been suggesting, the inner experience of time does not restrain itself to cognitive elements but incorporates visceral feelings (Wittmann, 2009). The results obtained with the subjective passage of time judgements emphasise the importance to investigate the relation of cognitive systems with affective elements and to instigate science to look into human body traces of these elements, albeit our time experiences remain private. This means that patients with MCI might experience time running slower, in spite of the experience of slowness being unique to each one.

Concluding Remarks

The experiments performed showed that persons with memory deficits, like patients with MCI, have alterations in experiencing time. In a quantitative task, participants did not count time intervals differently from healthy controls. However, in a qualitative assignment, they reported slower speed of time passage.

Time perception was one of the chief psychological themes at the end of the 19th century. It was a century dominated by discussions in the field of psychophysics. There was a belief that time perception could be measured and, therefore, the first attempts to quantify time perception in order to explain time distortions were made. Some philosophers and psychologists gave the first steps towards a more qualitative vision of time perception, like James and Guyau (Guyau, 1890; James, 1890). However, even James, with his specious present and Guyau, with his refusal of spatialized time, were unable to stand for a qualitative vision of time perception. It was Bergson who defended such a view and who suggested the linkage of time perception with memory. According to Heidegger, Bergson's philosophy contrasts with Aristotle's thoughts about time (Heidegger, 1925-26). That is the reason why we chose to oppose two philosophical models about time perception, one from Aristotle, and the other from Bergson. Both models bet that time perception is based on memory. However, they differ in one important aspect. For Aristotle, we experience time by counting time intervals, whereas for Bergson time experience consists of our feelings. Aristotle's model is quantitative and Bergson's model is qualitative.

The neuro-scientific work that we performed lead us to propose that, at the end, Aristotle and Bergson focused on two different kinds of conscious experience of time perception. One, Aristotelian, concerning time estimation abilities, and the other, Bergsonian, referring to feelings of time passage. These two time experiences are testable with different experimental protocols and probably rely on distinctive anatomical bases. On the other hand, both philosophers help us to frame and establish relations between the two time experiences and the different types of memory. Bergson associate the feelings of time passage with memory processes related to what is now considered episodic memory, whereas Aristotle posits a link between time estimation abilities and cognitive processes akin to what is presently known as working memory.

Most importantly, these conclusions direct us to speculate on the possible generalization of the philosophical insights to the experimental tasks involving time perception in MCI patients and in patients with memory impairment in general. Bergson's philosophy points to a possible linkage between the feelings of time passage and episodic memory impairment, suggesting that we should preferentially look to the qualitative aspects or the experience of time passage in patients with this type of memory dysfunction. On the other hand, time estimate and production abilities would be an interesting skill to study in patients with isolated working memory impairments, according to Aristotle's thoughts on the capability to count time intervals or quantities. Finally, the experimental results obtained with the delay-discounting task did not confirm Bergson's suggestion that the experience of time impacts upon dimensions of our life related to decision-making. It must be recognized that only one type of decision-making was experimentally assessed which may not capture Bergson's intuitions. To be entirely fair with Bergson's ideas, the French philosopher speaks about free acts and this concept, although implicating choices, is different from decision-making. Hence, further works are needed to explore the impact of time experience upon free acts, conceivably by using other type of decision-making experimental task that would better mimic Bergson's freedom concept.

FINAL DISCUSSION

Introduction

Philosophical ideas have been contributing to the theoretical foundations of psychological and neuro-scientific studies on time (Debiec, 2014). For some thinkers, like Newton and Einstein, the true time is the time of physics or objective time, while others focus on subjective time or the time of consciousness. Some philosophers, such as Aristotle, admitted a relation between subjective time and objective time, whereas others, such as Bergson, posited that subjective time is the only real time. To understand the temporal processes of subjective time it would be helpful, not only to comprehend consciousness, but also to explore concepts such as free will and self (Bergson, 1889).

Through psychological and neuro-scientific experimental protocols, time perception in patients with MCI can be assessed in several different ways, especially if we take into account temporal aspects such as temporal order, time perspective and time duration. Evidences that temporal order is impaired in MCI patients have already been reported (Gillis et al., 2013). As far as we know, there is no study available about time perspective in MCI patients. The study of duration in MCI, assessed through the time experiences of interval length judgments and passage of time judgments, is of crucial importance due to the implications that the experience of duration may carry out upon these patients' lives. Similar to Aristotle's thoughts, interval length judgments establish a relation between subjective time or the subject's counting activity and objective, real measured time. In contrast, like Bergson envisioned, passage of time judgments only evaluate subjective time or how people feel time without any reference to real measured time.

Overall, our studies showed that MCI patients present an unimpaired internal clock and no significant differences in intertemporal decision-making when compared to the healthy controls. However, regarding the feelings of time passage, MCI patients differ significantly from the age-matched control group. Presumably, the main explanation for this occurrence is that interval length judgments and passage of time judgements, although reflecting duration paradigms, are different time experiences. Moreover, interval length judgements and passage of time judgments, as assessed in the present experimental protocols, rely upon different time scales (the interval length judgements range from seconds to minutes whereas the passage of time judgments encompass days, months, years) and this could be another reason for the differences observed.

A suggestion to future work would be to apply a passage of time judgements task to MCI or AD patients using shorter intervals ('How fast did the previous 5 min pass for you?'). This experiment, created in a more real life experienced context, rather than in an artificial one (like time questionnaire items employed), might elucidate the impact of memory problems upon this type of task. Thus, it will endorse or not Bergson's speculation that time qualitative data embrace memory, now not only in longer time scales but also in shorter ones.

Interval Length Judgements

Regarding interval time judgements, MCI patients maintain the tendency to overestimate and underproduce time intervals common to healthy controls, thus not deviating from the normal aging process. At least two previous studies showed an acceleration of time perception with aging. One study with 86 healthy participants, aged 15-90 years old, using tasks of prospectively estimating and producing empty-time intervals of 7 s, 32 s and 58 s revealed a faster internal clock with aging (Coelho et al., 2004). These results were attributed to worse capabilities of the elders in attention and working memory domains. Another investigation submitted a group of 13 young adults and a group of 12 elderly participants to a task of prospectively reproducing a short interval of 10 s (Carrasco, Bernal & Redolat, 2001). Once again the results showed a faster internal clock in older participants and it was hypothesized to be due to aged-related cognitive changes in perceptual, attention, mnemonic and decision-making processes. The results found in our experimental work do not support that memory decline, particular of episodic memory, might be implicated in the internal clock changes detected by the studies mentioned above in the normal aging process (Carrasco, Bernal & Redolat, 2001; Coelho et al., 2004). Nevertheless, it must be referred that the present work did not control for the strategies used to do the internal counting, likely to recruit different neural networks, and this is a limitation that should be overcome in further work.

If patients with MCI had an impaired internal clock, this trend would probably be exacerbated at later stages of cognitive decline, such AD. As far as we know, there are at least two studies that evaluated time perception in AD patients, using time estimation and production tasks. A study using a prospective time estimation task on short filled intervals, e.g. in between 10 s and 60 s, found that AD patients are less accurate (deviate more from true time) and present greater variability (some AD participants significantly overestimate time while others significantly underestimate time) than controls (Rueda & Schmitter-Edgecombe, 2009). However, these results were not attributed to episodic memory impairments specific to AD, since there were no differences in the AD group verbal estimates between shorter intervals (<30 s) and longer intervals (>30 s). Besides that, if memory impairments had an impact on time perception, the tendency would be to overestimate time intervals and this is not verified (Nichelli, 1993; 1996). Another study comparing AD participants with age-matched controls employed a time production task of three short empty time intervals (5 s, 10 s and 25 s). It revealed that AD participants present deficits both in accuracy and precision of time interval judgements, meaning that they exhibited a greater variability in time judgements and deviate significantly from true time, respectively (Carrasco, Guillem & Redolat, 2000). Again, if episodic memory impairment had an impact on time judgements, the tendency would be to underproduce time intervals and this was not observed (Nichelli, 1993; 1996). Noteworthy, AD participants performed an empty time interval judgement task, meaning that their attention was not deviated by a concurrent non-temporal task. The failure to maintain attention during the production task may be the explanation for the results achieved since the allocation of few attentional resources to time monitoring could induce a greater variability and inaccuracy in temporal judgements (Brown, 1997). Thus, results from both studies in AD patients did not support an important role for episodic memory on time estimation abilities.

Taken together, the studies on interval length judgements on MCI patients and AD patients cast doubts on the fundamental role of episodic memory for this type of judgements, at least on a time scale ranging from seconds to minutes. This suggestion is supported by neuroimaging (Wittmann & Paulus, 2008; Lewis & Miall, 2003; Radua et al., 2014; Ortuño et al., 2011; Hinton & Meck, 2004), neuropharmacology (Meck, 1996; Mattell & Meck, 2004) and neuropsychology (Coull et al., 2004; Meck, 2005) studies that showed the activation of cortico-striatal-thalamic circuits during time estimation tasks, attributing to the hippocampus, which is the primary area of atrophy in MCI and AD patients, a modulatory but not critical role in time estimation abilities (Meck, Church & Matell, 2013; Yin & Troger, 2011).

Studies in patients with other memory disorders, such as amnestic patients, were not conclusive regarding the effect of memory abilities on time perception. Some studies attributed time estimation alterations to memory dysfunction (Palombo, Keane & Verfaellie, 2016), while others did not (Shaw & Aggleton, 1994). A classic and elusive case documented in the history of memory and time perception was H.M. patient, who after hippocampal ablation was found impaired judging temporal intervals above 20 s, although considered normal in estimating shorter intervals (Olton, Meck & Church, 1987; Richards, 1973). Probably, time estimation impairments in patients with memory disorders, particularly for longer intervals, such as those observed in H.M. case, are not caused by deficits in encoding and in retrieving temporal information. On the contrary, a gap in the maintenance of task instructions in short-term memory and attentional failures might be involved (Meck, 2005). This is specially the case if we take into account that hippocampus may play a role in attentional mechanisms (Yin & Troger, 2011; Buhusi & Meck, 2002; Buhusi et al., 2003). These findings underline the need of further work to clarify what is exactly the role of memory in timing abilities, paying attention to the possible biases that may interfere with this cognitive process. Those studies would eventually confirm Aristotle's suggestion of a major role of working-memory like cognitive processes in time experience.

Another interesting future avenue to explore is how patients with MCI perform on time perception for longer intervals (hours, days, months). The biological clock on a timescale of hours (circadian rhythms) rely on the suprachiasmatic nucleus (SNC), a group of cells located in the hypothalamus, related to the sleep-wake cycles (Gillette, 1986). There is evidence of sleep disturbances in MCI patients associated with altered circadian clocks or rhythms (Cochrane, Robertson & Coogan, 2012; Ortiz-Tudela et al., 2014; da Silva, 2015) and therefore MCI patients may exhibit an impairment in time estimation abilities in the range of hours. However, it is important to recognize that potential biases may interfere with the investigation on circadian timing in MCI patients. First, when time estimates are above one hour, there is always the risk that the experiences accumulated by the participants during the time estimation task may be used as temporal cues to answer the estimation query. Second, it must be highlighted that it is not possible to keep the focus of time awareness during one hour time interval continuously (Wackermann, 2007; Wittmann, 2011; Zakay & Block, 1997).

Notwithstanding, our conclusions point out a relation between episodic memory and qualitative data of a longer temporal projection. Recently, Wittmann (Wittmann, 2011; 2015), based on the work of Shau Gallangher (Gallangher, 2000) on self concepts, proposed a model of temporal integration that encompasses a notion of self. For Wittmann, a temporal experience ranging from seconds to minutes is a conscious experience where, thanks to working memory operations, we are able to maintain mental representations in an active state for a certain period of time. That mental state, conjoined with visceral and emotional body states (Craig, 2009; Pollatos, Laubrock & Wittmann, 2014; Wittmann & Wassenhove, 2009) gives a unified sense of presence, close to the notion of a narrative self. This sense of continuity over time contrasts with the time experience of a few seconds, which is assigned to the notion, advanced by Gallangher, of a minimal self. The minimal self is certainly experienced by the individual himself but it is unextended in time. To complete this proposal of corresponding temporal levels to self levels, we suggest a third self, related with the cognitive experience and the affective sensation of a longer time scale of hours, days, weeks, months. That would be a deeper self that, thanks to episodic memory operations, would enable us to recall ourselves, qualitatively and not quantitatively, in a longer distant past. Strictly speaking, the kind of inner self that Bergson envisaged, more subjective given the larger timescale (Pöppel & Yao, 2014) and that surely allows us to engage in mental time travel.

A recent line of investigation has been aiming to explain the lack of impairments in estimation abilities in patients with brain lesions, likely to damage temporal processes, on the basis of the ideas of redundancy and degeneracy of the timing systems. Redundancy supposes that, when one part of the brain is injured, multiple copies of the same timing mechanism may be displayed in the opposite hemisphere, contributing to recovery. In contrast, the degeneracy principle posits that time functions are distributed across structurally different networks (Lewis & Meck, 2012) and that within a range of neural timing architectures and hierarchies, a failure of one system or mechanism will be compensated by another one (Lewis & Meck, 2012; Wiener, Matell & Costell, 2011; Merchant, Harrington & Meck, 2013). Notwithstanding, these hypotheses seem more plausible in subjects with circumscribed brain lesions, such as subjects with specific basal ganglia lesions (Coslett, Wiener & Chatterjee, 2010), and not in patients with neurodegenerative disorders, such MCI or AD, that face impairments in multiple neural systems.

Passage of Time Judgements

The greatest achievement of this work was to discover that MCI patients have an altered sense of time passage, that is, they feel the time passing slower when compared to the age-matched controls. This alteration was not associated with changes in interval length judgements, suggesting that passage of time judgments represent a distinct time experience, encompassing a different scale. Two important factors seem to contribute to the altered sense of time passage in patients with MCI, the presence of memory deficits and feeling life more like a routine. However, it is not entirely clear which of these factors is likely to be determinant for the slowing of the speed of time judgement, or if they are related.

It is important to consider how the speed of time is felt in the normal aging process. Three studies assessed the speed of time in normal aging, applying the same 10-item questionnaire that we used (Friedman & Janseen, 2010; Janseen, Haka & Friedman, 2013; Wittmann & Lehnhoff, 2005). All studies revealed that both younger participants and older participants felt the time passing quickly, with no significant differences between the two, except on the item 10 (‘How fast did the last 10 years pass to you?’), where the older group reported the time passing quicker than the younger group. However, this result was attributed to feelings of time pressure, as well as to the common belief shared by all participants that time passes quicker as we get older, and not to possible decline of cognitive abilities in aging. Remarkably, our work showed that MCI patients perceive time passing slower than controls, exhibiting an inverted tendency regarding normal aging. The observation that MCI patients differ specifically at items of the time questionnaire related to the recent past (item 3, ‘How long does the past week pass to you?’ and item 4, ‘How long does the past month pass to you?’) reinforces the idea that memory influences the passage of time judgements. These items refer to remember duration, covering memories of past intervals, and not to experience duration (item 1) or imagined duration (item 2) or even memories of a distant past (items 5, 6) (Wittmann & Lehnhoff, 2005). The last two items may suffer the interference of other variables or cognitive biases, such the conviction that time passes rapidly when we get older (Friedman & Janseen, 2010; Janseen, Haka & Friedman, 2013). To this regard, the reported feelings of slower time passage in the recent past by patients with MCI may not be accounted for by the widespread assumption that time accelerates with age (Wearden, 2015).

Interestingly, we observed that MCI patients described their life as being more like a routine compared to the healthy controls. It is certainly important to look at interactions between the feelings of routine and cognitive and emotional factors of the participants. Routine activities associated with low levels of attention and negative hedonic value (depression) induce an impression of slow passage of time (Agarwal & Pati, 2010; Avni-Babad & Ritov, 2003; Droit-Volet & Wearden, 2016; Sucala, Scheckner & David, 2010; Wearden, 2005; Wearden, 2015). Interestingly, according to our results, neither the feelings of routine correlate significantly with executive functions nor with anxiety and depressive symptoms, despite the fact that MCI patients exhibited alterations in these domains. On the contrary, the only cognitive domain that the feeling of routine correlated with significantly was memory. This may point, as was referred before, to abandonment of complex daily activities by MCI patients (Pedrosa et al., 2010), but also to their inability to register novel events (Belleville, Ménard & Lepage, 2011), creating the false impression that life remains the same. As previous studies showed, there is a negative correlation between routine and memory because when routine increases, the amount of information attributed decreases (Avni-Babad & Ritov, 2003). In the same vein, a lower information processing load originates a sensation of slower passage of time (Wearden, 2005; Wearden, 2015). Thus, it is plausible that lower information load due to memory loss in MCI patients may increase the feelings of routine contributing to the feelings of slower time passage. At last, previous studies suggested that routine may influence time estimation (Avnid-Babad & Ritov, 2003; Agarwal & Pati, 2010), but this is not verified in the present study, where no differences in interval length judgements between the patients with MCI and healthy controls were observed. Taking together, the present evidence suggests that the feelings of routine in MCI patients may be a consequence of their memory impairments.

Intertemporal Choices

Significant differences in delay discounting were not detected between MCI patients and controls, accompanying the absence of significant differences in interval length judgements. The observed differences in the passage of time judgements between the two groups thus did not seem to impact on decision making, as evaluated by the intertemporal choices questionnaire.

It must be noted that only a specific type of decision-making was assessed in this protocol and that a possible relation between passage of time judgements and decision-making remains to be proven. Following Bergson's ideas that time-memory is necessary for free acts, we may speculate that another type of decision-making task with a different experimental protocol could reveal a connexion between decision-making and passage of time judgements and, ultimately, their dependence on memory abilities. The absence of alterations in MCI patients using the present experimental protocol might be due to the fact that they had at their disposal all the elements they needed to decide, since the intertemporal task involves the choice between two options that are patent. Previous studies (Zamarian, Weiss & Delazer, 2010) revealed that in tasks where information is missing, like decisions under ambiguity, MCI patients exhibit impairments in decision-making. We may wonder whether the difficulties that MCI patients show in real-life decision-making, where it is necessary to recruit several past memories to have all the elements at stake to decide, are caused by deficits in the retrieval of information. Following Bergson's philosophy, in patients with memory disorders it would be difficult for some memories to be updated, and this might constrain the process of memories selection to reach a decision. Lesser elements at our disposal will adversely influence the decision taken.

Final Remarks

In Primo Levi tale's "Time Checkmated", people, after taking a drug that induces an altered sense of time, began to project themselves into life differently (Levi, 1986). Likewise, we may wonder that feeling of time passing slower or faster will affect our ability to mental travel, leading us to project ourselves in the past or in the future in unusual ways. However, this is something to explore in further works.

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