



UNIVERSITÀ  
DEGLI STUDI  
DI PADOVA

Università degli Studi di Padova  
Dipartimento di Psicologia Generale

SCUOLA DI DOTTORATO DI RICERCA IN SCIENZA PSICOLOGICHE  
INDIRIZZO PSICOBIOLOGIA  
CICLO XXIV

**TIME PERCEPTION AND PROSPECTIVE MEMORY  
IN TRAUMATIC BRAIN INJURY PATIENTS**

**Direttore della Scuola:** Ch.ma Prof.ssa Clara Casco

**Coordinatore d'indirizzo:** Ch.mo Prof. Alessandro Angrilli

**Supervisore:** Ch.ma Prof. ssa Franca Stablum

**Dottoranda:** Giovanna Mioni



## INDEX

<b>INTRODUCTION</b>	1
<b>CHAPTER 1: TIME PERCEPTION</b>	1
<b>1.1 Introduction</b>	3
<b>1.2 Models of time perception</b>	5
<b>1.3 Factors that influence time perception</b>	12
<b>1.4 Methods to investigate time perception</b>	18
<b>1.5 High cognitive factors that influence time perception</b>	25
<b>1.6 Neuropsychology of time perception</b>	28
<b>1.7 Time perception in brain injury patients</b>	32
<b>1.8 Study 1</b>	38
1.8.1 Introduction	38
1.8.2 Materials and methods	40
1.8.2.1 Participants	40
1.8.2.2 Procedure	42
1.8.2.3 Temporal task	42
1.8.2.4 Executive functions tasks	43
1.8.3 Result	45
1.8.3.1 Temporal tasks	45
1.8.3.2 Executive functions tasks	47
1.8.3.3 Correlations between time perception, attention and working memory	48
1.8.4 Discussion	49
<b>1.9 Study 2</b>	53
1.9.1 Introduction	53
1.9.2 Materials and methods	55
1.9.2.1 Participants	55
1.9.2.2 Procedure	57
1.9.2.3 Temporal tasks	57
1.9.2.4 Neuropsychological evaluation	59
1.9.3 Results	60

1.9.3.1 Statistical analysis	60
1.9.3.2 Temporal tasks	61
1.9.3.3 Neuropsychological assessment	66
1.9.3.4 Correlation between temporal tasks and neuropsychological tasks	67
1.9.3.5 Correlation between temporal tasks	69
1.9.4 Discussion	70
<b>1.10 General discussion</b>	<b>75</b>
<b>CHAPTER 2: PROSPECTIVE MEMORY</b>	<b>78</b>
<b>2.1 Introduction</b>	<b>78</b>
<b>2.2 Models and theories of prospective memory</b>	<b>80</b>
<b>2.3 Processes involved in prospective memory performance</b>	<b>85</b>
<b>2.4 Factors that influence prospective memory</b>	<b>88</b>
<b>2.5 Monitoring behaviour in prospective memory</b>	<b>91</b>
2.5.1 Monitoring behaviour in time-based prospective memory	91
2.5.2 Monitoring behaviour in event-based prospective memory	96
<b>2.6 High cognitive abilities involved on prospective memory performance</b>	<b>98</b>
<b>2.7 Neuropsychology of prospective memory</b>	<b>100</b>
<b>2.8 Prospective memory in traumatic brain injury patients</b>	<b>102</b>
<b>2.9 Study 3</b>	<b>111</b>
2.9.1 Introduction	111
2.9.2 Materials and methods	114
2.9.2.1 Participants	114
2.9.2.2 Procedure	117
2.9.2.3 Time-based prospective memory task	117
2.9.2.4 Time perception task	118
2.9.2.5 Executive functions tasks	119
2.9.3 Results	119
2.9.3.1 Time-based prospective memory	119
2.9.3.2 Time perception task	121

2.9.3.3 Executive functions	122
2.9.3.4 Correlation analysis	122
2.9.4 Discussion	126
2.9.4.1 A comprehensive model for monitoring behaviour in time-based prospective memory	133
<b>2.10 Virtual task to investigate prospective memory</b>	137
<b>2.11 Prospective memory' virtual tasks and TBI</b>	138
<b>2.12 The Virtual Week: Characteristics and assessment in clinical population</b>	143
<b>2.13 Translation and adaptation to the Italian population</b>	148
<b>2.14 Study 4</b>	150
2.14.1 Introduction	150
2.14.2 Materials and methods	152
2.14.2.1 Participants	152
2.14.2.2 Procedure	154
2.14.2.3 Prospective memory task	155
2.14.2.4 Executive functions tasks	156
2.14.3 Results	157
2.14.3.1 Prospective memory task	157
2.14.3.2 Executive functions	160
2.14.3.3 Correlation analysis between PM and executive functions	161
2.14.3.4 Correlations between prospective memory, clinical features and neuropsychological tasks in TBI patients	162
2.14.4 Discussion	164
<b>2.15 General discussion</b>	165
<b>GENERAL CONCLUSION AND FUTURE DIRECTIONS</b>	169
<b>REFERENCES</b>	173

## CHAPTER 1

### TIME PERCEPTION

#### 1.1 Introduction

Time is a key factor to perform most of everyday activities and the interest to understand how subjects perceive time is still an engaging question (Block, Zakay, & Hancock, 1998). Good temporal skills are essential for normal social functioning, such as crossing a busy street, preparing a meal or organizing the daily activities. Prior research indicates that neurologically normal adults have efficient temporal abilities (Rao, Mayer, & Harrington, 2001) and that attention and working memory processes play an important role in the process of accurately estimate the passage of time (Block, 1990; Block & Zakay, 1996; Perbal, Droit-Volet, Isingrini, & Pouthas, 2002; Baudouin, Vanneste, Isingrini, & Pouthas, 2006a; Baudouin, Vanneste, Pouthas, & Isingrini, 2006b). Despite the fact that attention and working memory deficits are well documented in traumatic brain injury (TBI) patients (Azouvi, 2000; Leclercq, Couillet, Azouvi, Marlier, Martin, Strypstein, & Rousseaux, 2000; Boelen, Spikman, Rietveld, & Fasotti, 2009; Stuss, 2011) there has been little work investigating time perception following TBI. This is an important area of study as an impaired sense of time could affect the daily adaptive functioning of patients recovering from TBI. For example, an inability to accurately estimate the passage of time could interfere with time management abilities or lead to problems in the organization of daily life (Bauer, 2001).

Inaccurate and variable duration judgments have been reported in frontal patients and it has been associated to the involvement of the frontal lobes in working memory and attention processes (Nichelli, Clark, Hollnagel, Grafman, 1995; Binkofski & Block;

1996; Mangels, Ivry, & Shimizu, 1998; Casini & Ivry, 1999; Mimura, Kinsbourne, & O'Connor; 2000). Based on the studies conducted with frontal lobe patients, one can suggest that patients with TBI will probably exhibit impaired duration judgments since they generally show frontal lobe dysfunction (Azouvi, 2000; Leclercq et al., 2000) associated with deficits in attention and working memory. However, only four studies have been conducted so far, to investigate time perception in TBI patients (Meyers & Levin, 1992; Perbal, Couillet, Azouzi, & Pouthas, 2003; Schmitter-Edgecombe & Rueda, 2008; Anderson & Schmitter-Edgecombe, 2011). Durations ranging from 4 s to 60 s were employed with time reproduction, time production and verbal estimation tasks. The results reported lower accuracy and higher temporal variability in TBI patients compare to controls. None of the previous studies employed time discrimination task, which was widely used in studies with frontal lobe patients (Nichelli et al., 1995; Harrington, Haaland, & Knight, 1998a; Mangels et al., 1998; Casini & Ivry, 1999; Rubia & Smith, 2004; Picton, Stuss, Shallice, Alexander, & Gillingham, 2006). Testing time perception with a time discrimination task may give additional information about temporal abilities in TBI patients, in particular with range of durations not previously tested (above and below 1 s).

In this session I review the main theories and methodologies on time perception, moreover I will present two studies conducted with TBI patients to investigate their temporal abilities. Participants also performed attentional, working memory and executive functions tasks to investigate the involvement of these cognitive functions on time perception. In the first study TBI patients and controls performed a time discrimination task with standard durations of 500 ms and 1300 ms. In the second study

we used three temporal task: time reproduction, time production and time discrimination tasks with brief (.5, 1 and 1.5 s) and long durations (4, 9 and 14 s).

## **1.2 Models of time perception**

Time dimension is always embedded in any human experience and is an inseparable part of it. Studying time perception has always been complex, despite the importance of adequate temporal abilities no physical sense or organ is known by which time is directly perceived. It seems that time perception is a product of cognitive functioning and that can be understood as a manifestation of temporal information processes (Zakay, 1990). Researches, since the emergence of experimental psychology, have been trying to understand the secrets of cognitive processes responsible of sense of time but “time, is a slippery entity, sensitive to the condition under which it is measured” (Zakay, 1990, pp. 59).

For examples, in a situation where a person is relaxing on a beautiful beach, not having any deadline or scheduled meeting, time is not an important issue. If we asked to this person how long he or she has been on that beach, the duration that was felt is much shorter than the objective time that elapsed since coming to the beach. In a different situation in which a person is waiting for an important call, but is not sure whether or not the call will arrive; in this situation the person waiting will look again and again the watch, and will probably discover that the objective time did not advance much since the last check. The discrepancy between the two situations indicates that duration judgments in each case may rely on different cognitive processes. Although, in the first situation *retrospective duration judgment* processes were mainly involved, in the second situation *prospective duration judgment* processes were mainly involved (Block &



Zakay, 2006). This distinction relies on different cognitive processes that are involved in retrospective and prospective duration judgments. While retrospective duration judgments are inferred on the information retrieved from memory (Block, 1992), prospective duration judgments reflected the amount of attentional resources allocated in the duration judgment (Zakay, 1998). This work is conducted within the prospective memory framework<sup>1</sup>.

Since the first interest on temporal abilities hundreds of articles have been written and different models have been proposed. The first important theoretical distinction is between models that referred or not to a central clock (Grondin 2010). In fact, some authors have argued that there is no need to refer to a central clock for describing timing behaviour and described time perceptions in terms of cognitive mechanisms, without referring to the idea of central internal clock (Block, 1990, 2003; Buonomano, 2007). Support comes also from the field of visual perception that have lead to the development of modality specific perspective. Such a modality-specific perspective provides a potential explanation to why there are so many differences between sensory modalities when time intervals are to be discriminated or categorized (Grondin, 1993; Grondin, Roussel, Gamache, Roy, & Ouellet, 2005). The sensitivity to time is much higher (less variability) when the durations are presented with auditory rather than visual modality (Grondin, 2003), moreover sensitivity to time is much lower when discriminating intervals marker by brief sensory signals of different modalities (visual and auditory) rather than when are presented within the same modalities (either auditory or visual) (Grondin et al., 2005).

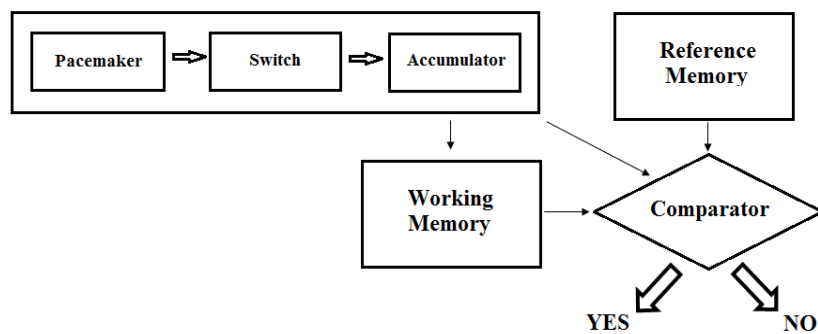
---

<sup>1</sup> See Block & Zakay, 1997, 2006; Grondin, 2010 for more extensive review on retrospective duration judgments.

On the other hand a longer tradition refers to a central mechanism as responsible for the estimation of time. Within theories and models that have hypothesised the presence of a central clock mechanism an additional distinction has to be made between two main perspectives: the pacemaker-counter process versus the oscillator process (Grondin, 2010). In the latter case, temporal control is usually reported to be based on a dynamic, nonlinear system (i.e. Dynamic Attending Theory, DAT; Jones & Boltz, 1989; Jones, 2006), in contrast with the linear perspective of a pacemaker-counter device that is most often embedded within an information-processing perspective (Treisman, 1963; Rammsayer & Ulrich, 2001). The latest perspective, which assumed that temporal judgments are based on a single internal clock, is the predominant perspective on the field of time perception, data collected in this study will be analysed according to this perspective.

One of the most influential models to explain time perception was proposed by Treisman (1963). The model postulated a single internal clock, the pacemaker that produces a regular series of pulses the rate of which varies as a function of arousal. A counter records the number of pulses in a pathway and the total is transferred into a store and into a comparator mechanism. The Scalar Expectancy Theory (SET; Gibbon, Church, & Meck, 1984; Gibbon, Malapani, Dale, & Gallister, 1997; Figure 1.1) extended Treisman's (1963) findings investigating time-related behaviour in animals like pigeons and rats during relatively short time durations and provided an excellent model widely used in time perception (Gibbon et al., 1984; Block & Zakay, 1996; Mangels & Ivry, 2000). According to the SET model, tasks requiring prospective timing involve three distinct stages: a clock stage, a memory stage and a decision stage. The clock stage is composed by a pacemaker that produces pulses at a constant rate. When

the gate is switched open the pulses from the pacemaker are directed into the accumulator. The accumulator integrates and holds the total pulses count during the time period. Perceived duration is a monotonic function of the total number of pulses transferred into the accumulator. When the presentation of the duration ends, the switch closed and the accumulation ends. On any trial, the contents of the accumulator are transferred into a working memory store for comparison with the content of a reference memory. The reference memory store contains long-term memory representation of the approximate number of pulses that accumulated on past trial. This number is then transferred to the decision stage (Gibbon et al., 1984; Mangels & Ivry, 2000).



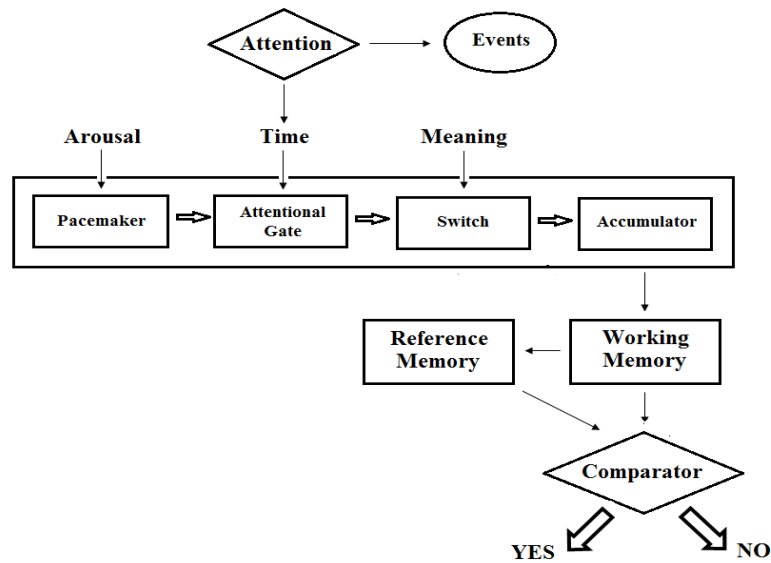
**Figure 1.1** The Scalar Expectancy Model of interval timing. Adaptation from Mangels & Ivry (2000) “Time perception” *The handbook of cognitive Neuropsychology: What deficits reveal about the human mind* (pp. 473).

However, the model does not take into account factors that are more prominent in human temporal processing. In particular, it is not able to explain why cognitive factors (attention, strategies, and information-processing) influence temporal behaviour (Block & Zakay, 1996). This limitation seems largely a consequence of methodological limitation; in fact few animal timing researches have explored the effects of attentional manipulations (which have been a focus on human prospective duration timing).

Moreover, this model does not take into account external strategies that may influence its time-related behaviour. Several studies have proposed models of psychological time in which attention to time plays a major role, one of these models, which had major influence of subsequent models of time perception, was proposed by Thomas and Cantor (1975). Briefly the model predicted that perceived duration depend on the amount of information encoded by two processes: a temporal information processor and a non temporal information processor. Attention is divided between the two processors, which function in parallel and perceived duration depends on more attentional allocation to one process or the other (Thomas & Cantor, 1975).

Interestingly, Block & Zakay (1996) proposed the Attentional-gate model, a comprehensive model that combined features of the Treisman's (1963) model, the SET model (Church, 1984; Gibbon et al., 1984), and Thomas's (Thomas & Cantor, 1975) model (Figure 1.2). The model propose a pacemaker that produces pulses at a rate which is influenced by arousal (circadian or stimulus induces; see also Triesman's, 1963 model). When people attend to time, as opposed to external stimulus events, open the gate allowing the pulses going to the accumulator. The meaning assigned to a situation influences the switch. When the meaning implies a beginning of a stimulus duration that should be timed, the switch opens, enabling the flow of pulses from the pacemaker to the accumulator. When the target event ends, the switch closes and the number of pulses stored in the accumulator is a representation of the duration of the stimulus duration. This number is then transferred to a working memory component. A representation of a target interval can be encoded in the reference memory. When a temporal task has to be performed the same process occur, but in this case the number of signals that have entered the accumulator is compared with a representation stored in reference memory

(Block & Zakay, 1996). The strength of the Attentional-gate model lies in its ability to provide coherent explanation of most phenomena that characterized prospective duration judgments. Temporal errors often occur and different predictions can be made on temporal behaviour depending on which model's component "brakes" along the process.



**Figure 1.2** The Attentional gate model, adaptation from “An Attentional-gate model of prospective time estimation” by Zakay & Block, 1994. I.P.A.Symposium, Liège.

Studies focused on properties of the pacemaker have argued that the pacemaker emitted pulses with a fixed frequency (Creelman, 1962), others proposed that the frequency is related to the arousal (Treisman, 1963; Block & Zakay, 1996). Studies conducted to investigate the effect of affective valence and arousal on time perception demonstrated that high significant valence by arousal interaction affected duration judgments. For low arousal stimuli the duration of negative slides were judged relatively briefer than the duration of positive slides. Opposite pattern of results were obtained for high arousal stimuli, for which the duration of negative slides was judged longer than

the duration of positive slides (Angrilli, Cherubini, Pavese, & Manfredini, 2007). Droit-Volet et al. (2004) demonstrated that intervals are perceived as longer when angry faces are presented during the intervals as compared with when neutral faces are shown (Droit-Volet, Brunot, & Niedenthal, 2004; see also Gil et al., 2007; Chambon, Gil, Niedenthal, & Droit-Volet, 2005). Moreover, age-related variables may also affect pacemaker. Different studies have reported older adults perceiving time going faster than it did when they were younger (Fraisse, 1984) and it has been suggested that might be the slowing down of the pacemaker that makes time to pass more quickly as become older (Joubert, 1983; Schroots & Birren, 1990). When compared older and younger adults' performances with same duration with verbal estimation or time production tasks the results revealed that older adults gave shorter verbal estimates and made longer productions than younger adults (Craig & Hay, 1999; Perbal et al., 2002). If the pacemaker emits pulses at a lower rate in older adults, a smaller number of pulses will be accumulated for a given duration, leading to shorter verbal estimates and longer productions (Perbal et al., 2002).

We already have reported that the opening of the gate is related to the amount of attention dedicated on time. Therefore, the difficulty of the secondary non-temporal task reduces attentional resources to temporal judgments, the more resources are allocated for the non-temporal task fewer resources are allocated for time and fewer pulses pass through the gate and enter the accumulator (Block & Zakay, 1996). Attentional resources are compromised not only by the secondary non-temporal task but also by age-related and clinical dysfunctions. In fact, frontal lobe patients and older adults, that often report attentional dysfunctions, showed also lower temporal abilities. Part of the

variance observed in timing tasks is also caused by the latency at the switch components both at the onset and the offset of the stimulus (Grondin, 2008; Grondin, 2010).

Finally, part of the variance in temporal tasks depends on memory and decisional processes. When the content of the accumulator is transferred to the working memory for the eventual comparison with the content stored in the reference memory (where a representation of the critical duration is kept) the duration retrieval from the reference memory might have been modified according to the characteristics of the memory system. The quality of the interval's representation is the major source of variability (Grondin et al., 2004; Grondin, 2010).

### **1.3 Factors that influence time perception**

The reason why someone makes errors on judging time depends on several factors. Researchers since the emergence of experimental psychology have been trying to crack the secrets of information processing responsible for the sense of time. However, time is “a slippery entity, sensitive to the condition under which it is measured” (Zakay, 1990, pp. 59). Already Hicks et al. (1976) pointed out the importance of investigating the different factors that influence time perception and listed four factors: 1- the nature of the measurement paradigm (prospective or retrospective); 2- duration of the intervals to be estimated; 3- the nature of the processing required during the interval to be estimated (filled or unfilled interval); 4- the method of time estimation (Hicks, Miller, & Kinsbourne, 1976). Block (1989) claimed that “a complete understanding of any kind of temporal experience is possible only if we consider complex interaction among all of these factors” (pp. 334).

In prospective duration paradigm participants know in advance that they will be asked to judge the duration, while in retrospective duration paradigm, participants do not know until after a time period that they are being asked to judge its duration (Block & Zakay, 1997; Block et al., 1998; Block & Zakay, 2006). In the prospective paradigm a person intentionally encode temporal information and temporal performance depends of the amount of attention dedicated to time; in the retrospective paradigm, a person incidentally encode temporal information and these are retrieved later from memory (Block & Zakay, 2006). Many studies have been conducted with prospective paradigms, but relatively few have used retrospective paradigms. The reason for this imbalance is that, after a participant is asked to provide a retrospective judgment, he/she became aware of the subsequent duration judgment that reduces the number of possible observation (Block & Zakay, 1997). Findings from some experiments that compared temporal performance within prospective or retrospective paradigms provided evidences that different processes or system subserve the two kinds of duration judgments (Hicks et al., 1976; Block, 1992). Prospective and retrospective duration judgments tend to be underestimated, but prospective duration judgments are typically more accurate than retrospective duration judgments. In addition, retrospective judgments show greater inter-subject variability than do prospective judgments (Block & Zakay, 1997).

The duration of the intervals that has to be perceived, is absolutely one of the main factor that influence time perception. The field of time perception has been more concerned with intervals in the range of 100 ms to few seconds. In particular durations in the range of 1 s have received great interest because of the debate of the *indifference interval* that is the interval in which there would be no tendency to overestimate or underestimate (Eisler, Eisler, & Hellström, 2008). Other authors have introduced the



concept of *psychological present* that is defined as the period of time during which an interval can be perceived as a unit (James 1890; Fraisse, 1984; Pöppel, 1972, 2004). Moreover, it has been emphasized a distinction between intervals above and below 1 s (Penny & Vaitilingam, 2008; Lewis & Miall, 2003a b); processing a brief intervals (below 1 s) is supposed to be sensory based, or benefits from some automatic processing, whereas the processing of longer intervals (above 1 s) requires the support of cognitive resources (Lewis & Miall, 2003a b).

It has also been demonstrated that temporal performance becomes less accurate with increasing duration of time interval to be estimated when evaluated with time reproduction, time production or verbal estimation tasks (Block et al., 1998; Craik & Hay, 1999). Opposite effect of lengthiness of intervals has been found when participants were tested with time discrimination tasks. In time discrimination tasks better performances have been found with increasing duration may be due to the greater relative differences between the two duration that have to be discriminated (Rammsayer, 2001; Paul, Le Dantec, Berbard, Lalonde & Rebaï, 2003; Smith, Taylor, Lidzda & Rubia, 2003; Gontier, LeDantec, Leleu, Paul, Charvin, Bernard, Lalonde & Rebaï, 2007; LeDantec, Grontier, Paul, Charvin, Bernard, Lalonde & Rebaï, 2007).

The second critical factor is the secondary task that occurs along with the temporal task. Time perception varies with the difficulty of the concurrent secondary task and time perception is adversely affected by the demands of any non-temporal secondary task (Zakay, 1993; Zakay & Block, 1997; Block & Zakay, 2008). Zakay and Block (2004) asked participants to perceive durations while reading sentences with or without syntactic ambiguity. Resolving syntactic ambiguity demands more resources than regular reading, fewer resources can be allocated for time perception in the first

condition than in the second. The results showed shorter time reproduction in the semantic-ambiguity condition than in the no-ambiguity condition. Vanneste and Pouthas (1999) also reported that simultaneously focus attentional resources on one, two or three temporal stimuli affect temporal performance. The authors reported that performance of both younger and older participants were deteriorated by the difficulty of the task (number of concurrent targets to control) but the old participants were more affected by interference (more variable and less accurate).

There are varieties of dual-task experiments in time research, including performing two temporal tasks concurrently (Brown & West, 1990; Brown, Stubbs, & West, 1992) and specifying in advance the percentage of attention allocated to each of the two tasks (Grondin & Macar, 1992; Casini & Macar, 1997). In sum, what it is usually found is a decrease of the perceiving length of an interval as more attention is dedicated to the non-temporal task (Zakay & Block, 1997, 2004).

Stimulus modality (auditory, visual or tactile) has also been demonstrated to affect time performance. The sensitivity to time is much higher when intervals are marked with auditory rather than visual stimuli (Grondin, 2003). Others authors have reported that auditory stimuli appearing to last for longer than visual stimuli. This effect is due to differences in the operation of the pacemaker, with faster pacemaker speeds for auditory stimuli than for visual stimuli (Wearden, Edwards, Fakhiri, & Percival, 1998; Penny, Gibbon, & Meck, 2000). Moreover, when intervals are marked by two brief stimuli from different sensory modalities, sensitivity to time is much lower than it is when intervals are marked by signals from the same modalities (either visual or auditory) (Grondin, 2003; Grondin et al., 2005).

An additional critical factor that influences time perception is the nature of the interval, in particular the distinction concerns the structure of the interval i.e. filled or unfilled interval. A filled interval is when the stimulus is continuous from the onset to the offset (i.e. sound that last the entire stimulus duration) while an un-filled interval is when the stimulus interval is marker by brief markers and nothing is presented in the interval between the two markers (Grondin, 2008). It is generally reported in literature that filled intervals are estimated longer in comparison with equal un-filled intervals (Allan, 1979; Grondin, 2008; Grondin, 2010). The employment of unfilled intervals however, is problematic because researchers have no control over what subjects are doing “internally” during the empty interval. Participants might involve complex or simple information processing or employing strategies that are not controlled by the experiments (Allan, 1979; Zakay, 1990). To avoid the employment of uncontrolled strategies, some researchers have instructed participants to count aloud to induce the same strategy in all subjects, or a concurrent reading condition that, on the other hand, prevented the use of counting and acted as a dual-task paradigm (Perbal et al., 2002; Baudouin et al., 2006a b).

In fact, it has been demonstrated that when participants are tested with stimulus durations of few seconds<sup>2</sup> (both filled and unfilled stimuli) it is very likely that participants tend to employed strategies by segmenting the interval into smaller parts (i.e. counting the seconds; Grondin, 2003; Grondin, Ouellet, & Roussel, 2004). The strategies could include counting or tapping the foot. The efficiency of the segmentation strategy for estimating relative long duration is recognized in timing literature (Petrušić,

---

<sup>2</sup> Different studies have reported different durations in which adopting counting strategies would have increased or reduced the performance. At the present there is no gold standard duration, performance not

1984; Grondin, Meilleur-Wells, & Lachance, 1999; Grondin, Oullet, & Roussel, 2004). A methodological issue lies in the possibility that using strategies such as counting might prevent the emergence of temporal experiences; for this reason concurrent secondary task are often employed to prevent the use of strategies. Finally, if the participants are required to make the duration judgment after some delay following the temporal interval, the result is a linear decline in accuracy with increasing delay (Block, George, & Reed, 1980; Zakay, 1990). Researchers that focused on reaction time used a warning signal to announce that a target signal will be presented; the foreperiod is the period between the warning and the target signals (Grondin & Rammsayer, 2003; Vallesi, Binns, & Shallice, 2008). Usually the reaction times get shorter (better performance) as the foreperiod get longer, which has been interpreted as an effect of better attentional preparation as the foreperiod get longer (Grondin & Rammsayer, 2003). Grondin and Rammsayer (2003) founded that as the foreperiod preceding an interval to be discriminated got longer the duration of the interval to be discriminated was perceived as longer (and often as less variable).

It is clear that subjective perception of time is largely influenced by various types of processes and factors, some of which related to specific characteristics of the model used to interpreted the data, others related to the characteristics of the stimulus used in temporal tasks. Finally, critical in time perception is the method employed to evaluate temporal abilities. A wild number of methods have been employed to test time perception and it is important to consider the intrinsic factors of these tasks because different cognitive factors characterized each methods.

---

only depend on stimulus durations, but also on others factors like age, methods or modalities (Block et al., 1998; Grondin, Meilleur-Wells, & Lachance, 1999; Grondin, Oullet, & Roussel, 2004).

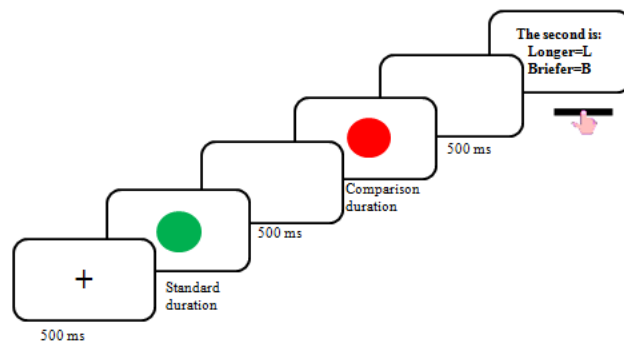
#### **1.4 Methods to investigate time perception**

Many methods have been proposed to assessing time perception and the appropriateness of a method may depend on the range of duration under investigation. It is easy to imagine that perceiving durations that last few seconds it not like perceiving durations lasting minutes (Grondin, 2010).

Traditionally, authors distinguishing four main methods in prospective timing: time comparison; time reproduction, time production and verbal estimation (Allan, 1979; Block, 1989; Zakay, 1993; Mangels & Ivry, 2000; Grondin, 2008; Grondin, 2010). Time comparison method has been mainly employed in psychophysical studies and the analysis of variability of estimations and the difference threshold have been the central issues. Instead, time reproduction, time production and verbal estimation methods not only investigate temporal abilities but also the effect of attention and the role of memory on time estimation.

*Comparison tasks:* In comparison tasks participants are required to compare the relative duration of two intervals and judge which is the longer or briefer one in this case participants are engaged in a two-alternative force-choice method (2AFC). The time discrimination task is one of the most common comparison task (Figure 1.3) and consist in the presentation of two subsequently stimuli, the first stimulus presented is often referred as the “standard” while the second presented the “comparison”. When the standard interval is always presented first, followed by the comparison, the approach is called “*reminder method*”, instead, when the standard and the comparison intervals vary from trial to trial is called the “*roving method*” (Macmillan & Creelma, 1991). Most of the time, the time discrimination task requires the first stimulus presented to be stored in the reference memory, whereas the second stimulus being held online. When compared

the time discrimination performances obtained with the reminder are much better than with the roving methods (Lapid, Ulrich, & Rammsayer, 2008; Grondin & McAuley, 2009). Temporal performance is modulated by stimulus duration and by the magnitude of the duration difference between the two stimuli. Greater difference between the two stimuli produces higher accuracy. Comparison methods investigate the subject's threshold; this notion refers to the minimal difference needed to discriminate between two stimuli (also called *Just Noticeable Difference*, JND) (Grondin, 2008; Grondin, 2010).



**Figure 1.3** Example of time comparison task: the discrimination task.

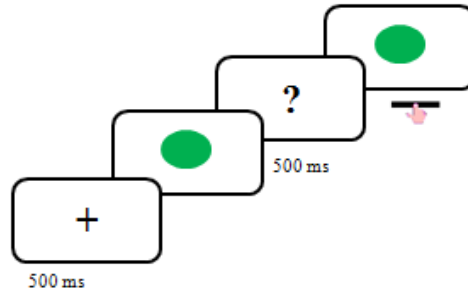
There are two main categories of methods for establishing the discrimination threshold: the method of constant stimuli and the adaptive method. In the constant stimuli method the difference between the standard and the comparison remain fixed from trial to trial, while in the adaptive method the comparison interval is adjusted from trial to trial depending on whether the observer provided a correct or incorrect response. There are several rules adopted to adjust the value of the comparison intervals, with the changes in difficulty levels being fixed steps (staircase method) or adjustable steps as in the parameter estimation by sequential testing (PEST) (Grondin, 2008).

There are some variant of the method of comparison, in particular the bisection and the temporal generalization methods (Grondin, 2010). In the bisection task two intervals (one brief and one long) are presented several times and are followed by intervals that have to be categorized as being closer to the briefer or the longer interval (Penny, Gibbon, & Meck, 2008). In the temporal generalization tasks the central interval (the standard a midpoint) is presented several times and participants are required to indicate (yes or no) whether the subsequent intervals are the same duration as the standard (Wearden, Norton, Martin, & Montford-Bebb, 2007).

The comparison tasks (in particular the time discrimination method) often present a *time-order error* that refers to the finding that the order of presentation influences the temporal judgment and it induced some bias in the perceived duration of intervals (Allan, 1979; Zakay, 1990; Eisler, Eisler, & Hellström, 2008). The time-order error can be either positive or negative. In a positive time-order error the first of the two temporal durations is perceived as longer, whereas in a negative time-order error the first duration is perceived as shorter (Hellström, 1985; Hellström, & Rammsayer, 2004). To avoid this methodological problem is usually dealt by counterbalancing the presentation order of the standard and the comparison interval (Zakay, 1990).

*Time reproduction task:* In time reproduction tasks, participants reproduce the duration of a stimulus previously presented (Figure 1.4). The first duration presented has to be encoded and stored in the reference memory to be subsequently retrieved and reproduced. This task involves storing the accumulated pulses according to the duration perceived, followed by reproduction in which the currently accumulated pulses are compared with those previously stored in reference memory (Block & Zakay, 2006). Time reproduction tasks also provide information about participants' working memory

capacity and attention abilities (Block et al., 1998; Perbal et al., 2002). Performance is influenced by stimulus duration and concurrent task (dual-task condition).



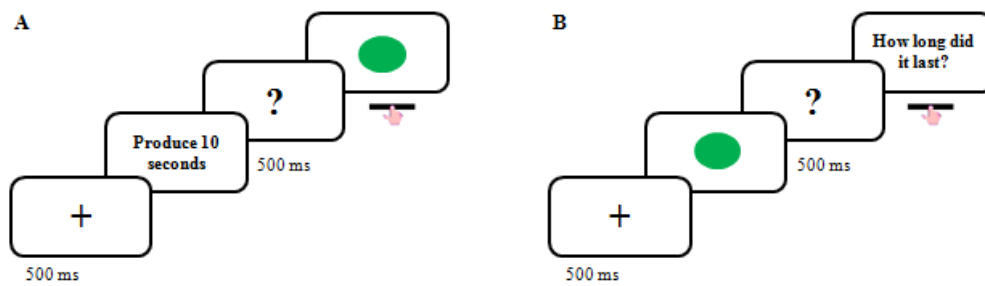
**Figure 1.4** Example of Time Reproduction task.

It has been demonstrated that performance becomes less accurate with increasing duration of time intervals to be reproduced (Block et al., 1998; Craik & Hay, 1999); moreover, a concurrent task performed during the encoding phase decreases reproduction accuracy reducing attentional resources devoted to timing. In a dual task condition the attentional resources have to be divided between the temporal and the non-temporal tasks, consequently, the fewer attentional resources dedicated to the timing task, the fewer signals pass through the gate resulting in under-reproduction of stimulus duration (Zakay, 1993; Block & Zakay, 2006; Baudouin et al., 2006a; Perbal, et al., 2002; Zakay & Block, 2004). Researchers have added concurrent non-temporal tasks both to investigate the effect of divided attentional resources on time perception (Vanneste & Pouthas, 1999; Zakay & Block, 2004) but it is also widely used to prevent participants to use uncontrolled strategies (i.e. internal counting strategies; Allen, 1979; Zakay, 1990; Perbal, et al., 2002; Baudouin et al., 2006a b; see also the previous section: “Factors that influence time perception”, pp. 12).



A variant of the time reproduction task is the peak interval procedure often used both on animal and human studies (Mangels & Ivry, 2000). Normally participants are carried out the task over two consecutive days. The first day of the procedure is the “training” session in which the subjects receive fixed interval trials several times. Once they have learned the duration of the fixed interval they are asked to reproduce it on a second day during the “testing” session (Malapani, Rakitin, Levy, Meck, Deweer, Dubois, & Gibbon, 1998; Mangels & Ivry, 2000; Rakitina, Sterna, Malapani, 2005). This procedure has been extensively used because produces especially stable estimates of timing accuracy and variability, as well as free-recall testing following a 24 h delay (Malapani, Deweer, & Gibbon, 2002).

*Time production* and *verbal estimation* tasks may be considered the two side of the same coin and reflect the same underlying temporal processes and mechanisms (Allan, 1979; Craik & Hay, 1999; Figure 1.5). In time production tasks participants are required to produce an interval equally to a duration that is previously indicated and translate from an objectively labelled duration to a subjectively experienced duration. In the verbal estimation tasks, participants experienced target duration and then are required to translate the experienced duration (objective duration) into clock units (subjective duration) (Block et al., 1998). Likewise, time reproduction tasks, performance on time production and verbal estimation tasks are affected by stimulus duration and concurrent secondary tasks (Block et al., 1998; Grondin, 2008). When a concurrent secondary task is embedded with the time production or verbal estimation task the common performance is relatively smaller verbal estimates and relatively longer productions (Allan, 1979; Block, 1989; Grondin, 2008).



**Figure 1.5** Example of Time production (A) and Verbal estimation tasks (B).

Time production and verbal estimation are suitable methods to investigate individual differences (or effects of variables that may influence the rate of internal processes). Researchers have successfully used them in studies of manipulations of the rate of internal pacemaker (Block et al., 1998; Meck, 1996; Rammsayer, 2001). Instead, in the method of time reproduction participant experiences a target duration and then is required to delimit another time period that is of the same length. Even if the rate of physiological and cognitive processes varies with age, the same rate will subserve a person's experiencing the target duration and reproducing it. Thus, the reproduction method may detect individual differences only if it is used in the framework of psychophysical studies, in which duration is varied or additional cognitive variable are engaged (secondary tasks with different cognitive load) (Zakay, 1990; Block et al., 1998; Grondin, 2010).

A variant of the production task is the finger-tapping task in which participants are required to tap tapping block, as regularly as possible at the pace they preferred (free tempo condition) or at a specified rate (i.e. 1 s tempo). Normally, participants are required to tap within an interval that is marked by two auditory or visual signals (Perbal Couillet, Azouzi, & Pouthas, 2003; Mangels & Ivry, 2000; Grondin, 2010).

Researchers are using the entire repertory of methods but in most cases they give no explanation for the selection of a specific one. It is obvious that each method activates different time-related processes and presents some specific perceptual bias. For example, the verbal estimation methods are prone to a response bias of reporting the estimated duration in round number (Hornik, 1985; Zakay, 1990), while the time discrimination method often presents a time-order error (Eisler et al., 2008). Time reproduction is considered to be more accurate and reliable than time production and verbal estimation (Block, 1990). Block (1989) remarked that time production and verbal estimation show more inter-subject variability than time reproduction or time comparison. Some authors pointed out that time production and verbal estimation deal with the relation of subjective time to clock and are successfully used in studies of manipulations of the rate of internal pacemaker (Block et al., 1998; Rammsayer, 2001). Others have pointed out that time discrimination is the purest measure to investigate time perception (Rubia, Taylor, Taylor, Sergeant, 1999). Findings support the assumption that the perception of stimulus duration depends on the method used (Zakay, 1990; Block et al., 1998) and Allan (1979) argued that no single method can claim consistent superiority and that there is no significant correlation among methods. In sum, when studying time it is particularly important to select the appropriate method depending on the theoretical hypothesis, Block (1989) proposed an interesting and particularly useful checklist for researchers on time perception.

### **1.5 High cognitive factors that influence time perception**

The impact of attention on temporal experience is evident in everyday life. When attention is directed to an absorbing activity we have the feeling that time flies,

however, when attention is focused on time the opposite effect occurs. Attentiveness to time often creates the temporal illusion called “The watched pot phenomenon”, when attention is actively directed to time (boiling water) time appeared to move more slowly (Cahoon & Edmonds, 1980). The Attentional-gate model theorized this phenomenon indicating that more attention is directed to time the wider the gate is open and more pulses enter into the accumulator; the results is a lengthening of perceived time (Block & Zakay, 1996; Block & Zakay, 2006). Research on time and attention covers a wide range of issues because attention itself is a complex topic with many different aspects and it has been divided in many subcomponents (i.e. alertness, selectivity, orienting and detecting, Posner & Boies, 1971). Zakay & Diamant (2011) recently investigate the involvement of different attentional functions (selective attention, orienting attention, sustained attention, and executive attention; Tsal, Shalev, & Mvorach, 2005) on time perception. Participants were divided in “high” and “low” groups according to their scores on each one of the attentional functions. Sustained attention was the only attentional functions that correlated with time performance. Participants with better sustained attention abilities were more accurate and less variable on time reproduction tasks. It was also found that the feedback on temporal performance was helpful in the “low” sustained attention group, whereas “high” sustained attention participants did not benefit from the feedback, probably because they were performing near their optimal level of performance (Zakay & Diamant, 2011).

A consistent line of research pointed out that executive functions are involved in time perception (Zakay & Block, 2004; Brown, 2006). Different studies have demonstrated that that cognitively controlled temporal perception is also closely related to executive functions, in fact, healthy individuals with low executive functions often

present greater timing errors than better functioning individuals (e.g., Barkley, Koplowitz, Anderson, & McMurray, 1997; Janowsky, Shimamura, & Squire, 1989; Kerns & Price, 2001; Lewis & Miall, 2006a b; Rammsayer, 1999; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005; Block & Zakay, 2006).

Recent studies explored which executive component is mainly involved in time perception. According with Miyake and co-workers model (2000), executive functions may be divided in three basic components: inhibition of prepotent responses; updating of working memory contents, and mental shifting (Miyake, Friedman, Emerson, Witzki, Howerter & Wager, 2000). Carelli, Forman & Mäntylä (2007) conducted two separate experiments on school age children and university students to investigate if participants' time reproduction performance were mediated by individual differences in executive functions. Participants were required to reproduce duration ranging from 4 to 32 s under simple and concurrent condition (school-age children performed time reproduction task only under simple condition). Results from the study conducted with school-age children revealed that participants with lower updating and inhibition executive component, but not in mental shifting, made greater errors than children with more efficient working memory and executive functions. Results from the study conducted with university students revealed that individual differences in inhibition and updating components of executive functioning were related to absolute errors in the concurrent condition.

Perbal and co-workers (2002) reported that age-related working memory limitations better account for the shorter reproductions whereas age-related slower processing speed better account for longer productions performance (Perbal et al., 2002). Baudouin and co-workers (2006) reported that time production correlated with

spontaneous motor tempo (finger tapping task) and reproduction correlate with working memory measures. The authors concluded that the pacemaker rate modulates the production of duration and that the reproduction performance varied according to the working memory capacity (Baudouin et al., 2006a).

Finally, different involvement of working memory storage and central executive functions was found in age-related differences in time perception (Baudouin et al., 2006b). Older and younger adults were involved in the study and performed time reproduction tasks (simple- and dual-task condition) with working memory tasks (measuring storage capacity and updating functions). Hierarchical regression analysis revealed that the storage capacity predicted reproduction performance in the simple-task condition, whereas updating predicted performance in the dual-task condition. The authors concluded that age-related decline in executive functions reduced the ability in older adults to divide attention between concurrent temporal and nontemporal task which determine their temporal dysfunctions (Baudouin et al., 2006b).

## **1.6 Neuropsychology of time perception**

Neuropsychological studies confirmed the relation between time perception and cortically and sub-cortically brain areas. Moreover, the emergence of new techniques also produced a large body of neuropsychological researches which evidenced that specific structures in the brain play a role on time perception (Coull, Vidal, Nazarian, & Macar, 2004; Cockburn, 2006; Rubia, 2006; Penny & Vaitilingam, 2008; Szlag, Dreszer, Lewandowska, & Szymaszek, 2008). The frontal cortex was one of the first brain regions to be related to time perception (Gibbon et al., 1997; Fuster, 2001; Rubia, 2004). Patients with lesions in frontal brain regions appear to be impaired in their ability

temporal abilities with duration ranging from hundreds of milliseconds to seconds (Nichelli et al., 1995; Harrington et al., 1998a; Casini & Ivry, 1999; Mangels et al., 1998; Meyers & Levin, 1992; Perbal, Couillet, Azouzi, & Pouthas, 2003; Schmitter-Edgecombe & Rueda, 2008; Anderson & Schmitter-Edgecombe, 2011; Rubia, 2006; Grondin, 2010). Considering that this thesis is focused on temporal perception in TBI patients, the next paragraph will be entirely dedicated to review the literature on temporal dysfunctions in frontal lobe patients and TBI patients. In this section I will briefly review the main literature on the role of cerebellum and subcortical structures, moreover, pharmacological evidences will also be summarized.

There is strong evidence for the implication of cerebellum on timing (Rubia, 2004; Rubia, 2006; Grondin, 2010). In particular the cerebellum has been mostly involved in motor timing<sup>3</sup> with very brief durations (Harrington & Haaland, 1999). In fact, the cerebellum is argued to be involved in tasks in which the timing of brief intervals is a central component, such as eyeblink conditioning and speech perception and production (Lewis & Miall, 2003a b; Bueti, Walsh, Frith, & Rees, 2008; Grondin 2010). Converging data from neuroimaging literature using position emission tomography (PET), have found increased in cerebellar blood flow during duration judgments both visual (Maquet et al., 1996) and auditory (Jueptner et al., 1995). Other studies based on neuroimaging have shown greater activation of the cerebellum for the discrimination of 600-msec rather than of 3s intervals (Lewis & Miall, 2003a). The cerebellum has also been reported to play a role in both production and discrimination tasks in cases with intervals briefer than 1.2 s (Bueti et al., 2008). Two studies conducted

---

<sup>3</sup> Motor timing refers to the timing aspects of the output of behavior such as temporal organization of motor and speech. It is measured with finger tapping or rhythm production and normally range from few milliseconds to seconds (Rubia, 2006).

with repetitive transcranial magnetic stimulation (rTMS) with a bisection task (Lee, Eagleston, Brown, Gregory, Barker, & Woodruff, 2007) and time reproduction task (Kock, Olivieri, Torriero, Salerno, Lo Gerfo, Caltagirone, 2007) also reported that timing was affected for durations between 400 and 800 ms but not for intervals above 1 s. However, others studies have shown that patients with cerebellar lesions display poor temporal performance also when tested with longer intervals in the range of few seconds (Meck, 2005; Grondin, 2010). Nichelli et al. (1996) using a bisection task, showed that cerebellar degeneration leads to temporal impairment when intervals were in the range of few seconds, but not when they briefer than 1 s (Nichelli, Always, & Grafman, 1996). Additionally, an imaging study conducted by Tracy et al. (2000) showed that the cerebellum provides codes for the processing of intervals lasting 12–24 sec (Tracy, Faro, Mohamed, Pinsk, & Pinus, 2000).

The relationship between cerebellum and prefrontal cortex on time perception has been directly investigated (Casini & Ivry, 1999; Mangels et al., 1998). Performance of cerebellar patients on finger tapping (motor task) and discrimination task was compared with the performance of patients with cortical lesions. Cortical patients showed deficits in finger tapping but not in time discrimination, while cerebellar patients on both temporal tasks (Ivry & Keele, 1989). Because time discrimination has been considered the pourer temporal task (Rubia, Taylor, Taylor, & Sergeant, 1999), and cerebellar patients were less accurate than controls when tested with time discrimination task, the authors interpreted these results confirming the role of cerebellum in time perception (Ivry, Keele, & Diener, 1988; Ivry & Keele, 1989). Imaging studies manipulating the temporal occurrence of events showed significant activation suggesting that the cerebellum might be involved in the attempt to temporal occurrence



of events (Dreher & Grafman, 2002). Whether the cerebellum is involved exclusively in the timing of very brief intervals or covers a wide duration range is still an open question. Many studies have demonstrated the role of cerebellum on timing brief duration, however, some other have shown that the role of the cerebellum might not be restricted to brief duration (Nichelli et al., 1996; Tracy et al., 2000; Meck, 2005; Grondin, 2010).

The basal ganglia have also been involved in time estimation (Rubia, 2004; Rubia, 2006; Grondin, 2010). Research using fMRI has demonstrated the involvement of the basal ganglia in timing processes (Harrington & Haaland, 1999). In particular, the caudate and putamen are shown to be activated by timing tasks both with brief (Pouthas et al., 2005; Tragellas, Davalos, & Rojas, 2006) and with duration longer than 1 s (Harrington, Lee, Boyd, Rapcsak, & Knight, 2004; Hinton & Meck, 2004). Moreover, the caudate and the putamen have been found to be activated in time discrimination in the milliseconds range (Jueptner et al., 1995; Rao, Mayer, & Harrington, 2001) and time production of several seconds (Lewis & Miall, 2002).

Relatively poorer performance of Parkinson's disease (PD) patients was interpreted as indicating the involvement of basal ganglia and associated thalamo-cortical connections in time perception (Cockburn, 2006; Rubia, 2006). A direct relationship between temporal deficits and dopaminergic level is in fact supported by the findings that pharmacological restoration of normal dopamine levels can significantly improve temporal dysfunctions in both schizophrenics and PD patients (Pastor, Artieda, Jahanshahi, & Obeso, 1992; Meck, 1996). Patients with schizophrenia, a disorder associated with increased dopamine levels, perceive subjective time as quicker than objective time (Wahl & Sieg, 1980). Conversely, patients with decreased

levels of dopamine resulting from Parkinson's disease have been found to have a perception of time that passes more slowly than objective time (Malapani, Rakitin, Levy, Meck, Deweer, Dubois, & Gibbon, 1998; Pastor, Artieda, Jahanshahi, & Obeso, 1992). In short, dopamine levels in the nigrostriatal pathway have been hypothesized to modulate the speed of the internal clock (for a review see Meck, 1996). Nevertheless, dopamine is not the only psychoactive substance that produce distortion on time perception caffeine and nicotine accelerate the internal clock (Arushanyan, Baida, Mastayagin, Popova, & Shikina, 2003; Gruber & Block, 2003; Terry, Dumas, Desai, & Wing, 2009), alcohol, instead, has the opposite effect (Terry et al., 2009).

Pharmacological studies also pointed out that, central nervous system (CNS) depressants are associated with reductions in verbal estimations of time intervals and thus arguably with the slowing of the internal clock, whereas CNS stimulants have the opposite effect (Friedman, 1990; Meck, 1996). For example, depressants such as secobarbital (Goldstone & Kirkham, 1968), ethanol (Tinklenberg, Roth, & Koppell, 1976), and cyclopropane (Adam, Rosner, Hosick, & Clark, 1971) are associated with reductions in verbal estimation, whereas stimulants such as amphetamines (Church, 1984; Goldstone & Kirkham, 1968) and marijuana (Hicks, Gualtieri, Mayo, & Perez-Reyes, 1984; Tinklenberg et al., 1976) are associated with increased verbal estimates of duration, implying that the internal clock is running too fast.

In sum, studies that have involved both brief (few milliseconds) and long intervals (seconds) have found that the right prefrontal brain regions (DLPFC) seem to mainly involved in perceiving long intervals, the cerebellum and the basal ganglia seem to be involved both in brief and long intervals (Jones, Rosenkranz, Rothwell, & Jahanshahi, 2004). These findings suggested that the cerebellum and the basal ganglia

might be crucially involved in hypothetical internal clock mechanisms, while the prefrontal lobes may mediate timing functions via the role of high cognitive functions, such as working memory, attention or executive functions, which are related with frontal areas (Rubia, 2004).

### **1.7 Time perception in traumatic brain injury patients**

Time perception relies on various cognitive processes, such as attention and working memory (Block & Zakay, 1996), which are related to frontal lobe functioning (Moscovitch, 1994; Shimamura, 1994; Lezak et al., 2004; Stuss, 2011). Given the vulnerability of the frontal lobes to damage as a result of a TBI (AharonPeretz & Tomer, 2007; Bigler, 2007) and the common occurrence of executive dysfunction following TBI (Boelen, Spikman, Rietveld, & Fasotti, 2009; Hartikainen, Waljas, Isoviita, Dastidar, Liimatainen, Solbakk, Ogawa, Soimakallio, Ylinen, & Ohman, 2010), it seems reasonable to expect that time perception would also be affected in TBI patients. In fact, temporal dysfunctions have been documented in patients with focal frontal lesions (Nichelli et al., 1995; Harrington et al., 1998a; Mangels et al., 1998; Casini & Ivry, 1999; Rubia & Smith, 2004; Picton et al., 2006).

Nichelli and co-workers (1995) used a time bisection task in focal frontal lesions patients. Patients were less accurate than controls with short durations (100 and 900 ms), but precision of the performance (i.e., consistency of classification criteria over repeated trials) was remarkably unaffected. When tested with long duration (8 and 32 sec) both accuracy and precision were impaired. The authors concluded that a deficit at the level of reference memory could explain the impaired accuracy at short durations, while a deficit in sustained attention is presumably associated with the long intervals

performance. Mangels et al. (1998) examined patients with frontal lesions and neocerebellum lesions with a time discrimination task (400 ms and 4 s). Frontal patients exhibit a significant timing deficit when judging 4 s intervals, while neocerebellum patients exhibited temporal impairment in both milliseconds and seconds ranges. According to the authors, attention and working memory processes appeared critical for maintaining information over long periods of time. Their results indicated that the integrity of the prefrontal cortex is critical for accurate temporal perception within seconds' duration range. These findings were supported by a later study, where the attentional load during temporal and non-temporal perceptual tasks was manipulated (Casini & Ivry, 1999). Patients with frontal lobe lesions, with cerebellum lesions, and healthy controls performed a discrimination task (first standard duration = 400 ms; the comparison stimulus ranged from 220 ms to 580 ms), either single (discriminate the temporal duration or the frequency of the auditory stimuli) or concurrently with a non-temporal perceptual task (discriminate both the temporal duration and the frequency of the auditory stimuli). In both single conditions patients performed poorly than controls, but no difference was found between the two patient groups. When participants had to make concurrent judgments on both dimensions, patients with frontal lobe lesions were significantly impaired on both tasks, whereas the variability of cerebellum patients increased only when time discrimination was required. The authors concluded that, whenever the attentional demands of a task are increased, patients with prefrontal lesions are challenged, regardless of whether the task requires temporal or non-temporal processing. The cerebellum group, on the other hand, did not show a generalized attentional problem. These findings confirm the influence of prefrontal cortex and attentional manipulation on temporal tasks (Casini & Ivry, 1999). Temporal dysfunction

was also observed in frontal lobe patients when tested with other methodologies like verbal estimation or time production (Binkofski & Block, 1996; Mimura et al., 2000).

To our knowledge only four studies have investigated time perception abilities in TBI patients (Meyers & Levin, 1992; Perbal, Couillet, Azouzi, & Pouthas, 2003; Schmitter-Edgecombe & Rueda, 2008; Anderson & Schmitter-Edgecombe, 2011; Table 1.1). Meyers and Levin (1992) tested 34 patients who had sustained TBIs of varying severity with time reproduction and verbal estimation tasks (the durations tested were: 5, 10 and 15 s). TBI patients were divided in two subgroups according to their orientation level evaluated with the Galveston Orientation and Amnesia Test; (GOAT; Levin, O'Donnell, & Grossman, 1979). No differences in verbal estimation or time reproduction tasks were found between the TBI and control groups. Orientation level (Disoriented TBI  $n=10$  GOAT=42.8 SD=23; Oriented TBI  $n=24$  GOAT=88.17 SD=10.07) was found to be related to performance at the 15-s interval, with greater under-reproduction by more disoriented TBI participants. Authors concluded that disoriented TBI patients can employ their immediate working memory to judge brief duration, but that they under-reproduce timing intervals as the interval became longer and exceed their immediate memory capacity.

Fifteen severe TBI patients (tested within a mean of 11 months post injury) and 15 matched controls were examined by Perbal and co-workers (2003). Participants performed time reproduction and time production tasks (4, 12 and 31 s) under control counting and concurrent reading conditions. No differences in time accuracy (analysed by the ratio score) were found between TBI and controls both in time reproduction and time production tasks; however TBI patients were more variable on both tasks in both conditions. The authors also analyzed the correlation between the variability index

calculated for time reproduction and time production, neuropsychological memory tests and processing speed. The results indicated that the variability index for the reproduction task correlated with memory and processing speed, while the variability index for the production task correlated only with the processing speed measure. The authors discussed the results as a difficulty of TBI patients to maintaining a stable representation of duration probably due to difficulties in sustaining attention and working memory.

**Table 1.1** Studies that investigated time perception in TBI patients.

<b>Author</b>	<b>Year</b>	<b>Patients</b>	<b>Clinical characteristics</b>	<b>Tasks</b>	<b>Condition</b>	<b>Durations</b>
<b>Meyers &amp; Levin</b>	1992	Disoriented TBI=10 Oriented TBI=24 Controls=12	18 severe, 5 moderate, 11 mild; PTA=16 days; post-injury time=37 days	Time Reproduction Verbal Estimation	Simple	5, 10 and 15 s
<b>Perbal et al.</b>	2003	TBI patients=15 Controls=15	GCS=6.4; PTA=88 days; post-injury time=11 months	Time Reproduction Time Production	Concurrent reading Control counting	5. 14 and 38 s
<b>Schmitter-Edgecombe &amp; Rueda</b>	2008	TBI patients=27 Controls=27	14 severe and 13 moderate TBI; PTA=24.11 days; post-injury time=41.93 days	Verbal estimation	Concurrent reading	10. 25. 45 and 60 s
<b>Anderson &amp; Schmitter-Edgecombe</b>	2011	TBI patients=15 Controls=15	8 severe and 7 moderate; PTA=23.27; post-injury time=432.13 days	Verbal estimation	Concurrent reading	10. 25. 45 and 60 s

Schmitter-Edgecombe & Rueda (2008) suggested that previous studies do not find reduced time estimation accuracy after TBI because the time duration intervals employed do not exceeded the working memory span (30 s). 27 severe TBI and 27 matched controls were tested with a time estimation task by using 10, 25, 45, and 60 s time intervals. TBI patients should significantly underestimate temporal intervals

exceeding immediate memory span. The results showed no group differences for short duration (10 and 25 s), while the magnitude of underestimation for longer duration (45 and 60 s) was significantly greater on TBI than controls. Some TBI studies (Schmitter-Edgecombe & Anderson, 2007; Anderson & Schmitter-Edgecombe, 2009) have demonstrated poorer performance on episodic memory tests in the early recovery stage, but a good recovery curve of episodic memory abilities within the first year postinjury (Christensen, Colella, Inness, Hebert, Monette, Bayley, & Green, 2008). Following these results, Anderson and Schmitter-Edgecombe (2011) retested the TBI patients and control participants of the Schmitter-Edgecombe and Rueda (2008) study. The authors were interested in examine whether the time estimation accuracy of the TBI participants for long intervals (45 and 60 sec) would improve to normal levels following a year of recovery due to improvements in episodic memory abilities. Contrary to their hypothesis, despite the presence of continued episodic memory impairment in the TBI group, there were no longer differences in the time estimates made by the participants with TBI and the controls. Episodic memory dysfunction may not have played a significant causative role in the TBI groups' underestimation of time for longer durations. These results suggested that not only episodic memory account for temporal dysfunction but other cognitive factors (i.e. attention, speed processing or working memory) could be involved, and biological processes, such as the "internal clock" (Anderson & Schmitter-Edgecombe, 2011; Perbal et al., 2003; Zakay & Block, 1997).

In sum, previous studies underlay a temporal dysfunction, when TBI patients were tested with duration that exceeds working memory span (Schmitter-Edgecombe & Rueda, 2008), and a greater variability in TBI performance also when patients were tested with durations not exceeding working memory span (Perbal et al., 2003).

However, the literature on time perception and frontal lobe patients shows temporal dysfunction even when frontal patients are engaged with duration in the seconds and milliseconds range (Nichelli et al., 1995; Harrington et al., 1998a; Mangels et al., 1998; Casini & Ivry, 1999; Rubia & Smith, 2004; Picton et al., 2006). As TBI and frontal patients may present lesions in similar brain regions and similar cognitive dysfunctions, we therefore predicted temporal dysfunction also when TBI patients were tested with durations in the few milliseconds range.

## **1.8 Study 1**

### ***1.8.1 Introduction***

In this study we investigate time perception in TBI patients employing a time discrimination task. Time discrimination task has previously been employed to investigate time perception in frontal patients (Nichelli et al., 1998; Mangels et al., 1998; Casini & Ivry, 1999; Rubia & Smith, 2004; Picton et al., 2006) but no studies have been conducted on TBI patients. In time discrimination tasks participants are required to perceive the stimulus duration; maintain the duration active in memory to quickly compare it with the second duration presented. High cognitive abilities are required to accurately perform time discrimination tasks, likewise working memory, attention and decisional processes (Paul et al., 2003; Le Dantec et al., 2007).

Moreover time discrimination tasks are particularly suitable to investigate the hypothesis of different temporal system engaged for duration above and below 1 s. In fact, different neural timing system has been associated with discrimination of duration sub- and supra-seconds (Rammsayer, 1999; Macar, Lejeune, Bonnet, Ferrara, Pouthas, Vidal, & Maquet, 2002; Lewis & Miall, 2003a, b). The timing of brief intervals is



frequently linked with motor control, because voluntary movements are typically of sub-second durations; the circuit used for brief durations may be located within the motor system (Matsuzaka, Aizawa, & Tanji, 1992; Arshavsky, Deliagina, & Orlovsky, 1997; Lewis & Miall, 2002). The cerebellum may also be involved in motor timing (Ivry & Keele, 1989) and it seems particularly appropriate for the measurement of brief durations (Lewis & Miall, 2003a). Therefore, several authors have suggested that time measurements of sub-seconds duration range are “automatic”, whereas judgments of supra-second durations required more “cognitively controlled” systems (Lewis & Miall, 2003a). Theoretically judgments of supra-second durations required additional attentional and working memory abilities (Block & Zakay, 1996; Rammsayer, 1999; Lewis & Miall, 2003a). Neuroimaging (Macar, Lejeune, Bonnet, ferrara, Pouthas, Vidal, & Maquet, 2002; Lewis & Miall, 2003a) and patients (Nichelli et al., 1995; Harrington et al., 1998a; Mangels et al., 1998; Casini & Ivry, 1999) studies showed involvement of the prefrontal and parietal cortices in timing associated with attention and working memory.

In this study we used the constant stimuli procedure and not an adaptive psychophysical procedure where the comparison stimulus varied from trial to trial. In classical adaptive psychophysical procedure participants are engaged with hundreds of trial to estimate the discrimination threshold; with constant stimuli procedure we could obtain performance accuracy testing participants within a short session time (approximately 10 min). The decision to employed constant stimuli discrimination task came from the necessity to used faster procedure that not engaged patients for a long session.

We predict that TBI patients would be less accurate than controls in particular when are required to discriminate few milliseconds duration because discriminating brief duration requires adequate attentional resources, working memory and high speed processing which are often compromise in TBI patients (Cooke & Kausler, 1995; McAllister et al., 1999; Azouvi, 2000). We explore the involvement of executive functions on time perception, participants with better attentional and working memory abilities would have better temporal abilities (Block & Zakay, 1996). Moreover, employing duration of 500 ms and 1300 ms we can investigate the hypothesis of different system involved to discriminate duration above and below 1 s.

## ***1.8.2 Materials and methods***

### ***1.8.2.1 Participants***

Twenty-seven TBI patients (F=8 and M=19) took part at the study. Demographic and clinical features of TBI patients were reported in Table1.2. The patients were all right-handed and had been referred to Modulo di Neuropsicologia Riabilitativa, UMR – Dipartimento di Neuroscienze/Riabilitazione Azienda Ospedaliero-Universitaria di Ferrara, Italy. Patients were tested at least 6 months post injury. All patients had CT or MRI scans, which showed mainly frontal lesions. Patients that had pre-existed neurological, psychiatric, or developmental disorders(s) or a history of treatment for substance abuse, or a history of previous head injury were excluded from the study. Patients provided verbal consent to participate in this study that was conducted in accordance with the Helsinki Declaration (59th WMA General Assembly, Seoul, 2008).

**Table 1.2** Demographic and clinical features of the TBI patients. Cause referred to the cause of accident; MB=moto-bike; Injury site referred to the prevalent site of injury; F=Frontal; F-T=Fronto-Temporal; F-P=Fronto-Parietal; DAD= Diffuse Axonal Damage; PTA= Post Traumatic Amnesia (days); GCS= Glasgow Coma Scale (Teasdale & Jennett, 1974); TPI=Time Post Injury (month); LCF=Level of Cognitive Function (Hagen, Malkmus, Durham, & Bowman, 1979); FIM/FAM= Functional Independence Measure/Functional Assessment Measure (Hall, Hamilton, Gordon, & Zasler, 1993).

	Sex	Age	Education	Cause	Injury site	PTA	GCS	TPI	LCF	FIM/FAM
1	M	49	13	car	F bilateral	90	11	18	7	93
2	M	19	8	car	F-T right	-	3	7	7	90
3	M	47	11	car	F bilateral	24	3	50	7	79
4	F	36	18	fall	F	120	6	49	8	81
5	M	46	7	car	F	-	-	15	6	86
6	M	42	18	bicycle	F-T left	35	10	6	7	96
7	M	18	8	car	DAD	28	5	6	7	95
8	M	22	8	car	DAD	-	-	20	6	90
9	M	32	8	car	F bilateral	42	-	14	6	86
10	F	44	13	car	F bilateral	-	8	26	7	93
11	F	46	13	fall	F	-	15	24	6	83
12	F	60	5	fall	F	24	-	24	6	85
13	F	18	8	bicycle	DAD	28	-	7	6	87
14	M	28	8	car	F-P left	-	6	34	6	86
15	F	41	18	car	DAD	-	-	21	6	86
16	M	58	18	MB	F bilateral	30	9	6	6	97
17	M	31	8	car	F right	120	-	80	6	82
18	M	32	8	car	F bilateral	-	6	108	8	95
19	M	28	13	car	F-P left	112	-	60	6	72
20	M	50	8	car	F-P left	150	-	90	6	67
21	M	43	8	car	F-T left	-	4	60	7	86
22	F	42	8	car	F-T left	35	5	21	7	83
23	M	31	16	MB	DAD	90	4	12	6	86
24	F	33	8	car	F-T right	-	15	15	6	74
25	M	50	5	car	F-P right	35	3	6	7	82
26	M	34	13	car	F right	42	6	10	7	94
27	M	20	13	car	DAD	-	-	25	8	82
	Mean	37.04	10.74	car		62.81	7	30.15	6.59	85.78
	(SD)	(11.98)	(4.10)	70%	frontal 83%	(43.00)	(3.84)	(27.78)	(0.69)	(7.38)

The control group included 27 participants (F=8 and M=19) all right-handed, who had never suffered from TBI. They have been recruited through the University of Padova and the community. Control group was matched to the patients on the basis of age and educational level. The mean age was 31.59 years (SD=7.04; range=22-45) and the mean level of education was 11.67 years (SD=3.47; range=8-18). The TBI group and the control group showed significant differences on age [ $t(52)=2.01, p<.05$ ] but not on level of education [ $t(52)=-.89, p=.375$ ]. None of control participants had any neuropsychiatric disorder or history of drug or alcohol abuse.

#### *1.8.2.2 Procedure*

TBI patients were tested individually in a quiet room at the Modulo di Neuropsicologia Riabilitativa, UMR–Dipartimento di Neuroscienze/Riabilitazione Azienda Ospedaliero - Universitaria di Ferrara, Italy. Controls were tested in a quiet room at the University of Padova. All tasks were presented on a 15-inch PC monitor and participants were seated from a distance of approximately 60 cm. E-Prime® 1.0 was used to program and run the experiments. All participants performed the experimental protocol in a fixed order: the time discrimination task, the Stroop task, the n-back task. Each task was preceded by a practice phase, no participants failed to understand the instructions displayed.

#### *1.8.2.3 Temporal task*

To test time perception participants performed a time discrimination task. Four pairs of stimuli were employed, each pair was composed by a standard and a comparison stimulus sequentially presented in a fixed order (standard-comparison). Two

standard durations were employed: 500 and 1300 ms. The comparison could have been longer (standard-long) or briefer (standard-brief). After the instruction, a 500-msec fixation point appeared on the computer screen and after 150 ms the standard stimulus. The comparison stimulus was  $\pm 25\%$  respect to the standard: standard-long (500 – 625 ms and 1300 - 1625 ms) or standard-brief (500 – 375 ms and 1300 – 975 ms). Each trial was presented 12 times. Participants were instructed to press two distinct keys marked with different letters: <L> if the second was longer than the first one [“L” referred to the Italian word “Lungo”=long] or press <B> if the second was shorter than the first one [“B” referred to the Italian word “Breve”=brief]. The stimuli used were smiley faces, black and white coloured presented centrally in a grey background. The participants were instructed to respond with their index fingers, and the response keys were balanced between subjects. A practice phase was included at the beginning of the task to clarify the instruction: Participants performed one time each pair of stimuli (500 – 625 ms; 500 – 375 ms; 1300 – 1625 ms; 1300 – 975 ms), the stimuli were the same used in the task, no feedback on performance was provided.

#### *1.8.2.4 Executive functions tasks*

A Stroop task was employed to study the attentional component. Each trial was composed by three colour words displayed centrally on the computer screen for 2 sec. The words were presented in Arial font 20 point size. The possible words were: RED, YELLOW, GREEN and BLUE. The central word was coloured in red, yellow, green or blue and the two laterals were always black coloured. The central word was the target stimulus whereas the two black lateral words were the possible responses (i.e. GREEN RED RED). Participants were instructed to judge the colour of the central word by

pressing a key on the keyboard marked with an arrow pointing either right (→) or left (←), depending on the position of the correct response. Whenever the answer was on the left, the (←) key had to be pressed with the left index finger, and whenever the answer was on the right, the (→) key had to be pressed with the right index finger. Two possible conditions were randomly presented: congruent and incongruent. In the congruent condition the colour of the central word corresponded with the written word (the word “RED” written with red ink. In the incongruent condition, the colour did not match the written word (the word “RED” written with green ink). Forty-eight stimuli were presented in each condition (total 96 stimuli) and equal number of correct responses were presented right or left (see Del Missier, Mäntylä, & Bruine de Bruin, 2010). A practice phase was included at the beginning of the task to clarify the instructions and to familiarize with the task: participants performed 10 trials, 5 in the congruent and 5 in the incongruent condition, no feedback on performance was provided.

N-back task was employed to study working memory component (for a review see Owen, McMillan, Laird, & Bullmore, 2005). The stimuli were common bi-syllabic words presented centrally in the computer screen displayed in Courier New font 36 point size, colour in white ink presented in a black background. Participants were instructed to indicate, by pressing the left mouse key, when they recognised the word as the same as the one 2 word back. The task comprised 48 target stimuli (24 different stimuli presented 2 times) and 48 non-target stimuli: 12 non-target stimuli were presented only one time, 12 stimuli were 3-back, 12 stimuli were 4-back and 12 stimuli were 5-back. A practice phase was included at the beginning of the task to clarify the

instructions and to familiarize with the task: Five target words and 10 non-target words were presented during the practice phase, no feedback on performance was provided.

### **1.8.3. Results**

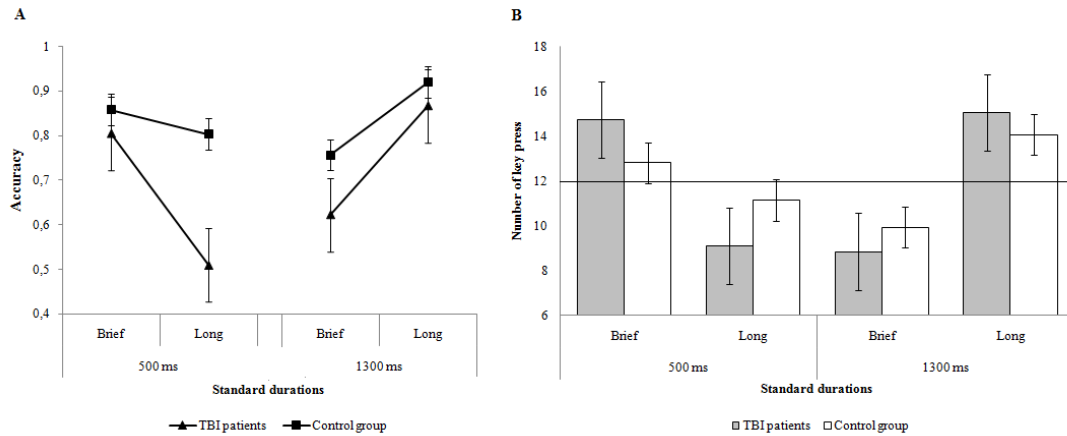
#### *1.8.3.1 Temporal task*

Time discrimination task were analyzed in term of response accuracy that reflects the percentage of correct responses. Data were included into mixed-model ANOVA with between factor of group (TBI vs. control) and within factors of standard duration (500 vs. 1300 ms) and presentation order (standard-brief vs. standard-long). The post-hoc analyses were performed with the Bonferroni correction.

The main effect for group [ $F(1,52)=27.60$ ,  $MSE=.035$ ,  $p <.0001$ ] and standard duration [ $F(1,52)=6.34$ ,  $MSE=.020$ ,  $p <.05$ ] were significant, whereas the main effect for the presentation order did not reach the significance level [ $F(1,52)=.22$ ,  $MSE=.050$ ,  $p=.64$ ,  $\eta^2_p=.004$ ]. The TBI patients were less accurate compared with the controls (70% vs 83%). Participants were more accurate when discriminating the 1300 ms compared with the 500 ms duration (79% vs 74%). The group  $\times$  standard duration [ $F(1,52)=4.34$ ,  $p<.05$ ] and standard duration  $\times$  presentation order [ $F(1,52)=79.02$ ,  $p<.0001$ ] interactions were significant. Interestingly, also the interaction group  $\times$  standard duration  $\times$  presentation order was significant [ $F(1,52)=14.22$ ,  $p<.0001$ ] (Figure 1.6A).

Significant differences were found between groups with 500 ms standard duration depending on the standard-comparison condition: TBI patients were less accurate than controls in the condition standard-long (500-625 ms). Opposite patter of results were found when the standard was 1300 ms: TBI patients were less accurate in the condition standard-brief (condition 1300-1625). No significant differences were

found between groups in the condition standard-brief when the standard was 500 ms and in the condition standard-long when the standard was 1300 ms.



**Figure 1.6 (A)** Accuracy in the time discrimination task as a function of standard duration, presentation order and group. “Brief” referred to the condition standard-brief condition and “Long” referred to the standard-long condition. **(B)** Number of key press as a function of standard duration, presentation order and group. Errors bar are presented in both figures.

TBI patients presented an order effect either with 500 than 1300 ms standard durations, patients were significantly impaired when discriminating standard-long order in the 500 ms and when discriminating standard-brief in the 1300 ms condition. No significant differences were found in the control group in the short-long order with the standard duration of 500 ms but significantly difference was found in the 1300 ms where controls performed worse when the discrimination was standard-short condition.

To further investigate the root of the interaction group  $\times$  standard duration  $\times$  presentation order we analysed the number of key press. Data were included into mixed-model ANOVA with between factor of group (TBI vs. control) and within factors of standard duration (500 vs. 1300 ms) and presentation order (standard-brief vs. standard-long). No main effects of group [ $F(1,52)=1.72$ ,  $MSE=.098$ ,  $p=.195$ ,  $\eta^2_p=.032$ ], stimulus



duration [ $F(1,52)=2.00$ ,  $MSE=.009$ ,  $p=.163$ ,  $\eta^2_p=.037$ ] or presentation order [ $F(1,52)=1.07$ ,  $MSE=.28.94$ ,  $p=.304$ ,  $\eta^2_p=.020$ ] were found. More interesting are the significant interactions stimulus duration  $\times$  presentation order [ $F(1,52)=121.50$ ,  $MSE=16.11$ ,  $p <.0001$ ] and group  $\times$  stimulus duration  $\times$  presentation order [ $F(1,52)=7.53$ ,  $p <.001$ ] (Figure 1.6B). Both groups showed a significantly greater tendency to respond “brief” with the 500 ms standard duration and “long” with the 1300 ms standard duration. With respect to the 500 ms standard duration significant difference was found between groups in the condition standard-long, TBI patients judged the comparison stimulus briefer than the standard even in the condition standard-long. When the standard duration was 1300 ms no significant differences were found between groups. In fact, both groups equally judged the comparison stimulus longer even in the condition standard-brief.

### 1.8.3.2. Executive functions tasks

We analysed the Stroop data in terms of reaction time (RT), and defined the attention index as the difference between incongruent and congruent RT. The results revealed significant differences between groups [ $t(45)=2.73$ ,  $p<.01$ ,  $d=1.27$ ]. TBI were more affected by interference compared to control (261 vs. 141 ms). N-back data were analysed in terms of number of errors (false alarms + omissions), and a significant difference was found between the groups [ $t(52)=1.97$ ,  $p<.01$ ,  $d=.53$ ] indicating that TBI patients produced more errors than controls (9.51 vs. 7.07).

### *1.8.3.3. Correlations between time perception, attention and working memory*

To examine the relationship between time perception, attention and working memory abilities a specific index for each task was calculated. Two separate indices were calculated for the two standard durations: Accuracy 500 and Accuracy 1300 indices were the mean of performance accuracy with the two standard durations in the time discrimination task. Two separate indices were also calculated for the number of key press for the two durations: the index Key 500 is the number of key press in the condition standard-brief for the 500 ms standard duration; while the index Key 1300 is the number of key press in the condition standard-long in the 1300 ms standard duration. The attention index (Attention) is the difference between RTs incongruent trials - RTs in congruent trials in the Stroop task. The working memory index (Working memory) is the number of errors made in the n-back task.

Two separate two-tailed Pearson correlation analyses were performed for TBI patients and controls (Table 1.3). In TBI patients significant correlations were found between working memory index and both Accuracy indices. TBI patients with better working memory abilities were also more accurate in time discrimination task. Moreover, significant correlation was found between Accuracy 1300 and Attention. Patients with better attentional resources had better temporal abilities. Concerning control group the only significant correlation was found between Accuracy 1300 and Working memory.

The two correlation analyses were also compared to better understand differences between TBI patients and controls ( $z$  Fisher). Working memory differently correlate with Attention 500 ( $z=2.53$ ,  $p<.01$ ). Significant correlation was found between the two variable in TBI patients ( $r=-.492$ ) indicating that TBI with better working

memory abilities had higher accuracy; no significant correlation was found in the control groups.

**Table 1.3** Pearson’s correlations between accuracy for the time discrimination task, number of key press, attention and working memory. The analysis has been conducted separately on TBI patients and controls.

	TBI patients		Control group	
	Attention	Working memory	Attention	Working memory
Accuracy 500	-.237	<b>-.492**</b>	-.322	.188
Accuracy 1300	<b>-.546**</b>	<b>-.617**</b>	-.358	<b>-.518**</b>
Key 500	-.119	-.141	.050	-.196
Key 1300	.356	-.088	-.248	.118

\* p<.05 \*\* p<.01

### **1.8.4 Discussion**

Previous studies conducted on TBI patients reported higher variability (Perbal et al., 2003) and less accuracy performance when patients were tested with durations that exceeded the working memory span (above 30 s; Schmitter-Edgecombe & Rueda, 2008; Anderson & Schmitter-Edgecombe, 2011). However, the literature on time perception and frontal lobe patients showed temporal dysfunction even when frontal patients are engaged with shorter duration in the milliseconds range (Nichelli et al., 1995; Harrington et al., 1998a; Mangels et al., 1998; Casini & Ivry, 1999; Rubia & Smith, 2004; Picton et al., 2006). This study was aimed to investigate temporal dysfunction in TBI patients engaging durations above and below 1s (500 and 1300 ms). Moreover, we investigate the involvement of attention and working memory on time perception and we predicted that participants with lower attentional and working memory abilities would present lower temporal abilities.

The novelty of this work was to investigate temporal ability in TBI patients with a time discrimination task. The time discrimination task it has been previously employed with frontal patients (Casini & Ivry, 1999) and it is a common task to investigate time perception (Block et al., 1998). Our results showed temporal dysfunction in TBI, in fact, patients were less accurate than controls when the standard duration was either 500 ms or 1300 ms. Moreover, TBI were significantly less accurate when discriminating 500 ms than 1300 ms, while no significant difference were found between durations within the control group. Discriminating 500 ms durations seem to be extremely challenging for TBI patients compare to control, maybe due to additional cognitive functions involved in time discrimination task in particular speed processing. Mangels's et al. study (1998) indicated that the human prefrontal cortex is involved in the active maintenance, monitoring and organization of time-based representation in working memory therefore the damage of frontal areas presented in TBI patients could explain the lower performance presented in patients.

Interesting are the results of the number of key press. Previous studies on time perception have already pointed out the interaction between standard duration and presentation order, often called time-order error (Hellström, 1985; Hellström & Rammsayer, 2004; Wiener, Turkeltaub, & Coslett, 2009). However the presence of this phenomenon is often neglected and it has never been investigate in TBI patients. We believed that the analysis of the interaction standard duration and presentation order may add further interest to the study of ability to discriminate time in TBI patients and gives additional information about cognitive processing in TBI. Our data are in line with previous studies that point out significant interaction between standard duration and presentation order in health adults (Paul et al., 2003; LeDantec et al., 2007; Gontier et

al., 2007; Gontier, Paul, Le Dantec, Pouthas, Jean-Marie, Berbard, Lalonde, & Rebai, 2009).

Different possible reasons may be offered for explaining this pattern of results. One could be a memory interference in which the representation of any stimulus in memory decay after a certain time (Baddeley, 1992). The memory interference may have made the first stimulus appearing briefer than the second one. This interpretation may be true for the 1300 ms standard duration when the standard-long condition achieved the higher performance. It is may be possible that because of the shortening of the standard stimulus due to a memory interference the difference between the standard and the comparison is more detectable (Paul et al., 2003). However, this is not the case for the 500 ms standard duration where the higher performances were obtained in the reverse condition (in the condition standard-brief). For these brief durations at the limit of the subjects' capacities, the standard-brief condition may have appeared easier because of a response bias in reporting the comparison stimulus as shorter (Paul et al., 2003; Le Dantec et al., 2007). Lewis and Miall (2003a) reported that briefer intervals are generally processed in a less controlled manner than longer ones, with the former relying more on subcortical regions (Mangels et al., 1998). Thus, at few milliseconds stimulus range, a briefer stimulus may be more easily detected as comparison stimulus than at standard duration. A wider interpretation that take into account short and long durations has been proposed by Gontier et al. (2007): participants create a "anchor" stimulus in memory and classified stimuli below approximately the "anchor" as short and above the "anchor" as long (see also Oshio, Chiba, & Inase, 2006). This could also be the case in our study: participants create a memory representation of "anchor" duration by averaging out the shorter (375 ms) and the longer (1625 ms) durations

presented and classified stimuli below approximately the “anchor” as short and above the “anchor” as long.

In this study we also investigate the involvement of attention and working memory in time discrimination task. In the TBI patients Accuracy 500 significantly correlate with working memory, no significant correlation was found in the control group, probably because this duration is within the control’s working memory capacity and does not required additional cognitive ability to be performed. In both groups Accuracy 1300 significantly correlate with working memory. Working memory resources seem to be involved when participants are required to discriminate longer duration (standard 1300 ms). No significant correlations were found between attention and Accuracy 500 consistent with the hypothesis that brief duration (above 1 sec) are may be processed in a less controlled manner (Lewis & Miall, 2003a, b; Mangels et al., 1998). Neither for TBI or controls number of key press correlated with attention or working memory component confirming that higher number of key pressing presented in the standard-brief condition (when standard duration is 500 ms) or standard-long condition (when standard duration is 1300 ms) is not cognitive controlled but probably more subcortical controlled (Lewis & Miall, 2003 a, b).

Taken together our results showed that TBI patients present temporal dysfunction even when tested with duration ranged within few milliseconds. TBI patients pressed significantly more the “brief” key when the standard duration was 500 ms, indicating that patients consistently underestimate the second stimulus presented. Instead, patients pressed significantly more the “long” key when the standard duration was 1300 ms indicating that patients consistently overestimate the second stimulus. Clinical assessments of TBI patients typically report attentional difficulties; when

patients are ensure about the stimulus duration they tend to give the most automatic response, whereas the controls did not demonstrated such strong bias. The nature of group differences on this task points to a disruption at the decision level, with patients adopting a more automatic strategy. When patients are forced to make a rapid decision they tend to produce the less effortful response. Attention and working memory were involved in time perception in particular when participants are required to discriminate duration above 1 s. Our data give additional support to the notion that two different systems may be responsible for elaborate duration above and below 1 s (Lewis & Miall, 2003a b).

## **1.9 Study 2**

### ***1.9.1 Introduction***

Results from Study 1 have demonstrated temporal dysfunction in TBI patients when tested with very brief duration ranging from 500 to 1300 ms. To our knowledge, Study 1 was the first study that point out temporal dysfunction in TBI patients with brief duration in fact, previous studies have found temporal dysfunction when patients were tested with duration longer than 30 s and discussed the results according to working memory dysfunction that affect temporal performance (Schmitter-Edgecombe & Rueda, 2008; Anderson & Schmitter-Edgecombe, 2011).

An important consideration has to be made on the methodologies employed to investigate time perception. As already point out (Methods to investigate time perception, pp. 18) different methodologies may be employed to test time perception and each one rely on different cognitive abilities (Allan, 1979; Zakay, 1990; 1993). In this study we investigate time perception in TBI patients employing three different

temporal tasks (time reproduction, time production and time discrimination) to have a wide overview on temporal abilities in TBI patients. We have selected those task because widely used on timing literature and because allowed us to employed different duration and they rely on different cognitive functions. In fact, when participants are tested with a time reproduction task after the presentation of the duration participants have to encode the duration, transfer the information to the memory stage and maintain the information active in the memory for the subsequent reproduction (Block & Zakay, 1996). According to the Attentional Gate model, attention and working memory abilities are involved in time reproduction tasks. Time production and verbal estimation tasks required to translate an objective duration into a subjective one and vice versa (Block et al., 1998). Since production and verbal estimation appear to reflect the same underlying temporal processes and mechanisms (Craig & Hay, 1999), but the latter method results in less accuracy than the former one (Zakay, 1990), the method of verbal estimation was not employed in the present study. Differences in the pacemaker rate are shown with time production task and it rely on attentional resources, in particular inhibition. Finally, time discrimination tasks required to quickly comparing two durations and estimate with one is the briefer or the longer one. Attention and speed processing are particularly involved in this task.

Participants performed the three temporal tasks under the same durations: brief (.5, 1 and 1.5 s) and long (4, 9, and 14 s) durations to investigate the suitability on each task in relation of brief and long durations. Participants undertake a neuropsychological evaluation to investigate attentional and working memory abilities. Correlation analysis would be subsequently conducted to investigate the different involvement of executive functions on time perception. We predict attentional and working memory involvement



on time reproduction task, in particular with long durations; attentional and inhibition abilities in time production tasks, while attention on speed processing would be mainly involved in time discrimination task.

An additional aim of this study is investigate possible similarities between temporal tasks and common underlying processes on time perception. Allan (1979) argued that no single method can claim consistent superiority and that there is no significant correlation among methods. Rammsayer (2001), however, point out that time discrimination is more sensible to detect temporal impairment in older adults when tested within the psychological present<sup>4</sup> (Rammsayer, 2001).

We hypothesise that TBI patients would present temporal impairment for long durations, when tested with time reproduction and time production tasks, which rely on attentional and working memory abilities. We also hypothesise a method superiority of time discrimination task to investigate temporal abilities with brief duration. In fact we predict temporal dysfunction in TBI, when tested with brief duration, only when performing the time discrimination tasks.

## ***1.9.2 Materials and methods***

### *1.9.2.1 Participants*

Fifteen TBI patients (F=6 and M=9) took part at the study (Table 1.4). Patients were all right-handed and had been referred to Neuroriabilitazione del Presidio Ospedaliero di Fossano-Caraglio (A.S.L. di Cuneo). Patients were tested at least 6 months post injury. Nine patients had sustained a head injury as a result of car accidents,

---

<sup>4</sup> The psychological present is defined as the period of time during which an interval can be processed as a unit (Rammsayer, 2001).

two as a result of bicycle accident and six as a result of motor vehicle accident. All patients had CT or MRI scans, which showed mainly frontal lesions. Patients that had pre-existed neurological, psychiatric, or developmental disorders(s) or a history of treatment for substance abuse, or a history of previous head injury were excluded from the study. Patients provided verbal consent to participate in this study that was conducted in accordance with the Helsinki Declaration (59th WMA General Assembly, Seoul, 2008).

**Table 1.4.** Demographic and clinical features of the TBI patients. Injury site referred to the prevalent site of injury; F=Frontal; F-T=Fronto-Temporal; F-T-P=Fronto-Temporo-Parietal; DAD= Diffuse Axonal Damage; T-P=Temporo-Parietal; TPI=Time Post Injury (month); LCF=Level of Cognitive Function (Hagen, Malkmus, Durham, & Bowman, 1979); GCS= Glasgow Coma Scale (Teasdale & Jennett, 1974).

	Gender	Age	Education	Injury site	Time post Injury	Days of coma	LCF	GCS
1	M	27	8	F	12	10	-	-
2	F	43	8	F-T-P	22	18	9	4
3	M	44	11	F dx	65	90	-	-
4	F	52	11	T-P	9	-	9	8
5	M	53	11	F	25	-	8	5
6	F	29	8	T-P	90	-	-	-
7	F	44	16	DAD	24	-	-	-
8	F	20	13	DAD	15	3	7	-
9	M	46	8	F-T-P	31	8	-	-
10	M	34	11	DAD	9	0	-	-
11	M	54	8	T-P	85	-	-	7
12	M	40	8	F bilateral	6	4	-	3
13	F	52	16	F-T-P	23	5	6	3
14	M	22	13	F	29	30	-	-
15	M	54	8	F-T dx	26	3	9	-
	M (SD)	40.94 (11.84)	10.54 (2.90)		31.4 (26.75)	17.1 (27.13)	8 (1.26)	5 (2.10)

The control group included 15 participants (F=7 and M=9), all right-handed, who had never suffered from TBI. They have been recruited through the community in Cuneo or at the University of Padova, Italy. Control group was matched to the patients on the basis of age and educational level. The mean age was 40.53 years (SD=11.63; range=20-54) and the mean level of education was 10.73 years (SD=2.81; range=8-16). The TBI group and the control group did not showed significant differences on age [ $t(28)=.093$ ,  $p=.92$ ] or on level of education [ $t(28)=-.192$ ,  $p=.849$ ]. None of control participants had any neuropsychiatric disorder or history of drug or alcohol abuse.

#### *1.9.2.2 Procedure*

TBI patients were tested individually in a quiet room at the Neuroriabilitazione del Presidio Ospedaliero di Fossano-Caraglio (A.S.L. di Cuneo). Controls, if recruited in Cuneo, were tested in a quiet room in their own house otherwise if recruited in Padova they were tested in a quiet room at the Department of General Psychology, University of Padova. All tasks were presented on a 15-inch PC monitor and participants were seated from a distance of approximately 60 cm. E-Prime® 2.0 was used to program and run the experiments. All participants performed the experimental protocol in two separate sessions: in the first session participants performed the temporal tasks, while in the second session they performed the neuropsychological assessment.

#### *1.9.2.3 Temporal tasks*

##### *Time reproduction task*

Participants were instructed to reproduce the duration of a previously seen stimulus under two conditions, simple and concurrent. In the simple condition, a

stimulus (“smiley” face) appeared at the centre of the computer screen for one of three short (500, 1000 and 1500 ms) or long (4, 9, 14 s) durations. Durations were randomly presented 4 times for a total of 24 stimuli presentations. After a 500 ms inter-stimulus interval, a question mark appeared on the computer screen and participants were instructed to press the spacebar for the same duration that the stimulus was on the screen. In the concurrent condition, we used the same apparatus and stimuli as employed in the simple condition, but in addition, digits appeared at the centre of the stimulus and participants should read these digits aloud. Digits ranged from 1 to 9 and were randomly presented with an inter-digit interval that varied from 400 to 1000 msec (Baudouin et al., 2006b). Participants completed a practice phase of both conditions before beginning the task (one time each duration); no feedback was provided.

#### *Time production task*

Participants were instructed to produce duration both in simple and concurrent condition. In the simple condition a sentence appeared at the centre of the computer screen indicating the duration to produce (e.g. “produce 10 seconds”). After a 1-second inter-stimulus interval, a question mark appeared on the computer screen and participants were instructed to press the spacebar for the duration required. A “smiley face” appeared at the centre of the computer screen as long as the participants keep press the space bar. Participants were required to produce short (500, 1000 and 1500 ms) and long (4, 9 and 14 s) durations four times (total 24 stimuli).

In the concurrent condition, we used the same apparatus and stimuli as employed in the simple condition, but in addition, digits appeared at the centre of the stimulus and participants should read the digits aloud. Digits ranged from 1 to 9 and were randomly presented with an inter-digit interval that varied from 400 to 1000 ms (Baudouin,

Vanneste, Pouthas, & Isingrini, 2006). Participants completed a practice phase of both conditions before beginning the task (one time each duration); no feedback was provided.

#### *Time discrimination task*

The time discrimination task was the same employed in Study 1 (see pp. 42). Participants were instructed to judge two different durations. Each trial was composed by a standard and a comparison stimulus sequentially presented in a fixed order (standard-comparison). However, in this study we used three different durations to be consistent with the brief durations employed in time reproduction and production tasks. The standard durations employed were: 500, 1000 and 1500 ms. The comparison stimulus was +/-25% respect to the standard: standard-long (500 – 625 ms, 1000- 1250 ms and 1500-1875 ms) or standard-brief (500 – 375 ms, 1000-750 ms and 1500-1125 ms). Participants completed a practice phase before beginning the task and no feedback was provided.

#### *1.9.2.4 Neuropsychological evaluation*

Participant performed Alertness, Go/Nogo and Working memory subtasks from Test of Attentional Performance 2.2 (TAP, Zimmerman & Fimm, 2002). Alertness refers to the condition of general wakefulness that enables a person to respond quickly and appropriately to any given demand. It is the pre-requisite for effective behaviour, and is in this respect the basis of every attention performance. The task measures the simple reaction time in response to a visual stimulus (a cross presented on the monitor). The Go/Nogo task taps the ability to perform an appropriate action under time pressure and to simultaneously inhibit an inappropriate behavioural response. Five different

configurations appeared at the centre of the computer screen, participants are required to press a designed key in response to the target stimulus and inhibit the distracter configuration. Finally the Working memory task tap the ability to actively maintain available and update information for solving complex problems. A sequence of numbers is presented on the computer screen. Participants are required to determine whether each number corresponds with the 2 back number. Moreover, participants performed the Trial Making Test (TMT, Bowie & Harvey, 2006) to measure the cognitive domains of attention, processing speed, mental flexibility and visual–motor skills. In part A, participants are required to connect a series of 25 numbers in numerical order. In part B, participants connected 25 numbers and letters in numerical and alphabetical order, alternating between the numbers and letters. The Digit span (forward) was used for measuring working-memory's storage capacity from WAIS-R (Wechsler, 1981). A sequence of three to eight numbers are presented and the participants had to immediately recall the sequence in the exact order.

### ***1.9.3 Results***

#### *1.9.3.1 Statistical analyses*

Time reproduction and production tasks data were analysed in terms of absolute and relative errors and coefficient of variation (CV) (Perbal et al., 2003). Three separate mixed-model ANOVA were run for each of the three dependent variables with group (TBI vs. control) as the between-subjects factor. Condition (simple and concurrent) and Stimulus duration (500 ms, 1000 ms, 1500 ms, 4 s, 9 s and 14 s) were entered as within factors. Absolute error reflected the number of timing errors (in seconds) regardless of their direction. Relative error was obtained by dividing each participant's time

reproduction by the time duration of the sample interval presented for that trial. This measure provided a standard score across the different time intervals, with coefficients above and below 1.0 indicative of overproductions and underproductions, respectively. The CV is computed by taking the ratio of the standard deviation (SD) over the reproduction mean. The CV index represents the variability in temporal judgment for each participant, and evaluates the consistency of time reproductions of the same target duration. Time discrimination task was analyzed in term of response accuracy that reflects the percentage of correct responses, and CV. Two separate mixed-model ANOVA were run for each of the two dependent variables with group (TBI vs. control) as the between-subjects factor. Standard duration (500, 1000 and 1500 ms) and presentation order (standard-brief vs. standard-long) were entered as within factors. For all the analyses the post-hoc were performed with the Bonferroni correction. *T*-test analyses were conducted to investigate different performances between TBI and controls on the neuropsychological tasks. To investigate the involvement of different cognitive functions on time perception we have run to separate two-tailed correlation analyses separately for TBI and controls. Moreover, correlation analyses were also conducted between the three temporal task to investigate common processes underlying temporal tasks.

### 1.9.3.2 Temporal tasks

#### *Time reproduction task*

Analysis of *absolute errors* revealed significant differences between group [ $F(1,28)=5.15, p<.05, \eta^2_p=.155$ ]. TBI patients were less accurate than controls (1.62 vs. 1.11 s). Moreover, condition [ $F(1,28)=18.95, p<.0001, \eta^2_p=.404$ ], and duration

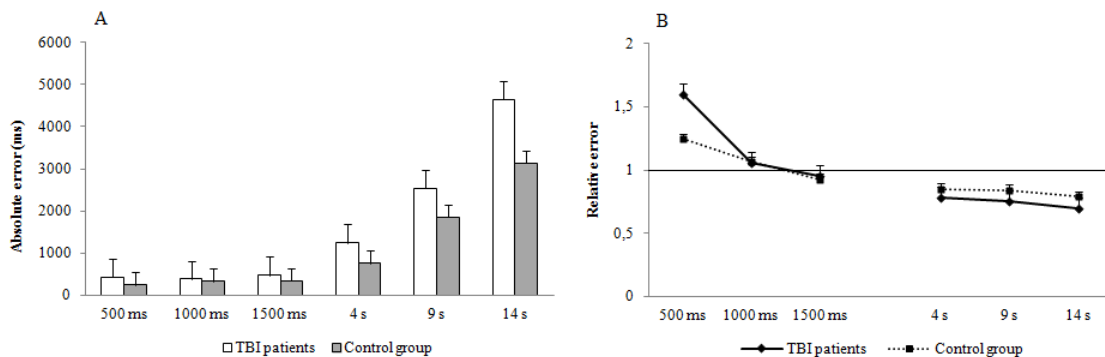
[ $F(1,28)=84.03, p<.001, \eta^2_p=.750$ ] main effects were significant. Performing a temporal task along with a concurrent non-temporal task increased the magnitude of errors compared with the simple condition. The magnitude of errors also increased with the duration to be reproduced. The condition  $\times$  duration [ $F(5,140)=20.55, p<.001, \eta^2_p=.423$ ] interaction was significant. Significant differences were found between condition only with the longer duration of 9 and 14 s. Participants were less accurate when the longer durations were performed with a concurrent non-temporal task. Within the simple condition, significant differences were found between brief and long durations and between all long durations. No significant differences were found between the short durations. The same pattern of results was found in the concurrent condition. Moreover, the group  $\times$  duration [ $F(5,140)=3.05, p<.05, \eta^2_p=.098$ ] interaction was also significant (Figure 1.6A). Significant differences were found between groups, TBI patients were less accurate than controls in the 500 ms duration and when reproducing longer durations. Within group TBI patients accurately reproduced the brief durations and were less accurate when reproducing longer durations. On the contrary controls were less accurate only when reproducing durations of 9 and 14 s.

Analysis of *relative errors* revealed no significant differences between group [ $F(1,28)=.063, p=.803, \eta^2_p=.002$ ]; both groups equally under-reproduced the durations presented (.97 vs. .95). The main effect of duration was significant [ $F(5,140)=27.778, p<.0001, \eta^2_p=.498$ ], participants over-reproduced the 500 ms duration, accurately reproduced 1000 ms and 1500 ms durations and under-reproduced the longer durations. No effect of condition was found [ $F(1,28)=1.13, p=.296, \eta^2_p=.039$ ]. Moreover the condition  $\times$  duration [ $F(5,140)=7.40, p<.001, \eta^2_p=.209$ ] interaction was found



significant. Participants were less accurate in the concurrent condition than in the simple condition. When participants were tested in the simple condition no difference were found between durations, whereas in the concurrent condition the brief durations were over-reproduced while the longer durations were under-reproduced. The group  $\times$  duration [ $F(5,140)=3.19$ ,  $p<.001$ ,  $\eta^2_p=.102$ ] interaction was also significant (Figure 1.6B). Significant difference was found between groups in the 500 ms duration. TBI patients significantly over-reproduced the duration. Within the TBI patients significant differences were found between all durations, while in the control group significant difference was only found between 2 and 4 s durations.

Analysis of CV revealed significant differences between groups [ $F(1,28)=7.78$ ,  $p<.0001$ ,  $\eta^2_p=.218$ ]: TBI patients were more variable than controls (.30 vs. .21). Significant effect of duration was found [ $F(5,140)=12.97$ ,  $p<.0001$ ,  $\eta^2_p=.317$ ], but no significant effect of condition was found [ $F(1,28)=.001$ ,  $p=.982$ ,  $\eta^2_p=.01$ ]. Moreover the condition  $\times$  group interaction was also significant [ $F(1,28)=7.78$ ,  $p<.001$ ,  $\eta^2_p=.228$ ]. TBI patients were more variable than controls in the simple condition while both groups were equally variable in the concurrent condition.



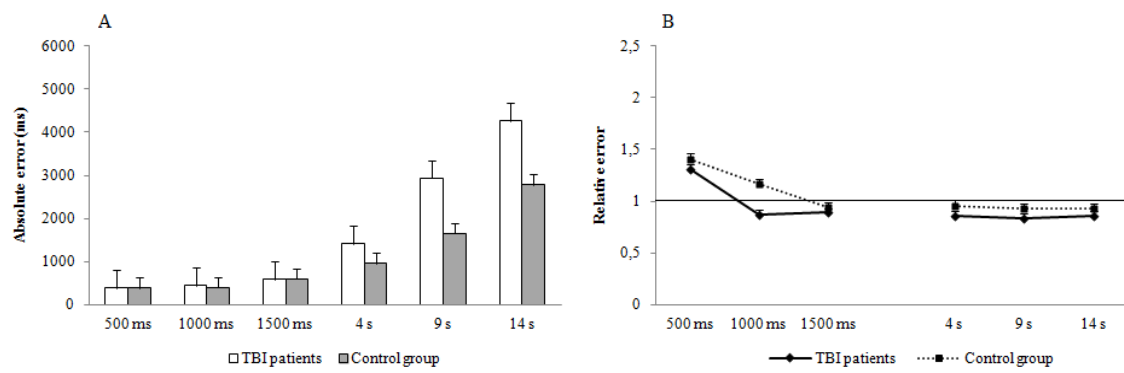
**Figure 1.6** Interaction between group and duration in time reproduction task. (A) Absolute error; (B) Relative error.

### *Time production task*

Analysis of *absolute errors* revealed significant differences between group [ $F(1,28)=11.20, p<.001, \eta^2_p=.286$ ], TBI patients were less accurate than controls (1.67 vs. 1.13 s). Significant main effect of duration was found [ $F(5,140)=116.37, p<.001, \eta^2_p=.806$ ], significant differences were found between all durations and the magnitude of absolute errors increased as the stimulus duration increased. No significant effect of condition was found [ $F(1,28)=.128, p=.723, \eta^2_p=.005$ ]. Moreover the group  $\times$  duration [ $F(5,140)=8.46, p<.001, \eta^2_p=.232$ ] interaction was also significant (Figure 1.7A). Significant differences were found between groups in all long durations, while TBI were as accurate as controls when producing brief durations. Significant differences were found between brief and long durations in both groups.

Analysis of *relative errors* revealed no significant difference between group [ $F(1,28)=1.24, p=.275, \eta^2_p=.040$ ], TBI patients slightly under-produced the duration while the controls slightly over-produced the durations (.93 vs. 1.05). Condition [ $F(1,28)=47.37, p<.001, \eta^2_p=.629$ ], and duration [ $F(5,140)=8.60, p<.001, \eta^2_p=.235$ ] main effects were significant. Producing durations in the simple condition determine an under-production, while producing durations in the concurrent condition an over-production (.82 vs. 1.17). Durations above 1 s were over-reproduced while duration above 1 s were under reproduced (1.35, 1.02, .91, .90, .88, and .89). Moreover the condition  $\times$  duration [ $F(5,140)=2.63, p<.05, \eta^2_p=.086$ ] interaction was significant, durations were significantly over-reproduced in the concurrent condition. No significant interaction group  $\times$  duration [ $F(5,140)=.473, p=.796, \eta^2_p=.017$ ] was found (Figure 1.7B).

Analysis of CV revealed significant difference between group [ $F(1,28)=12.64$ ,  $p<.001$ ,  $\eta^2_p=.311$ ]: TBI patients were more variable than controls (.30 vs. .20). The main effect of duration was significant [ $F(5,140)=13.49$ ,  $p<.001$ ,  $\eta^2_p=.325$ ], more variability was found when participants were asked to produce brief durations. No effect of condition was found [ $F(1,28)=.870$ ,  $p=.350$ ,  $\eta^2_p=.033$ ] and no significant interactions were found.

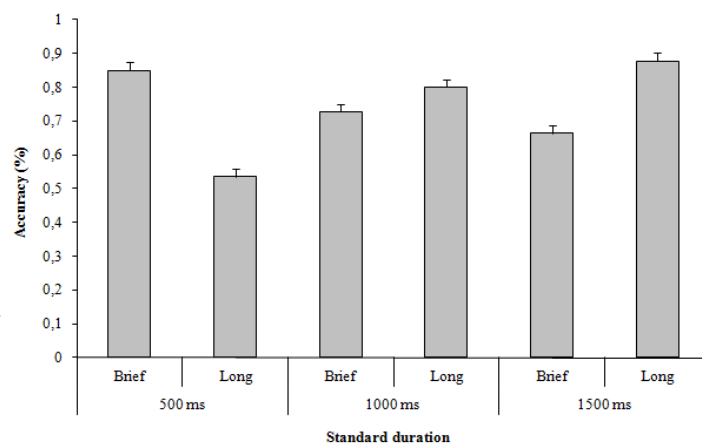


**Figure 1.7** Interaction between group and duration in time production task. (A) Absolute error; (B) Relative error.

### *Time discrimination task*

Analysis of *accuracy* revealed significant difference between groups [ $F(1,28)=5.89$ ,  $p<.05$ ,  $\eta^2_p=.174$ ]: TBI patients were less accurate than controls (68% vs. 80%). Significant effect of duration was also found [ $F(2,56)=5.63$ ,  $p<.001$ ,  $\eta^2_p=.167$ ] and a significant interaction duration  $\times$  presentation order [ $F(2,56)=33.21$ ,  $p<.001$ ,  $\eta^2_p=.543$ ] was found (Figure 1.8). Participants were more accurate in the condition standard-brief when the standard duration was 500 ms while, they were more accurate in the condition standard-long when the standard duration was 1500 ms. No effect of presentation order was found when the standard duration was 1000 ms.

Analysis of CV revealed significant difference between group [ $F(1,28)=6.46$ ,  $p<.01$ ,  $\eta^2_p=.187$ ]: TBI patients were more variable than controls (.75 vs. .47). Moreover, significant effect of duration [ $F(2,56)=6.05$ ,  $p<.001$ ,  $\eta^2_p=.178$ ] and significant interaction duration  $\times$  presentation order [ $F(2,56)=15.15$ ,  $p<.001$ ,  $\eta^2_p=.351$ ] were found. Data from the CV confirmed the results of accuracy, patients were more variable in the condition standard-long when the standard duration was 500 ms while, they were more variable in the condition standard-brief when the standard duration was 1500 ms. No effect of presentation order was found when the standard duration was 1000 ms.



**Figure 1.8** Time discrimination task. Interaction between standard duration and presentation order.

### 1.9.3.3 Neuropsychological assessment

TBI patients were generally less accurate than controls (Table 1.4). Patients produced more errors in Go/Nogo sub-task of TAP battery indicating attentional and working memory dysfunctions. Analysis of TMT task revealed that TBI patients were slower than controls on execution of both part A and part B, indicating attentional and shifting dysfunction in TBI patients. Patients presented lower performance in the digit

span task forward indicating attentional dysfunction. No differences were found between groups in the Alertness and Working memory sub-tasks.

**Table 1.3** Mean and standard deviation (SD) from the neuropsychological evaluation. Table also reports *t* and Cohen's *d*.

	<b>TBI patients</b> (n=15)	<b>Control group</b> (n=15)		
	M (SD)	M (SD)	<i>t</i>	<i>d</i>
<b>Alertness (error)</b>	3.53 (1.99)	4.47 (3.29)	-.93	-.34
<b>Go/Nogo (error)</b>	3.67 (3.92)	1.34 (.72)	2.67*	.83
<b>Working memory (error)</b>	13.46 (11.38)	8.34 (7.02)	1.49	.54
<b>TMT a (s)</b>	47 (11)	31 (11)	3.64*	1.45
<b>TMT b (s)</b>	137 (43)	84 (24)	4.15*	1.52
<b>Digit span</b>	5 (.88)	6 (.67)	-3.01*	-1.27

\**p*<.05

#### 1.9.3.4 Correlation analysis between temporal tasks and neuropsychological tasks

Two-tailed correlation analyses were conducted separately on TBI patients and controls. Time reproduction and time production indices referred to absolute errors on time reproduction and time production tasks with brief and long durations. Time discrimination index referred to accuracy performance on time discrimination task. Alertness, Go/Nogo and Working memory indices, referred to the number of errors in those tasks. TMT A and TMT B indices referred to the total time employed to perform the tasks, while Digit span index referred to the performance in the digit span task (forward) (Table 1.5).

Different pattern of results were found within the TBI patients and in the control group. Working memory and attentional abilities are involved in time reproduction in the control group, in fact significant correlations were found between time reproduction

task (long duration), Working memory and Digit span indices. Alertness and Go/Nogo indices significantly correlate with time production (long duration), indicating that controls participants with lower attentional and inhibitory abilities had lower performance in the time production task. Time discrimination index significantly correlate with Digit span index both in TBI patients and in controls. Participants with better attentional resources were also more accurate in the time discrimination task. Only for TBI patients time discrimination task significantly correlate with Alertness index indicating that TBI patients with better alertness abilities had higher performance in time discrimination task.

**Table 1.4** Correlation analysis conducted separately on TBI patients and control group between temporal and executive functions tasks. Time reproduction and time production indices referred to the absolute errors on these tasks conducted with brief durations and long durations. Time discrimination index refers to accuracy in time discrimination task. Alertness, Go/Nogo and Working memory indices referred to the number of errors. The TMT A and TMT B referred to time to perform the TMT parts. The Digit Span index referred to the performance (number of correct responses) on the forward digit span task.

	TBI patients					Control group				
	Time Reproduction		Time Production		Time Discrimination	Time Reproduction		Time Production		Time Discrimination
	Brief durations	Long durations	Brief durations	Long durations		Brief durations	Long durations	Brief durations	Long durations	
<b>Alertness</b>	.355	.207	.197	.375	<b>-.496*</b>	.138	-.128	.131	<b>.558*</b>	-.043
<b>Go/Nogo</b>	.318	.087	-.361	.189	-.121	.335	.033	.060	<b>.682**</b>	.184
<b>Working Memory</b>	.198	.236	.052	.205	-.147	-.112	<b>.510*</b>	.164	.062	.057
<b>TMT a</b>	.050	-.213	-.153	-.041	-.081	-.164	.187	.061	.016	.307
<b>TMT b</b>	.248	-.043	-.150	.183	-.174	-.222	.019	-.186	-.350	-.120
<b>Digit Span</b>	-.233	.051	-.003	-.354	<b>.561*</b>	-.273	<b>-.484*</b>	-.368	.082	<b>.604**</b>

\* $p < .05$ ; \*\* $p < .01$

### 1.9.3.5 Correlation analysis between temporal tasks

Two-tailed correlation analyses were conducted separately on TBI patients and controls to investigate possible underlying processes in temporal tasks (Table 1.6). Indices included in these analyses are the same used in the previous correlation analysis. In time reproduction and time production task we considered the data from the simple condition conducted with brief durations. We did not include the data from the concurrent conditions because we did not have similar condition in the discrimination task, for the same reason we included only the data of the brief durations.

**Table 1.5** Correlation analysis conducted separately on TBI patients and controls between temporal tasks. Time reproduction and time production indices referred to the absolute errors on these tasks conducted under simple condition with brief durations. Time discrimination index refers to accuracy in time discrimination task.

	TBI patients (n=15)		Control group (n=15)	
	Time Production	Time Discrimination	Time Production	Time Discrimination
<b>Time Reproduction</b>	.270	-.604*	.529*	-.581*
<b>Time Production</b>		-.352		-.812**

\* $p < .05$ ; \*\* $p < .01$

Significant correlation was found between time reproduction task and time discrimination task both in TBI and controls. Participants that were less accurate in time reproduction tasks were also less accurate in time discrimination task. In the controls group significant correlations were also found between time reproduction and time production and between time production and time discrimination. Nevertheless, in the TBI

group the same correlations were not significant the correlation coefficients were medium according to Cohen (1992).

#### ***1.9.4 Discussion***

This study was conducted to investigate time perception in TBI patients and the involvement of executive functions on temporal performance. To this end we tested participants with three different temporal tasks that underline different temporal abilities and involved different attentional and working memory abilities (Allan, 1979; Zakay, 1990; Grondin, 2008, 2010). Previous studies have found temporal dysfunction in frontal lobe patients (Nichelli et al., 1995; Harrington et al., 1998; Casini & Ivry, 1999) considering that there is a high incidence of frontal lobe dysfunction with TBI patients (Cooke & Kausler, 1995; McAllister et al., 1999) and considering that timing relies on various cognitive processes such as attention and working memory which are often affected in patients with TBI (Gronwall, & Wrightson, 1981; Azouvi, 2000; Mangels, Craik, Levine, Schwartz, & Stuss, 2002) is not surprising to expect temporal dysfunction in TBI patients.

We expected temporal dysfunction in TBI patients in particular when performing a concurrent secondary task. Performing a concurrent no-temporal secondary task reduce the attentional resources to time (Block, 1990; Block & Zakay, 1996) producing lower temporal performance, therefore, TBI patients with reduced attentional resources should be particularly affected by the concurrent secondary task. Moreover, we hypothesised an effect of duration on temporal performance. In particular we predict accurate performance for brief durations (500, 1000, and 1500 ms) and lower performances for long durations (4, 9, and 14 s) that required more attentional and



working memory resources. Participants also performed neuropsychological tasks to investigate the involvement of attention, working memory and executive functions on temporal abilities.

Temporal dysfunction was observed in TBI patients in fact they were less accurate and more variable than controls in all temporal tasks. Time reproduction and time production temporal performance was analysed in term of absolute and relative errors and CV. Each score reflects different characteristics of temporal performance, in particular: absolute errors reflected the magnitude of the participant's errors in timing regardless of the direction of the error; relative errors reflect the direction and magnitude of the error; and the CV is a measure of timing variability and allowed us to evaluate how consistent participants were in their temporal performance of the same target interval. Time discrimination performance was evaluated in term of accuracy (percentage of correct responses) and CV.

Analysis of absolute errors revealed that temporal performance of TBI patients on time reproduction and time production was significantly impaired when patients performed longer durations. This pattern of results is consistent with the notion that temporal performance decrease as the length of the stimulus duration increase probably due to reduction in attentional and working memory resources (Zakay & Block, 2004; Meyers & Levin, 1992; Perbal et al., 2002, 2003). This was particularly true for TBI patients that presented attentional and working memory dysfunctions and performed significantly worse than controls on longer durations. Analysis of relative errors showed similar pattern of over- and under-reproduction in TBI patients and controls. Participants over-reproduced 500 ms duration, where accurate when reproducing 1000 and 1500 ms and under-reproduced longer durations. The analysis of CV revealed that

TBI patients were more variable than controls. Similar performances were observed when participants performed time production task. The analysis of absolute errors revealed lower performance when TBI produced longer durations that were also significantly under-reproduced. The analysis of time production CV revealed higher variability in TBI patients likewise it was observed in the time reproduction task.

Analysis of temporal performance in time discrimination task revealed temporal dysfunction in TBI patients when tested with brief duration. This pattern of results confirmed our previous finding (Study 1) and extended them with different intervals (Study 1 two standard durations: 500 ms to 1300 ms; Study 2 three standard durations: 500, 1000, and 1500 ms). Significant interaction between duration and presentation order was also found. Participants were more accurate in the condition standard-brief when the standard duration was 500 ms while, they were more accurate in the condition standard-long when the standard duration was 1500 ms, while, no effect of presentation order was found when the standard duration was 1000 ms. Analysis of CV revealed greater variability in TBI patients compare to controls.

Higher temporal variability in TBI patients is explained in terms of difficulties in attention and working memory processes and/or in the decision mechanism (Brouwer et al., 1989; Nichelli et al., 1995). In sum, TBI patients were less accurate when tested with long durations in time reproduction and time production tasks, but, when tested with brief durations, TBI patients were less accurate with the time discrimination task.

Previous studies have point out the involvement of attention and working memory in time perception in particular when participants were tested with long durations (Schmitter-Edgecombe & Rueda, 2008; Anderson & Schmitter-Edgecombe, 2011). In Schmitter-Edgecombe and Rueda (2008) study significant differences were

found between groups when participants were tested with 45 and 60 s. The authors concluded that episodic memory dysfunctions occurred for temporal dysfunctions with long duration that exceeded the memory span. However, their conclusion was not confirmed by a subsequent study conducted by Anderson and Schmitter-Edgecombe, (2011) that retested Schmitter-Edgecombe and Rueda's participants under the same temporal task. TBI patients verbally estimate all duration as accurate as control despite the presence of episodic memory dysfunctions. Important considerations have to be made regarding the temporal methodology employed in these studies.

Our study extends previous findings and showed that TBI patients and controls differently recruited executive functions to perform temporal tasks. In fact, significant correlations were found between working memory, attention (digit span) and time reproduction task (long durations) in the control groups while no significant interactions were found in the TBI patients. Concerning the time production task, significant correlations were found between inhibition (Go/Nogo), alertness and time production task (long duration), while no significant correlations were found in the TBI patients. Finally, concerning the time discrimination task, significant correlations were found with attention (digit span) both in TBI patients and controls, while alertness significantly correlated with time discrimination task only in TBI patients. It is possible that control participants with better executive functions recruited the cognitive abilities required to accurately perform the temporal tasks. Inaccurate or variable duration judgments reported in frontal patients have been mainly related to the involvement of the frontal lobes in working memory and attention processes (Binkofski & Block, 1996; Mimura et al., 2000). Binkofski and Block (1996) reported the case of a single patient with left frontal lesions whose production of a 60 s duration was lengthened considerably in

comparison with the actual time. According to the authors, the frontal lesions could have either reduced the available attentional resources or slowed the rate of the internal clock.

To the best of our knowledge only four studies have been conducted to investigate temporal abilities in TBI patients (Meyers & Levin, 1992; Perbal et al., 2003; Schmitter-Edgecombe & Rueda, 2008; Anderson & Schmitter-Edgecombe, 2011) and direct comparison between studies is complicated by different durations and methodologies employed. The novelty of this study was to test participants with three temporal tasks, not only to have a wide view on temporal abilities on TBI patients but also to investigate intrinsic characteristics of each temporal task, in particular the relationship between temporal intervals and temporal task employed.

Each method activates different time-related processes and lead to different responses. Allan (1979) argued that no single method can claim consistent superiority and there is no correlation among methods. Our data contrast these conclusions and pointed out significant correlations among different temporal tasks and superiority to time discrimination task when employed brief duration (in the range between hundreds of millisecond to very few second). We agree with previous finding that pointed out differences between temporal tasks, in fact different processes are involved when performing different temporal tasks (Block, 1990; Zakay, 1990, 1993). Our finding, however, suggested the existence of common processes that underlie temporal tasks.

Moreover, our finding showed task sensitivity to the temporal duration employed. When participants are engaged with longer durations time reproduction and time production better point out group differences, while, when participants were tested with brief duration better groups differences emerged with time discrimination task.

Rammsayer (2001) tested young and older adults in time reproduction and time discrimination within the same protocol and found superiority of time discrimination task to investigate temporal abilities within the framework of psychological present.

### **1.10 General discussion**

In this session we investigate temporal abilities in TBI patients. Temporal dysfunctions were expected in TBI patients due to the frontally mediated executive dysfunctions often present in TBI patients (Lezak et al., 2004, Boelen et al., 2009; Hartikainen et al., 2010; Stuss, 2011) that might have affected temporal abilities (Perbal et al., 2002 Rubia, 2006;). Temporal impairment was found in frontal lobe patients both when tested with brief (Nichelli et al., 1995; Harrington et al., 1998a; Mangels et al., 1998; Casini & Ivry, 1999;) and long durations (Binkofski & Block, 1996; Mimura et al., 2000). However, past researches on time perception and TBI patients have not pointed out clear temporal impairment in TBI patients (Meyers & Levin, 1992; Perbal et al., 2003; Schmitter-Edgecombe & Rueda, 2008; Anderson & Schmitter-Edgecombe, 2011) and they have never investigated time perception with brief duration (ranging hundreds of milliseconds; see Table 1.1). However, investigating temporal abilities in the range of hundreds of milliseconds gives important information about temporal abilities in TBI patients. Perceiving and act in the range of brief duration is commonly required in daily life activities in fact it is crucial for motor control, speech generation and recognition and playing music (Buhusi & Meck, 2005).

In the first study we have employed durations between 500 and 1300 ms and tested participants with a time discrimination task which Rubia et al. (1999) have pointed out to be purest measure to investigate time perception. The results showed

temporal dysfunction in TBI patients in particular when tested with 500 ms. Discriminating 500 ms durations seem to be extremely challenging for TBI patients compare to control, maybe due to additional cognitive functions involved in time discrimination task in particular speed processing. Interesting were the results of the number of key press that indicated a response bias due to the interaction between stimulus duration and presentation order (time-order error; Hellström & Rammsayer, 2004). Both TBI and controls were less accurate when discriminating standard-brief order in the 1300 ms but only TBI patients presented also a response bias when discriminating standard-long order in the 500 ms. Correlation analysis were conducted to investigate the involvement of attention and working memory in time discrimination task. Working memory abilities are involved in discrimination 500 and 1300 ms in TBI patients while only with 1300 ms duration in the controls group probably because this duration is within the control's working memory capacity and does not required additional cognitive ability to be performed. Attentional resources were also involved in TBI patients when the standard duration was 1300 ms. No significant correlations were found between attention and Accuracy 500 consistent with the hypothesis that brief duration (above 1 sec) are may be processed in a less controlled manner (Lewis & Miall, 2003a, b; Mangels et al., 1998). Neither for TBI or controls number of key press correlated with attention or working memory component confirming that higher number of key pressing presented in the standard-brief condition (when standard duration is 500 ms) or standard-long condition (when standard duration is 1300 ms) is not cognitive controlled but probably more subcortical controlled (Lewis & Miall, 2003 a, b).

Study 2 was conducted to further investigate temporal abilities in TBI patients by testing participants with a wide number of temporal tasks that pointed out different

characteristics of temporal performance. Participants performed the time reproduction, time production and time discrimination tasks under two range of durations: brief (.5, 1, and 1.5 s) and long (4, 9, 14 s). TBI presented a temporal impaired when tested with long duration in the time reproduction and time production tasks while no significant differences were found between groups when tested with brief durations. Although, time discrimination tasks seems to be a better task to underlay temporal differences when participants are tested with brief durations. Our finding showed task sensitivity to the method and to the temporal duration employed.

Likewise in Study 1, temporal impairment was observed in TBI patients when tested with time discrimination task and it was also observed a standard duration and presentation order effect. Participants were more accurate in the condition standard-brief when the standard duration was 500 ms while, they were more accurate in the condition standard-long when the standard duration was 1500 ms. No effect of presentation order was found when the standard duration was 1000 ms. These and results from Study 1 give additional support to the notion that two different systems may be responsible for elaborate duration above and below 1 s (Lewis & Miall, 2003a b).

## **CHAPTER 2**

### **PROSPECTIVE MEMORY**

#### **2.1 Introduction**

Our capacity to shape and direct our future behaviour is of fundamental importance in the development, pursuit, and maintenance of an independent and autonomous lifestyle from early childhood to late adulthood. Prospective memory is the ability to form an intention and to remember to perform the future actions (Ellis, 1996; Kliegel, McDaniel, & Einstein, 2008a). Prospective memory is essential for many daily activities, such as remembering to pick up something at the market after work, remembering a birthday, or remembering to call a friend. Prospective memory dysfunctions can be particularly frustrating for traumatic brain injury (TBI) patients because their returning to independent lifestyle may depend upon proper prospective memory abilities (Fleming, Shum, Strong, & Lightbody, 2005). For example, forgetting to take medications or to go to the doctor's appointment could have serious consequences in rehabilitation of TBI patients. Thus it is important to understand the mechanisms involved in prospective memory, the effect on TBI independence living and developing adequate rehabilitation projects. In this second section we review the literature on prospective memory, focusing on main theories and studies that involved TBI patients. We also present two studies developed to investigate prospective memory dysfunctions in TBI patients and the underlying mechanisms involved on prospective memory performance.

In the first study we focused on TBI time-based prospective memory performance, in which participants are required to perform an action when a specific



amount of time was elapsed. A recent work by Shum and co-workers (2011) reviewed 14 behavioral studies that investigated prospective memory performance on TBI patients (Shum, Levin, & Chan, 2011). TBI patients presented event-based prospective memory dysfunctions and their lower performance was explained according to memory rather than executive dysfunctions (Kinch & McDonald, 2001; Maujean, Shum, & McQueen, 2003). TBI patients, however, often present executive functions deficit and the involvement of executive functions are often showed on time-based prospective memory tasks. Thus, it is not surprising to find time-based prospective memory dysfunctions in TBI patients but fewer studies have been conducted to investigate this issue (Shum, Valentine, & Cutmore, 1999; Kinch & McDonald, 2001; Carlesimo, Formisano, Bivona, Barba, & Caltagirone, 2004a; Mathias & Mansfield, 2005). It seems particularly interesting to investigate time-based prospective memory dysfunctions in TBI patients not only for the clinical implications but also for theoretical reason to further investigate the involvement of executive functions on time-based prospective memory. Moreover, no previous studies have investigated the involvement of temporal abilities on time-based prospective memory on TBI patients. Considering the temporal dysfunction present in TBI patients (Study 1 and Study 2) and that temporal abilities maybe involved on time-based prospective memory tasks (Glickson & Myslobodsky, 2006) we hypothesized that time-based prospective memory dysfunctions in TBI patients maybe also due to temporal dysfunction beside executive dysfunctions.

The second study investigates event- and time-based prospective memory in TBI patients with an ecological task. The Virtual Week has already been used in studies with healthy older adults (Rendell & Craik, 2000; Rose, Rendell, McDaniel, Abele, & Kliegel, 2010; Abele, Rendell, Rose, McDaniel, Kliegel, 2010) and different

pathologies, like Alzheimer disease (Ozgis, Rendell, & Henry, 2009; Will, Rendell, Ozgis, Pierson, Ong, & Henry, 2009; Thompson, Henry, Rendell, Withall, & Brodaty, 2010), multiple sclerosis (West, McNerney, & Krauss, 2007; Rendell, Jensen, & Henry, 2007a) alcohol and drugs users (Rendell, Gray, Henry, & Tolan, 2007b; Rendell, Mazur, & Henry, 2009) to investigate prospective memory and we recon is a promising method to investigate prospective memory also with TBI patients. A strong point of this task is the intuitive format that looks like a board game with a dice to roll, decision to make and activities to remember. After the training phase, participants easily move through the game with no particular trouble. Moreover, it includes both event-and time-based tasks, but also regular and irregular activities giving information about possible learning effect on regular tasks. Regular activities refer to routine and recurring activities whereas irregular activities are refer to tasks than change every day.

## **2.2 Models and theories of prospective memory**

Prospective memory is the ability to carry out later intention, is the memory for activities to be performed in the future, such as remembering to purchase a loaf of bread on the way home or remembering to give someone a telephone message (Ellis, 1996; Kvavilashvili, 1987). Prospective memory differentiates from retrospective memory, which is the memory for past events, such as remembering the characters from a movie or remembering the words from a list learned in an experiment (Brandimonte, Einstein, & McDaniel, 1996). Unlike retrospective memory, we know very little about prospective memory and the remembering intention (Baddeley & Wilkins, 1983; Ceci & Bronfenbrenner, 1985; Kvavilashvili, 1987; Brandimonte et al., 1996; Kliegel et al., 2008a); only in the last years an increasing number of studies have been conducted on

prospective memory (Kvavilashvili, 1992; Einstein & McDaniel, 1990; Einstein, McDaniel, Richardson, Guynn, & Cufer, 1995; Brandimonte et al., 1996; Ellis & Kvavilashvili, 2000; McDaniel & Einstein, 2000; Henry, MacLeod, Phillips, & Crawford, 2004; Kliegel et al., 2008a).

The majority of the first studies conducted on prospective memory involved older adults probably because memory dysfunctions are well documented in older adults (Light, 1991). Craik (1986) suggested that older adults have difficulty performing self-initiated retrieval process. Prospective memory tasks that provide subjects with little external support for retrieval should show large age-related decrements compare to prospective memory tasks that provide higher environmental support. However, when older and younger adults were tested in naturalistic settings and were required mailing post cards, telephoning the experimenter or sending a questionnaire at specified times in the future different patterns of results have been obtained (Wilkins & Baddeley, 1978; Meacham & Leiman, 1982; West, 1988; Dobbs & Rule, 1987; Einstein & McDaniel, 1990). Specifically, some studies showed age-related differences between older and younger adults (Dobbs & Rule, 1987), while others studies showed similar performances between groups (West, 1988). Considering that participants were tested in naturalistic setting, authors have suggested that they may have used different external aids to perform the prospective memory tasks, sometimes efficiently others times inefficiently. Moreover, authors could not even be sure that a subject's failure meant a failure to remember; in fact a number of non-memory factors (contingent or motivational) might have prevented a subject from mailing or phoning.

To solve the methodological issues rising from studies conducted in naturalistic setting, Einstein & McDaniel (1990) developed a more controlled laboratory method to

investigate prospective memory. The essential characteristic of their paradigm was to have subjects performing an ongoing task (i.e. a short-term memory task), while at the same time requiring participants to perform an activity at future specified times (press a designed key when the target word appeared during the short-term memory task). The authors also varied whether or not participants could use external memory aid (Experiment 1) or varied the familiarity of target event (Experiment 2) and expected large age-related decrement in prospective memory performance. The results confirmed the sensitivity of the paradigm for studying prospective memory and allowed a clear level of control when evaluating the influence of variables, however, surprising the results showed no age-related differences on prospective memory tasks. Older adults accurately remembered to perform the prospective memory tasks, regardless of the availability of external aids and regardless of the familiarity of the target event (Einstein & McDaniel, 1990).

The results obtained by Einstein and McDaniel (1990) seem to contradict Craik's (1986) theory that prospective memory tasks are highly self-initiated. Perhaps a reasonable explanation is that, prospective memory tasks like retrospective memory tasks (Herman & Neisser, 1978) vary in the degree to which they require self-initiated retrieval processes for successful memory. In fact, different situations may occur when performing prospective memory tasks. In a situation requiring to deliver a message to a friend when we see him or to press a key on the keyboard when the target word appear, the actions have to be done when a certain external event or cue occur. Different situation is when we have to meet a friend at 5:00 pm or that a medication every 6 hours. In these situations no external cue drive our actions and subjects must remember to monitor and initiate the prospective memory action on their own. Researchers

referred to the former situation as *event-based* and to the later one as *time-based*. From this perspective, event-based prospective memory tasks, like the one used in Einstein & McDaniel (1990) might not be so demanding because contained external cues that guided retrieval. On the other hand, time-based prospective memory tasks, because involved more self-initiated retrieval than do event-based tasks, might be more demanding (Einstein & McDaniel, 1990; Einstein et al., 1995).

Although past researches tended to characterize prospective memory task as a unitary process, prospective memory is a very complex process and contain different characteristics. For example, considering the situation in which your father's friend phone and asks you to deliver a message to you father, now you committed yourself to two memory tasks: one is remember the content of the message and second remember to deliver it to our father. Remembering the content of a prospective memory task seems essential to perform the prospective memory task and we refer to this as the *retrospective component* of a prospective memory task. However, remembering only the content of the prospective memory task will not produce successful performance. We have to remember to perform this action in the appropriate moment in the future. This may be labelled the *prospective component* of prospective memory tasks (Einstein & McDaniel, 1996).

Thus, a critical aspect of success on a prospective memory task is not only due to recall the content of that task, but also to retrieve the action at an appropriate moment. Prospective memory requires that at some point in the future, individuals remember to perform an action without being put in a retrieval mode by an external agent. Attentional processes are involved to switch from the ongoing task to the intended action that has to

be performed (McDaniel & Einstein, 2000; Einstein, McDaniel, Thomas, Mayfield, Shank, Morrisette, & Breneiser, 2005).

One approach to understanding how people accomplish this kind of retrieval is to assume that human beings have an executive attentional system that consciously monitors the environment for prospective memory target events (the Supervisory Attention System; SAS, Shallice & Burgess, 1991). The SAS would monitor the environment for the cue to perform the intended action, once the cue is encountered would interrupt the ongoing activity in order to execute the action (Burgess & Shallice, 1997; Smith, 2003). The key assumption is that some attentional resources are voluntarily developed for continuously monitoring environment and periodically bring the intended action into mind (McDaniel & Einstein, 2000; Smith, 2003; Smith & Bayen, 2004). Another approach is to assume that the cognitive system relatively automatically responds to the occurrence of the target events in the environment (Einstein & McDaniel, 1996). Following this approach, people rely on spontaneous attentional processes to retrieve intentions when prospective memory cue are encountered. The assumption is that participants do not monitor the environment for the cue and instead that remembering occurs when the cue is presents (Einstein & McDaniel, 1996; Guynn, McDaniel, & Einstein, 2000). McDaniel and Einstein (2000) proposed the multiprocess view, which takes into account evidence for both monitoring and spontaneous retrieval processes. The central tenet of this model is that people use multiple approaches in retrieving an intention, and depending on task, context and individual differences, tasks can be initiated by automatic monitoring (where cues seemingly ‘pop into mind’) or instead by strategic, effortful monitoring (Smith, 2003; see also Einstein Thomas, Mayfield, Shanck, Morisette, et al., 2005; McDaniel, Einstein, & Rendell, 2008).

### **2.3 Processes involved in prospective memory performance**

Due to the complexity of processes involved during prospective memory tasks the realization of delayed intention has been described through various phases (Ellis, 1996; Kliegel, Martin, McDaniel, & Einstein, 2002; Kliegel, MacKinlay, & Jäger, 2007):

- a- Formation of intention (i.e., to plan which actions shall be performed at what time in the future, and then to encode the plan).
- b- Retention interval (to keep the intention in mind while working on other tasks).
- c- Intention retrieval (to inhibit ongoing activities, and re-instantiate the intended plan. The success in this phase depends heavily on how well one monitors the environment).
- d- Intention execution (the intended action has to be carried out as previously planned).

*Formation of intention:* The first phase consists on the formation of the delayed intention. Different degree of motivation may influence the strength of the encoding of the delayed intention. In fact, the strength of an intention may reflect not only the personal importance, but also the potential benefits or the costs of realizing the delayed intention (Conway, 1992). Interesting, Goscheke and Kuhl (1993) identified an Intention Superiority Effect (ISE) that describes the enhanced activation or increased accessibility of materials associated with the intended action and reflects the reduction of response latency of materials previously encoded. The authors observed shorter latency for items intended to carry out relative to neutral items. Gollwitzer (1999) postulated the concept of an Implementation Intention to specify the conditions under which an intention can

be realized through a specific action. Thus, whereas an intention defines what the person intends to achieve, an implementation intention describes when, where and how the intended action can be instantiated (Gollwitzer, 1999; Ellis & Freeman, 2008). An extended body of studies have demonstrated that the encoding of an implementation intention improves the performance of the delayed intention. Thus, for examples, difficult actions were performed more accurately when they were associated with implementation intention instructions (Ellis & Freeman, 2008). An additional element that may influence the encoding of the delayed action is the repetition of intention (or instruction in a laboratory setting). This element describes a degree of commitment: people may write down the intended action or in a laboratory setting repeat aloud or subvocally the instructions (Ellis & Freeman, 2008).

*Retention interval:* the retention intervals can vary both in their duration and in their content and describe the delay between the formation of the intended action and the execution. Despite, in RM it has been found that the performance declines with increasing delay between the study phase and the test phase (Ebbinghaus 1887-1964), this effect of delay on prospective memory has yielded equivocal findings (Ellis & Freeman, 2008). Some authors found lower performance after a long delay compared to shorter delay (Meacham & Leiman, 1982), others failed to find any decline in performance after longer delay (Einstein, Holland, McDaniel, & Guynn, 1992; Guynn, McDaniel, & Einstein, 1998) or even better performance with the longer delay (Carlesimo et al., 2004a). Beyond the different methodologies employed, different delayed intervals were used in the previous studies and no univocal duration exist to identify short and long intervals that may varied from few minutes (15 vs. 30 min, Einstein et al., 1992; 4 vs 20 min, Guynn et al., 1998; 10 vs 45 min, Carlesimo et al.,



2004a) to days (1 vs 8 days, Meacham & Leiman, 1982). In addition to the length of the delay interval, the cognitive load added during the delay interval (filled or un-filled intervals) may influence the performance (Einstein et al., 1992; Henry et al., 2004; Henry, Phillips, Crawford, Kliegel, Theodorou, & Summers, 2007a).

*Intention retrieval:* Successful performance on prospective memory tasks, not only required to accurately encode the intended action and maintain the intended action active during the interval delay, but also to recognize the cue for the intended action, retrieving the action associated with that intention and performing the action. People may fail on their performance not only because they fail to recall the intended action, when the target occurs, but also because their cognitive resources were captured by the demands of the ongoing task (Einstein, McDaniel, Smith, & Shaw, 1998).

*Intention execution:* This may be considered the final stage to the execution of the delayed intention. However, after having been successfully went through all the previous phases, errors can occur and the delayed intention not performed. Distractions or failure to complete the task due to external circumstances may compromise the performance. For example, the intention to phone a friend may be interrupted by the door-bell or fail because the friend is not at home. When the delayed intention is not executed it is necessary to re-establish the intention and re-form the plan (Ellis, 1996). Ellis (1996) proposed a fifth phase that is concerned with monitoring the output of the executions of the intended action: *Evaluation of outcome*. The evaluation of outcome describes the process of which a person checks if the intended action has been accurately performed. Two errors may occur here: omissions, that are due to the incorrect belief that the action was completed and repetition of the action due to the

incorrect belief that the action was not completed (Marsh, Hicks, Hancock, & Munsayac, 2002).

## **2.4 Factors that influence prospective memory**

As attentional resources decline with age (Craik, 1986) and after TBI (Mathias & Wheaton, 2007) the multiprocess model (McDaniel & Einstein, 2000) predicts that more strategic processing are required for the prospective memory, the larger the age-related and frontally-mediate prospective memory impairment (Altgassen, Phillips, Henry, Rendell, & Kliegel, 2010). Therefore, some critical factors are involved on prospective memory performance and they determine the extent to which prospective memory depends more on strategic-attention-demanding process versus a relatively more automatic process (McDaniel & Einstein, 2000).

The aspects of the target that act as cue or the ongoing task may influence the prospective memory performance. For example, the distinctiveness of the target not only produces attentional switching from the ongoing activity, but also provides a frame for quickly recognizing its significance. The accuracy of prospective memory tasks is nearly perfect when perceptually distinct target are used (i.e. Upper case words). The distinct target may engage an involuntary orienting process that supports prospective memory performance (Einstein, McDaniel, Marzi, Cochran, & Baker, 2000). Moreover, the target can vary in the degree to which it is associated with the intended action. Better performances have been reported when the target was related to the action (i.e. buying oranges when shopping at the fruit-market) that when the action was unrelated to the intended action (i.e. buying shoes when shopping at the fruit-market) (Moscovitch, 1994; McDaniel et al., 1998). If the cue is part of the information extracted for

performing the ongoing activity more automatic attentional processes are required to monitor for the cue, on the other hand, if the cue is not part of the ongoing task more strategic attentional resources are required to monitor for the cue. There are also conditions in which the cue is embedded in the ongoing activity, but it still not focus for the prospective memory task. An example is the condition in which the target cue is a particular pair of letters in a word and the ongoing activity is processing the meaning of the word. In this case the automatic processes that support the intended action is unlikely and therefore prospective memory performance have to be supported by a more strategic or self-initiated process (Maylor, 2000). Einstein and McDaniel extended these finding and proposed the distinction between focal and non-focal cues (Einstein & McDaniel, 2005; McDaniel & Einstein, 2000, 2007). Focal prospective memory tasks are those in which the ongoing task involves processing the defining features of the prospective memory cues. In this case, the prospective memory cues are sufficiently processed during the ongoing task to automatically retrieve. By contrast, non-focal prospective memory tasks are those in which the prospective memory cues are not part of the information being extracted in the service of the ongoing activity In non-focal tasks, prospective remembering is thought to require strategic attentional resources to carry out extra monitoring for the cues to perform an intended action (Einstein & McDaniel, 2005 Rendell, McDaniel, Forbes, & Einstein, 2007c; Kliegel, Jäger, & Phillips, 2008c; Altgassen et al., 2010).

Although, the effects of prospective cue salience have been investigated in terms of familiarity or distinctiveness (Einstein & McDaniel, 1990; McDaniel & Einstein, 2000) or focality and non-focality (Einstein & McDaniel, 2005 Rendell, McDaniel, Forbes, & Einstein, 2007c; Kliegel, Jäger, & Phillips, 2008c) Altgassen et al. (2010)

extended the concept of salience of cue' emotional valence and investigated the effect of emotional stimuli on prospective memory performance. The results pointed out that emotional prospective memory cues were better remembered than emotionally neutral cues, indicating that the difficulties in carry out intentions are eliminated when the cues are emotionally salient.

As already pointed out, performing prospective memory tasks required to execute a delayed intention while engaged in an ongoing activity (McDaniel & Einstein, 2000). In a naturalistic setting this may be remembering to pick up the laundry while driving back home or remembering the appointment with the hairdresser after the lecture. In a laboratory setting this would be pressing a key while watching a movie or performing a secondary working memory task. The degree of attentional resources occupied to perform the ongoing activity also determines the prospective memory performance (Maylor, 1996; Park, Hertzog, Kidder, Morrell, & Mayhorn, 1997; McDaniel & Einstein, 2000). In fact, the ongoing activity may also vary in terms of how absorbing, engaging and demanding it is; the more absorbing the ongoing activity, less resources would be available for prospective memory task. In a laboratory setting this is made by varying the number of ongoing task to be performed. Less absorbing single ongoing task condition would allow a higher level of strategic monitoring than the multiple-ongoing task condition; thus, in a single ongoing task, prospective memory performance should be higher because more attentional resources might be employed in a strategic monitoring (Rendell et al., 2007c).

Some researchers have also observed that the perceived importance of the prospective memory task may influence the performance. Tasks perceived as more important will tend to required more strategic monitoring in the hope to increase the

performance. For less important tasks, a strategic and constant monitoring process is effortful and less needed, thus prospective memory performance may be left to more spontaneous and automatic processes (Kvavilashvili, 1987; Maylor, 1990; Andrzejewski et al., 1991; McDaniel & Einstein, 2000). Kliegel et al. (2001) extended these speculations by considering separately event- and time based tasks and distinguishing the influence of instructions on these prospective memory tasks. Manipulating the importance of the prospective memory task, by varying the instructions, affected the time-based but not the event-based performance. Importance improves prospective memory performance to the degree the task requires the strategic allocation of attentional resources (Kliegel, Martin, McDaniel, & Einstein, 2001).

As it is clear an extensive number of factors may influence prospective memory performance from more individual-personality related to individual cognitive difference or more procedural (cues and ongoing task characteristics). Further studies need to be conducted to deeply understand how all different factors interact to each other's and influenced prospective memory performance.

## **2.5 Monitoring behaviour in prospective memory**

### ***2.5.1 Monitoring behaviour in time-based prospective memory***

A specific interest of this thesis is the study of time-based prospective memory and the components that influence time-based prospective memory performance. Time-based prospective memory tasks differed from event-based prospective memory tasks mainly on events that retrieval the intended action. In time-based prospective memory tasks the appropriateness of the action is determined by the passage of time rather than

by the occurrence of an event (Einstein & McDaniel, 1996). For this reason to perform time-based tasks a person must rely heavily on internal processes.

Harris and Wilkins (1982) proposed a specific model (Test-Wait-Test-Exit, TWTE) for strategic monitoring in time-based prospective memory, assuming that monitoring is involved in a series of test-wait circles until a final test is made during a critical period. According to the authors, participants first synchronize their internal clock with the external clock, during the middle time they could rely on their internal clock to keep track of time, finally, as the response time approach they rely frequently on the external clock to be as accurate as possible in performing the task. The authors tested this model asking participants to watch a movie and hold up cards respecting to the times written on it (3 or 9 min). Subjects monitored the time by turning to look at the clock placed on the wall behind them. The results showed that the monitoring of the clock was closely related to the latency of responding, with shorter latencies associated with greater rate of monitoring, especially during the period immediately preceding the target time. Persons who were less accurate tended to monitor the clock very infrequently during the period immediately preceding the target time. Harris and Wilkins (1982) point out that “if subjects observed the clock during the *critical period*, they always responded within a few seconds” (pp.126). The authors considered the critical period the 15 seconds interval that proceeds the target time. When performing successfully, subjects progressively reduced the interval between clocks checking (increasing monitoring frequency) within the critical period until the target time occurs. Failures to respond on time were associated with a low rate of observation before and during the critical period (Harris & Wilkins, 1982).

Cohen, Atkin, & Hansen (1994; Atkin & Cohen, 1996) focused on classifying different types of monitoring strategies and on understanding how strategies depend on features of the task and environment. The authors point out that monitoring will always have some kind of cost, even if it is very small. Moreover, they concluded that the monitoring strategies can be divided in two general categories, namely, *periodic monitoring* and *interval reduction*. The distinction between the two monitoring categories is made respect to the goal and the environment. *Interval reduction* assumes that the subject monitors to find out where it is with respect to a goal. If the subject doesn't have a goal (i.e. press the key every 5 minutes), or if the environment provides no information about it (i.e. no clock to keep temporal information) then the interval reduction will not help and a periodic monitoring it is more likely. But, if the task and the environment provide information about when future events will occur, then the authors believed that the *interval reduction* is more appropriate process.

In sum, efficient monitoring requires a strategy or a scheme, for scheduling actions and balance the cost of monitoring against the cost of having inaccurate information about the environment. Various studies examined the relation between monitoring frequency and accuracy at the target time in children (Ceci & Bronfenbrenner, 1985, Kerns, 2000; Mäntylä et al., 2007), younger adults (Einstein & McDaniel, 1996; Mäntylä et al., 2007), older adults (Einstein, McDaniel, Richardson, Guynn, & Cufer, 1995; Einstein, Smith, McDaniel, & Shaw, 1997; Maylor, Smith, Della Sala, & Logie, 2002; Logie et al., 2004; Henry et al., 2004), and patients (Shum et al., 1999; Kerns & Price, 2001; Carlesimo, Casadio, & Caltagirone, 2004b; Cuttler & Graf, 2007; Altgassen, Williams, Bölte & Kliegel, 2009) and showed some regularities of behavior prior to successful task performance. Participants first test the time by

checking the clock, than wait a certain time until another check appear appropriate. In spite of differences in monitoring frequency the number of clock-checking increased when the deadline approach and the data showed a typical J-shape. Efficient monitoring requires a strategy for scheduling actions, balance the cost of monitoring against the cost of having inaccurate information about the environment (Mäntylä & Carelli, 2006).

Monitoring frequency has been a central feature of explanations of time-based prospective memory since the beginning of the studies on the topic (Ceci & Bronfenbrenner, 1985; Harris & Wilkins, 1982; Einstein et al., 1995; Mäntylä & Carelli, 2006; Guynn, 2008). Since the first studies on time-based prospective memory, self-initiated monitoring behavior has been demonstrated to be a strong predictor of prospective memory performance (Harris & Wilkins, 1982; Einstein et al., 1995). Monitoring frequency provide a window or a proxy to the participant's strategic behavior during the interval that precedes the deadline (i.e., clock checking indicates withdrawal of attentional resources from the ongoing activity). Thus, a time-based prospective memory performance can (and should) be examined in terms of multiple outcome measures, including response accuracy, monitoring frequency and primary task performance (Mäntylä & Carelli, 2006). A critical feature of time-based prospective memory tasks is that the available clock is hidden so that checking the clock requires on additional behavior. Collectively, participants periodically check the clock. The clock checking is generally strategic and participants increased their monitoring frequency closer to the target time. This strategic behavior determines higher accuracy, so that participants with a more strategic behavior would also have better performance (Einstein et al., 1995; Mäntylä, & Carelli, 2006; Einstein & McDaniel, 2007; Guynn, 2008).



Researchers agree on the notion that monitoring performance is mediated by higher-order control functions (Mackinlay et al., 2009; McFarland & Glisky, 2009; Mäntylä, & Carelli, 2006). According to this view, individuals with less efficient executive functions are expected to rely on less efficient monitoring strategies than individuals with better functioning processes. Studies showing age-related differences in time-based prospective memory tasks are consistent with the notion that executive functions mediate strategic monitoring. Specifically, assuming age-related decrement on executive functions older adults would be expected to use less efficient monitoring strategies than younger adults (Einstein et al., 1995; Park et al., 1997; Maylor et al., 2002; Martin et al., 2003; Logie et al., 2004; Mäntylä, Del Missier, & Nilsson, 2009; Mackinlay et al., 2009; McFarland & Glisky, 2009). Similar results have been expected with patients that presents executive dysfunctions (Shum et al., 1999; Carlesimo et al., 2004a).

Mäntylä and Carelli (2006) tested a wide group of younger, middle-age and older adults with time-based prospective memory task and 6 tasks to tap inhibition, updating and shifting executive components (see also Mäntylä et al., 2007). Correlation analysis showed that participants with lower performance in the inhibition and updating tasks showed less efficient monitoring performance than individuals with better performance in inhibition and updating executive tasks. Interestingly, McFarland and Glisky (2009) investigated the role of frontal lobe and medial temporal lobe functions on time-based prospective memory performance, in particular on monitoring frequency and plan execution. Older adults were divided in four groups upon their score on frontal<sup>5</sup> and

---

<sup>5</sup> The frontal lobe factor is hypothesized to tap executive control processes that have been shown to be dependent on frontal lobe (Wisconsin Card Sorting Test; Mental Control from WMS-III; Backward digit span from WMS-III; and Controlled Oral Word Association Test).

medial temporal<sup>6</sup> lobe functions tasks. High-frontal functioning participants had better prospective memory performance than low-frontal functioning. Older adults with high-medio-temporal lobe score performed significantly better than older with low-medio-temporal lobe score, but only if they were high on frontal functioning. Frontal lobe functions, but not medio-temporal functions predicted monitoring frequency behaviour (McFarland & Glisky, 2009). Importantly, performance of older with high-frontal score did not differ from younger participants. The results suggested that it is not aging per se that influence prospective memory performance but it is mainly the diminished frontal lobe functioning. Taken together, these findings suggested that time-based prospective memory performance, both in terms of monitoring frequency and accuracy, is closely related to individual differences in executive controls functions.

### ***2.5.2 Monitoring behavior in event-based prospective memory***

The early focus on monitoring on time-based tasks probably reflects the fact that there are obvious ways to measure this process (head turn or key press) and that time-based performance cannot be completely analyzed and understood without considering the monitoring behavior associated (Einstein et al., 1995; Mäntylä & Carelli, 2006; Guynn, 2008). In fact when participants are engaged in time-based tasks have to actively monitor the progress of time by checking the clock to accurately perform the prospective memory task. Probably less intuitive is the monitoring behavior present during event-based prospective memory tasks. In fact, in event-based tasks participants are required

---

<sup>6</sup> The medio-temporal lobe factor is hypothesized to tap executive control processes that have been shown to be dependent on medio-temporal lobe (Logical Memory, Verbal and Visual Paired Association and Faces from WMS-III; Long-Delay cue recall from the California Verbal Learning Test).

to respond when the external target stimulus is present, in this case the monitoring behavior occurs to monitor for the prospective memory target stimulus (Guynn, 2007).

A recently interesting new model has been proposed to investigate monitoring behavior in event-based tasks. The technique for measuring event monitoring derives from the fact that in event-based tasks the target events are embedded in the ongoing activity. To measure the monitoring, the performance on the ongoing task, when the prospective memory activity is required, is compared to the performance on the ongoing task when the prospective memory task is not required. Impaired performance on the ongoing task when the prospective memory tasks is present compared to the condition when is not required provides evidence for monitoring (Brandimonte, Ferrante, Feresin, & Delbello, 2001; Guynn, 2003; Kliegel, Martin, McDaniel, & Einstein, 2004; Kvavilashvili, 1987; Smith, 2003).

Guynn (2005; 2008) proposed a theory of monitoring, called the retrieval mode + target checking (RM + TC) theory, to understand how this process mediates prospective memory performance. The retrieval mode is conceptualized as a mental set that is a prerequisite for the attempt to retrieve information and for prospective memory when prospective memory is mediated by monitoring, and may be independent of the extent of target checking (Guynn, 2008). The retrieval mode is a continuous or constant process that operates after a prospective memory task has been assigned and until it has been completed. Instead checking the environment for the target is more periodic and intermittent; in fact there are costs of continuous checking behavior (Harris & Wilkins, 1982). Thus, when a target is present and a target check is made, the combination of these two process (retrieval mode and target check) support the monitoring, but when the target is present and the target check is not made, the retrieval mode can by itself

support the monitoring (Guynn, 2008). This theory is extremely interesting and it is not incompatible with the previous theories of prospective memory, likewise the multiprocess model (McDaniel & Einstein, 2000; Einstein et al., 2005; McDaniel, Guynn, Einstein, & Breneiser, 2004) or the preparatory attentional and memory process model (Smith, 2003; Smith & Bayen, 2004), but may complete the existing theories.

## **2.6 High cognitive abilities involved on prospective memory performance**

Considering the complexity of cognitive processes it is important to understand their involvement of high cognitive executive functions on remembering future intention. An initial hypothesis was that prospective memory performance depended on the prefrontal systems and on executive functions integrity (Stuss & Benson, 1987; Glisky, 1996; McDaniel, Glisky, Rubin, Guynn, & Routhieaux, 1999; Burgess, Veith, de Lacy Costello, & Shallice, 2000). In particular it has been hypothesized that participants with lower frontally mediated executive functions would present lower performance on prospective memory tasks (Kidder, Park, Hertzog, & Morrel, 1997; Martin, Kligel, & McDaniel, 2003; Logie, Maylor, Della Sala, & Smith, 2004; McFarland & Glisky, 2009). Considering that the executive functions are not a unitary system (Miyake, Friedman, Emerson, Witzki, Howerter, & Wager, 2000) it is still under discussion which executive functions components are mainly involved on prospective memory performance.

Following the studies of Miyake and colleagues (2000), Mäntyla and colleagues (2007) found that monitoring performance was related to the inhibition and updating components of executive functions (Mäntyla, Carelli, & Forman, 2007). Participants with lower performance in updating and inhibition showed more inefficient monitoring

performance than did participants with better updating and inhibition abilities. Instead, shifting did not correlate neither with prospective memory accuracy or monitoring frequency. McFarland and Glisky (2009) found that clock monitoring (last interval), frontal lobe factors (hypothesized to tap executive control processes that have been shown to be dependent on the frontal lobes) and plan quality better correlate with prospective memory performance. Mackinlay, Kliegel, and Mäntylä (2009) explored the involvement of working memory, task switching and planning on time-based prospective memory performance. The results confirmed the involvement of working memory, task switching and planning on prospective memory accuracy, while only planning correlates with monitoring frequency. These findings are in line with the hypothesis that strategic behavior as well as executive functions improves time-based prospective memory performance: participants with better strategic and executive abilities would have better time-based prospective memory performance. In particular the planning abilities that one engaged to perform the prospective memory task is likely to affect the nature and the activation of the prospective memory representation and this in turn should affect the extent to which prospective remembering is likely to occur with more spontaneous or automatic processes (Mäntylä, 1996; McDaniel & Einstein, 2000). Good planning obviate the need for strategic monitoring, also it seems likely that some conditions require more planning than others. For examples, with very salient target events less planning may be needed (Guynn, McDaniel, & Einstein, 1998).

Not only different executive functions components are hypothesized to be involved on prospective memory performance but also different executive functions may differently be involved in one of the four phases of the prospective memory process (Kliegel et al., 2002; Kliegel et al., 2007; Ellis, 1996; West, 1996). Martin et al. (2003)

examined the relationship between the performance on the four phases of prospective memory process (intention formation, intention retention, re-instantiation and intention execution) and executive functions in younger and older adults. Four prospective memory tasks were selected with respect to the hypothesized mainly involvement of executive functions of planning, inhibition and self-initiated monitoring: Multitask Prospective Memory Paradigm (MTPM, Kliegel, McDaniel, & Einstein, 2000); event- and time-based tasks, and Remembering-a-Belonging subtest from Reversed Behavioural Memory Test (RBMT, Wilson, Cockburn, & Baddeley, 1985). In particular the authors used the RBMT because emphasized the retention and re-instantiation phases, the event- and time-based tasks focused on the intention execution phase, and the MTPM focused both on intention formation and execution. Results showed that executive functions did not predict performance in the RBMT task, but executive functions did predict the performance both in event- and time-based prospective memory tasks. Both age and executive functions predicted the performance in the most complex MTPM task (Martin et al., 2003). It seems clear that different cognitive factors are involved on prospective memory performance across different prospective memory paradigms.

## **2.7 Neuropsychology of prospective memory**

Prospective memory is a complex cognitive process that relies on distinct phases (Ellis, 1996; Kliegel, McDaniel, & Einstein, 2000; McDaniel & Einstein, 2000; Kliegel et al., 2002). Efficient encoding of the intended action is needed during the first phase *intention formation*, moreover planning skills are assumed to be the most influential cognitive function, especially when an intention is complex. *Intention retention* seems

to primarily require storing the content of the intention in memory. Finally, *intention initiation* and *execution* seem to rely on processes such as monitoring, cognitive flexibility and inhibition. Although distinct executive processes are suggested to be involved during *intention formation*, *intention initiation*, and *intention execution*, executive functions seem to play only a marginal role during *intention retention* (note that some authors have suggested that executive control may be required during intention retention to some degree to periodically rehearse or check for uncompleted intentions; Carlesimo et al., 2004b; Kliegel et al., 2008a). However, not only frontally mediated executive functions have been suggested to be involved on prospective memory performance. Other cognitive processes (less frontally mediated) could play a primary role on the process of retrieving the content of the intention and the specific actions that have to be carried out (retrospective component of a prospective memory task; Einstein, Smith, McDaniel, & Shaw, 1997; McDaniel, Guynn, Glisky, Rubin, & Routhieaux, 1999).

In sum, it has been suggested that the prefrontal cortex mostly mediates those processes involved in prospective memory that are thought to be executive, such as the planning of an intention or the executive control mechanisms required to successfully initiate and execute an intention. Because of the link between executive functions and the prefrontal cortex (Miller, 2000; Miller & Cohen, 2001; Burgess, Quayle, & Frith, 2001), a strong involvement of this brain region in specific phases of the prospective memory process has been suggested. Moreover, the memory system of the medial temporal lobes is assumed to be essential for the retrospective component of prospective memory tasks to retrieve the content of an intention (Cohen & O'Reilly, 1996; Guynn, McDaniel, & Einstein, 2001; Kliegel, Jäger, Altgassen, & Shum, 2008b).

Prospective memory dysfunctions have been reported in different clinical population like Alzheimer patients (Smith, Della Sala, Logie, & Maylor, 2000; Maylor et al., 2002; Jones, Livner, & Bäckman, 2006, Thompson et al., 2010), Parkinson patients (Katai, Maruyama, Hashimoto, & Ikeda, 2003; Kliegel, Phillips, Lemke, & Kopp, 2005; Costa, Peppe, Caltagirone, & Carlesimo, 2008; Kliegel, Altgassen, Hering, & Rose, 2011; Raskin, Woods, Poquette, McTaggart, Sethma, Williams, & Tröster, 2011), Multiple sclerosis (Rendell et al., 2007a; West et al., 2007), substance and alcohol user (Ling, Heffernan, Buchanan, Rodgers, Scholey, & Parrott, 2003; Rendell et al., 2007b; Leitz, Morgan, Bisby, Rendell, & Curran, 2009; Rendell et al., 2009), and Schizophrenia patients (Henry et al., 2007b).

A consistent number of studies have been conducted with TBI patients (Shum et al., 2011 for a review). The relevance of studying prospective memory in TBI patients is reflected in patients' reports that failure to execute future intended action are their most significant memory impairment (Hannon, Adams, Harrington, Fries-Dias, & Gibson, 1995). In the light of cognitive and neural correlates of prospective memory, TBI patients were expected to be impaired on both event and time-based prospective memory tasks (Guynn et al., 2001).

## **2.8 Prospective Memory in traumatic brain injury patients**

Memory impairment is one of the most common TBI symptoms (Shum et al., 2000; Shum et al., 1996). The effect of this impairment is often long-term, debilitating and difficult to remediate (Glisky & Glisky, 2002). Despite several studies have been conducted on retrospective memory dysfunction on TBI patients (Levin, 1991; Ponsford, Sloan, & Snow, 1995, Lezak et al., 2004; Stuss, 2011) fewer studies have



been conducted on prospective memory dysfunction (Shum et al., 2011 for a review). For individuals with TBI, frequent prospective memory failures (e.g. forgetting to repay a loan to a friend, forgetting to turn up for an appointment, forgetting to take medication, forgetting to turn off a stove) can be frustrating, embarrassing and sometimes even life threatening. These failures have the potential to limit the independence of these individuals, causing them to rely on a caregiver for prompting. Moreover, these failures may affect their chance to return to work or to start a new vocation (Maujean, et al., 2003; Fleming et al., 2008).

Because the frontal and temporal areas are common sites of damage after TBI (Levin & Kraus, 1994) and because these areas are related to processes required for successfully prospective memory task execution (e.g., initiation and execution of planned intention, cue-recognition, interruption of ongoing activity; McDaniel, et al., 1999; Guynn et al., 2001; see also Crawford & Henry, 2005), it is expected that participants with TBI are impaired on both event- and time-based prospective memory tasks. It is expected that performance on the time- and event-based task would differ according to the complexity and requirement of the tasks for both participants with TBI and controls (Kliegel et al., 2001; Kliegel et al., 2004a; Henry et al., 2007a). When tested both on event- and time-based tasks TBI patients are expected to be particularly impaired on time-based tasks because time-based tasks requires more on self-initiation (due to the absence of an external cue; Ellis, 1996; McDaniel & Einstein, 2000). Dysfunctions on time-based tasks may also be due to less strategic monitoring behaviour. In fact, based on Einstein et al.'s (1995) results, it was expected that performance on the time-based task would be related to frequency of monitoring behaviour (especially in the period most proximal to the target time). Specifically, it was

expected that, controls would monitor the time more strategically than participants with TBI would.

The earliest studies that examined the effect of TBI on prospective memory performance used self-rating scales (Hannon et al., 1995) or very few test items (Bisiacchi, 1996; Kinsella, Murtagh, Landry, Homfray, Hammond, O'Beirne, Dwyver, Lamont, & Ponsford, 1996; see also Cockburn, 1996). In Hannon et al. (1995) study participants were tested with a Prospective Memory Questionnaire (PMQ; Hannon, Gipson, Rebmann, Keneipp, Sattler, Lonero, Day, & Bolter, 1990), together with attentional and memory tasks. Adults with TBI and older adults performed more poorly than younger adults on short-term prospective memory tasks, and adults with brain injury rated themselves more poorly than younger adults on the Short-Term Habitual subscale of the PMQ. Bisiacchi (1996) reported preliminary studies conducted by Sgaramella et al. (1993) on three TBI patients and showed the presence of different processes on event- and time-based prospective memory tasks. Kinsella and colleagues (1996) used only two tasks to assess prospective memory; the first task involved telling the participants about a self-report memory questionnaire at the beginning of an assessment session and instructing them to ask for the questionnaire at the end of the session (event-based task). The second task involved asking the participants to return (by mail) an evaluation form with the date written in the top corner (time-based task). Because of the small number of items used and because of the correct/incorrect nature of these items, the prospective memory scores obtained using these tasks were limited in range and unreliable. To assess prospective memory more accurately and reliably, it is necessary to increase either the number of items used or the number of responses required for each item. More recent studies (Table 2.1) took these limitations into

consideration and developed more appropriated tasks to investigate the effects of TBI on event- and time-based prospective memory performance.

**Table 2.1** Studies that used behavioral tasks to investigate prospective memory performance on TBI patients. GCS= Glasgow Coma Scale; Time refers to the time post injury (months); NPS assessment refers to the neuropsychological tasks included in the studies; WCST=Wisconsin Card Sorting Test; COWAT=Controlled Oral Word Association Test; DASS=Depression, Anxiety, Stress Scale; TOL= Tower of London; LNST=Letter-Number Sequencing Test; TMT= Trial Making Test; CAMPROMPT=Cambridge Behavioural Prospective Memory Test; MIST=Memory for Intention Screening Test.

Study <sup>7</sup>	Year	Sample	TBI characteristics		NPS assessment <sup>8</sup>	Type of prospective memory tasks	
			GCS	Time		Event-based	Time-based
<b>Shum et al.</b>	1999	12 TBI and 12 controls	8 or less	24.58 (15.58)	-	Response to questions and the target word	Press a key every 5 min and monitor the time
<b>Kinch &amp; McDonald</b>	2001	13 TBI and 13 controls	6.6 (3.3)	1.8 (0.7)	WCST, COWAT and DASS	Deliver a message (unfilled and filled conditions)	Stop the timer after 5 min (unfilled and filled conditions)
<b>Maujen et al.</b>	2003	14 TBI and 14 controls	3 to 15	9.71 (7.5)	TOL, COWAT and LNST	Response to a cue (low and high cognitive demand)	-
<b>Carlesimo et al.</b>	2004a	16 TBI and 16 controls	8 or less	108	-	Perform actions when the target appeared (related-unrelated cues) (10 vs. 45 min delay)	Perform actions after the interval (related-unrelated cues) (10 vs. 45 min delay)
<b>Kliegel et al.</b>	2004b	7 TBI, 21 older and 19 younger controls	severe	41.71 (11.79)	Verbal intelligence and WCST	Complex tasks following the multiprocess model	-
<b>Schmitter-Edgecombe &amp; Wright</b>	2004	24 TBI and 24 controls	8 or less	25.75 (21.63)	Attention, WM span, RM, COWAT, Stroop, TMT and WCST	Press a designed key on focal cue or peripheral cue	-

<sup>7</sup>Studies included here have been conducted with behavioral measures.

<sup>8</sup>References of neuropsychological tasks are not reported because the authors referred to different version of the tasks. Please refer to the specific articles for the appropriate references.

Study	Year	Sample	TBI characteristics			Type of prospective memory task	
			GCS	Time	NPS assessment	Event-based	Time-based
<b>Mathias &amp; Mansfield</b>	2005	25 TBI and 25 controls	8 or less	7	Declarative memory, digit span, TMT, COWAT and WCST	Remember the belongs, the appointment and delivering a delayed message	Stop a timer and send the envelop
<b>Henry et al.</b>	2007a	17 TBI and 16 controls	11.67 (3.50)	41.28 (32.52)	-	Response to a cue (one or four cue targets)	
<b>Fleming et al.</b>	2008	44 TBI but no controls	7.08 (3.89)	-	TMT, COWAT and metacognitive variables	CAMPROMPT	CAMPROMPT
<b>Tay et al.</b>	2010	31 TBI and 31 controls	13-15	0.89 (0.22)	-	MIST	MIST

Among the studies identified only one included mild TBI patients (Tay, Ang, Lau, Meyyappan, & Collinson, 2010), maybe due to the difficulty to recruit mild TBI patients because these patients are generally treated and discharged from the emergency center (Shum et al., 2011). All studies included evaluated event-based prospective memory performance and 6 of them examined both event- and time-based performance. When both event- and time-based tasks are included in the studies, TBI patients obtained lower performance on time-based tasks (shum et al., 1999; Kinch & McDonald, 2001 Carlesimo et al., 2004a; Mathias & Mansfield, 2005) confirming that time-based tasks are more difficult probably due to more self-initiated retrieval (Einstein & McDaniel, 1990). Generally TBI patients showed prospective memory dysfunctions

compared to health controls but the degree of this impairment varied according to the characteristics of the tasks employed. Varying the cognitive demand on the ongoing task Maujean et al. (2003) found that TBI patients performed more poorly than controls on high-demand but not in the low-demand condition. Schmitter-Edgecombe & Wright (2004) varied the location of the event cue. The cue was either integrated with the ongoing working memory task (focal cue) or peripheral to it. TBI patients and controls did not differ on the ongoing task but prospective memory performance was poorer on TBI patients in both focal and peripheral cue conditions, suggesting that even with highly salient cue TBI patients' exhibit prospective memory failures. Moreover, both TBI and controls self-reported that monitoring for the event cue in the peripheral-cue conditions required more effort than the focal-cue conditions. Instead, Henry et al. (2007a) maintained the cue in a focal condition, but varied the number of distraction during the ongoing task. TBI patients performed more poorly both on one and four target conditions. Finally, Carlesimo et al. (2004a) varied the delay between encoding and task performance (10 vs 45 min) expecting lower performance in the longer delay condition (45 min) and varied the functional link (inter-item associative link, i.e. semantic) between intended actions expecting better performance when the actions had functional link. TBI performed significantly lower than controls, however no significant effects of delay interval or the functional link of the intended actions were found.

Interestingly, Carlesimo et al. (2004a) also investigated the monitoring behavior in TBI patients on time-based prospective memory tasks by recording the number of times participants monitored their own watch or the wall clock. Controls monitored an average about twice as often as TBI patients and controls showed an increasing number of monitoring frequencies closer to the target time. In controls the number of monitoring

significantly predicted accuracy at the target time. However, TBI patients showed similar monitoring frequency across the intervals, demonstrating no involvement of strategic monitoring prior to time-based prospective memory performance. Before Carlesimo's et al. (2004a) study only Shum et al. (1999) have analyzed monitoring behavior in TBI patients. Differently to Carlesimo's et al. (2004a) study, Shum and colleagues (1999) found similar monitoring frequency in TBI and controls and in both groups number of monitoring frequency predicted time-based performance. Direct comparison between these two tasks is difficult due to the different methodologies employed and the different allocation of attention required to monitor the clock (Kliegel et al., 2001; 2004a).

A subset of studies included executive functions tasks to determine whether impairment on prospective memory was associated with difficulties on executive functions. Different pattern of results were presented, with studies indentifying significant correlations between prospective memory performance and executive functions (Maujean et al., 2003; Kinsella et al., 1996) and other studies showing no significant correlations (Mathias & Mansfield, 2005). For example, Maujean et al., 2003 found that working memory significantly correlate with prospective memory performance in the low cognitive demand condition both in TBI and controls. This result suggested that for the dual-task event-based paradigm employed in their studies, participants had to actively maintain in memory the requirement while undertaking the ongoing task. Surprising, this was true only in the low-demand condition. Spontaneous flexibility assessed through the Controlled Oral Word Association Test (COWAT, Spreen & Strauss, 1998) was found to significantly correlate with event-based prospective memory performance in the high-demand condition in TBI patients.

Schmitter-Edgecombe & Wright (2003) revealed that TBI event-based prospective memory performance significantly correlated with attention/speed processing measures, adding further support to the notion of a strong relationship between attention and prospective memory performance (Maater, Sohlberg, & Crinean, 1987; Craik & Kerr, 1996). In particular the authors point out that prospective memory dysfunctions may be due to momentary lapses of attention to task details rather than to a complete forgetting to the task instructions. Kinch and McDonald (2001) reported that RM accounted for a significant amount of variance in prospective memory tasks of TBI patients independently of executive functions. In particular, it was found that executive functions was involved both on time- and event-based prospective memory performance, but it was particularly influenced in time-based prospective memory performance, while RM was found to contribute most to event-based performance. Finally, Kliegel et al. (2004b) adopted a complex prospective memory paradigm (Kliegel et al., 2000) to investigate which of the four phases of prospective memory were affected in TBI patients. Prospective memory impairment was found on intention formation, intention re-instantiation and intention execution confirming that executive function are involved on these three phases rather than intention retention.

In addition to the executive functions involvement on prospective memory performance, two studies have also investigated prospective memory performance according to demographic, clinical and metacognitive variables (Kinch & McDonald, 2001; Fleming et al., 2008). Feeling of depression were shown of adversely affect successful performance on the timing component of the time-based task (see also Hannon et al., 1995) while feeling anxiety adversely affected performance on event-based tasks (Kinch & McDonald, 2001). In Fleming et al. (2008) study the localization

of the damage (mainly frontal) significantly correlated with event-based CAMPROMPT scores, whereas duration of post traumatic amnesia (PTA) and metacognitive variables significantly correlate both with time- and event-based scores.

In sum, previous studies point out prospective memory dysfunction on TBI patients and the involvement of executive functions on prospective memory performance (Kinch & McDonald, 2001; Maujean et al., 2003; Schmitter-Edgecombe & Wright, 2004). However, the mechanisms underlying TBI's prospective memory performance are not well known and there are aspects that have not been considered yet. In particular in time-based prospective memory no studies have been conducted to investigate the involvement of time perception on TBI prospective memory performance.

Studies on time perception conducted with frontal patients (Nichelli et al., 1995; Harrington et al., 1998; Mangels et al., 1998; Casini & Ivry, 1999; Rubia & Smith, 2004; Picton et al., 2006), TBI patients (Meyers & Levin, 1992; Perbal et al., 2003; Schmitter-Edgecombe & Rueda, 2008; Anderson & Schmitter-Edgecombe, 2011) and our studies (Study 1 and Study 2) showed temporal impairment on TBI patients both when tested with briefer durations (Study 1 and Study 2) and with longer durations (Study 2; Meyers & Levin, 1992; Perbal et al., 2003; Schmitter-Edgecombe & Rueda, 2008; Anderson & Schmitter-Edgecombe, 2011). It is possible that TBI patients (but also health participants) with lower temporal abilities would have lower time-based prospective memory performance? Support for this notion come from the hypothesis that not only executive functions are involved on time-based tasks but also a high degree of temporal abilities, in particular when monitoring time. In fact, strategic monitoring behaviour is fundamental to accurately perform the prospective memory task (Einstein



et al., 1995). Participants with high monitoring frequency that increased their monitoring frequency closer to the target time had higher prospective memory accuracy (Einstein & McDaniel, 1996; Einstein & McDaniel, 2007; Guynn, 2008). However, the process is more complex; efficient monitoring requires a strategy or a scheme for scheduling actions and it is a balance between the costs of frequently monitoring the clock against the cost of having inaccurate information about the environment (Mäntylä & Carelli, 2006; Glickson & Myslobodsky, 2006). We hypothesized that adequate temporal abilities may support time-based prospective memory performance by improving temporal perception within time monitoring checking. To investigate this hypothesis we have tested TBI patients and controls with time-based prospective memory task (Time monitoring task), temporal task (time reproduction task) and executive functions tasks (Stroop and N-Back tasks).

## **2.9 Study 3**

### ***2.9.1 Introduction***

In this study we investigate time-based prospective memory performance in TBI patients. In particular we investigate the involvement of time perception and executive functions on time-based prospective memory performance. Two previous studies investigated this hypothesis on healthy participants. Labelle, Graf, Grondin, & Gagné-Roy (2009) investigate whether the same temporal processes are involved in time-based prospective memory task and time production task. Participants were asked to make category-membership decision, while engaged either in a time production task (press a key after 30, 60 and 90 sec) or in a time-based prospective memory task (press a key after 30, 60 and 90 sec). In the time-based prospective memory task participants were

also instructed to check the clock, by pressing the spacebar, any time they wished. The results showed no significant correlation between time-based prospective memory accuracy and time production task. The authors concluded that these two tasks do not share the same temporal abilities and are controlled by two distinct types of timing mechanisms. Mackinlay et al. (2009) investigate temporal and executive processes that are involved in time-based prospective memory in school-age children. Participants were instructed to press a key on the keyboard every 2 min, while performing the ongoing one-back task. Moreover, participants performed four temporal tasks<sup>9</sup> (in which the time to be estimated was 2 min), planning (Zoo Map test), working memory (digit span backward) and switching (task switching subtest from TAP battery) tasks. Results showed no significant correlation between time-based prospective memory performance and time estimation, but only significant correlation between time-based prospective memory and executive tasks. The authors concluded that executive functions were the likely candidate for explaining individual and developmental differences in children's time-based prospective memory performance (Mackinlay et al., 2009).

Both previous studies asked participants to perform temporal task with the same interval duration required as target in the prospective memory task (30, 60 and 90 sec or 2 min). However, in our point of view, the trigger temporal process in time-based prospective memory tasks does not come out with the accuracy at the target time. Is not only requiring the subjects to perform an action every 30 sec or 2 min that makes time-

---

<sup>9</sup> The Prospective verbal estimation task in which participant were presented with two tones (a bell ringing) and were asked to provide a verbal estimation of the time between the tones; The Prospective production unfilled task in which participants were asked to produce a time duration; The Prospective production filled task, once again, the participants were asked to produce a time duration. However, in this version of the task, the delay was filled by a concurrent non temporal task. The Retrospective estimation task in which participants were asked to reproduce the duration of the stimulus previously presented.

based prospective memory tasks time-related, but the monitoring strategies that subjects used to get to that target. Focusing on the monitoring strategies we may understand the executive and time-related processes involved in time-based prospective memory tasks. We are aware that in time-based prospective memory tasks participants could check an external clock any time they wish to respond at the target time, for this reason it is reasonable to think that in time-based prospective memory tasks participants may not rely as heavily on their internal clock as in other temporal tasks. However, we could hypothesized that every time participants monitor the external clock they may reset the internal clock, store new pulses, make new comparisons and estimate time to the next external clock check.

With this study we investigate how temporal and executive processes are involved in time-based prospective memory tasks in TBI patients and healthy controls. To this end we employed a time monitoring task, in which participants are instructed to watch a movie and to press a designed key every 5 minutes, one timing task (time reproduction) and two executive functions tasks (n-back and Stroop tasks) to tap updating and inhibition executive functions components. Different temporal tasks may be employed to investigate temporal abilities (Block et al., 1998). In this study we used a time reproduction task with a concurrent secondary task to create the same dual-task condition present in the time-based prospective memory task, where participants are required to divide their attention between the ongoing and the prospective memory task. Participants are required to reproduce short intervals (4, 9 and 14 sec) that are close to the time related to frequency of clock checking.

We hypothesized that 1) TBI patients would be less accurate than healthy controls on a time-based prospective memory task, and that the frequency of monitoring

behaviour would correlate with time-based prospective memory performance, and 2) that time perception would be involved in monitoring frequency performance, such that participants with better timing abilities would display reduced monitoring frequency. To this end participants were required to reproduce durations similar to the time elapsed between clock checking.

## ***2.9.2 Materials and methods***

### *2.9.2.1. Participants*

Eighteen patients with severe TBI (12 men and 6 women), and 18 healthy participants (9 men and 9 women), matched for age and educational level, participated in the study. Demographic and clinical features of the patients were reported in Table 2.2. All patients referred to Modulo di Neuropsicologia Riabilitativa (Azienda Ospedaliero-Universitaria Ferrara, Italy). The patients were tested at least 6 months post their injury and severity was addressed with Level of Cognitive Functioning (LCF; Hagen, Malkmus, Durham, & Bowman, 1979), Post Traumatic Amnesia (PTA), Glasgow Coma Scale (GCS; Teasdale & Jennett, 1974), Functional Independence Measure/Functional Assessment Measure (FIM/FAM; Hall, Hamilton, Gordon, & Zasler, 1993). Patients also performed a battery of neuropsychological tasks to evaluate cognitive competences that included: Trial Making Task (Bowie & Harvey, 2006); Action Programme and Zoo Map subtasks from the Behavioral Assessment of Dysexecutive Syndrom (BADs; Wilson, Alderman, Burgess, Emslie, & Evans, 1996), Wisconsin Card Sorting Test (Laiacona, Inzaghi, De Tanti & Capitani, 2000) and Divided Attention and Go/Nogo subtasks from the TAP battery (Zimmermann & Fimm, 2002). All patients had available neuroimaging information (computed tomography,

magnetic resonance imaging) that showed damage in a wide variety of cortical areas, with the majority of participants having frontal lesions.

According to available clinical records, the participants were not densely amnesic or aphasic, and had no prior or current psychiatric pathology. We excluded participants who had motoric deficits, or history of drug or alcohol abuse. All patients were physically and mentally able to understand and complete the experimental tasks, and they provided verbal consent to participate in this study that was conducted in accordance with the Helsinki Declaration (59th WMA General Assembly, Seoul, 2008).

The control group was matched to the TBI patient group on the basis of age and educational level: The mean age was 34.50 years (SD=6.52; range=22-52) and the mean level of education was 13.33 years (SD=3.88; range=8-18). The TBI group and the control group did not show significant differences with respect to age [ $t(34)=1.20$ ,  $p=.236$ ] and education [ $t(34)=-.947$ ,  $p=.347$ ]. The difference in gender was not significant,  $\chi^2=1.02$ ,  $df=1$ ,  $p=.50$ .

**Table 2.2** Demographic and clinical features of TBI patients. Cause referred to the cause of accident; MB=moto-bike; TPI=Time Post Injury (month); Injury site referred to the prevalent site of injury; F-P=Fronto-Parietal; DAI=Diffuse Axonal Injury; F=Frontal; F-T=Fronto-Temporal; LCF=Level of Cognitive Functioning ; PTA=Post Traumatic Amnesia (day); GCS=Glasgow Coma Scale; FIM/FAM=Functional Independence Measure/Functional Assessment Measure; TMT (msec)= difference between execution time on TMT part B and TMT part A; Action Programme and Zoo map score from the Behavioral Assessment of Dysexecutive Syndrom; WCST global=global score in the Wisconsin Card Sorting Test; Divided attention (msec) and GO/Nogo (msec) tasks from the Test of Attentional Performance.

Patients	Gender	Age	Education	Cause	TPI	Injury site	LCF	PTA	GCS	FIM/FAM	TMT	Action Programme	Zoo Map	WCST global	Divided Attention	Go/Nogo
1	M	42	18	bicycle	6	F-P left	7	4	10	96	71	110.88	-	-	891	609.5
2	M	22	8	car	20	DAI	6	-	9	90	66	-	88.74	22.7	716	524
3	M	32	8	car	14	F bilateral	6	21	7	86	-	116.08	113.29	25.1	644	526
4	F	44	13	car	26	F bilateral	7	-	8	93	-	105.69	113.29	24	-	-
5	F	46	13	fall	24	F	6	-	7	83	214	84.9	nv	53	-	658
6	M	28	8	car	34	F-P left	6	-	7	86	-	110.88	88.24	34.7	288	542
7	F	41	18	car	21	F bilateral	6	-	-	86	20	95.3	96.92	45.7	836	-
8	M	58	18	MB	6	F-T left	6	4	9	97	87	-	92.83	-	251	559
9	M	31	8	car	80	F right	6	16	8	82	58	-	-	22.1	781	585
10	M	43	8	car	60	F-T left	7	-	-	86	32	105.69	105.12	43.8	-	-
11	F	42	8	car	21	F-T left	7	-	-	83	160	110.88	113.29	13	731	513.5
12	M	31	16	MB	12	DAI	6	12	4	86	99	79.72	92.83	23.4	873	648
13	F	33	8	car	16	F-T right	6	-	-	74	229	69.33	68.27	-	922	648
14	M	50	8	car	6	F-P right	7	5	3	82	90	-	-	-	-	-
15	M	34	13	car	16	F right	7	6	6	85	19	-	-	74.7	730	566
16	M	20	13	car	14	DAD	8	-	-	82	-	-	-	73.4	738	652
17	M	49	13	car	18	F right	7	14	4	93	68	110.88	113.29	55.6	841	600.5
18	F	36	18	car	47	F right	8	24	6	81	104	116.08	88.74	33.1	770	469
	Mean (SD)	37.89 (9.97)	12.05 (4.15)	car 70%	24.50 (19.67)	frontal 83%	6.61 (0.69)	11.78 (7.56)	6.77 (2.13)	86.16 (5.79)	94.07 65.28	101.26 15.57	97.90 14.11	38.54 19.37	715.14 203.88	578.51 59.93

### 2.9.2.2. Procedure

TBI patients were tested in a quiet room at Modulo di Neuropsicologia Riabilitativa (Azienda Ospedaliero-Universitaria Ferrara, Italy) while controls were tested at Department of General Psychology, Padova, Italy or in their own home. All tasks were presented with laptop and participants were sitted approximately 60 cm far from the screen. Prospective memory, temporal and executive functions tasks were performed during one experimental session that lasted proximately 1 hour. TBI apteints performed the neuropsychological evaluation in a separate session prior to the experimental session.

### 2.9.2.3 Time-based prospective memory task

We used a time monitoring task (Mäntylä et al., 2007) to test time-based prospective memory performance. For this task, participants watched a 20-minute cartoon-movie (*Madagascar*), and were instructed to mark the passage of time by pressing a key on a keyboard at every 5 minute interval. Subjects were not informed of the duration of the movie. The participants had available two response buttons (red and green) and were instructed to press the red key every 5 minute (at 5:00, 10:00, 15:00 and 20:00 min). Participants could press the green key at any time during the task to monitor the passage of time. When the green key was pressed, the corresponding time appeared for 2 seconds on the right bottom portion of the computer screen. Importantly, participants were also told to watch the film carefully, because they would be asked to complete a 10-item questionnaire about the movie content. To clarify instructions and ensure familiarization with the task, participants completed a practice where they watched and responded to a five-minute movie (*Sanpei*). The experimenter

demonstrated that the clock would start at 00:00 and that, for example, 2:00 means 2 min. No feedback was provided. Time-based prospective memory performance was evaluated in terms of prospective memory accuracy (target time response accuracy, PM-accuracy), monitoring frequency (number of clock checking) and ongoing task performance (response accuracy about the movie content).

#### *2.9.2.4. Time perception task*

Participants were instructed to reproduce the duration of a previously seen stimulus with a concurrent secondary task. Apparatus and stimuli were the same reported in Study 2. Participants were required to reproduce three durations, 4, 9, or 14 seconds (see pp. 57 for more details about the procedure). The durations employed in this study were selected following the results of a pilot study conducted with older and younger adults and following Shum et al. (1999) and Einstein et al. (1995) results<sup>10</sup>. Analysing the monitoring frequency (in particular at the last minute closer to the target time) controls monitored on average every 12 s while TBI patients every 7 s (Shum et al., 1999) while, in Einstein et al. (1995, Exp 3) study younger adults monitored on average every 6 s, middle-age adults on average every 5 s and older adults on average every 15 s<sup>11</sup>. Following these results participants were required to reproduce durations in the range of 4 to 14 s that are durations similar to the intervals between monitoring. Data were analysed in term of relative errors and CV.

---

<sup>10</sup> Carlesimo et al. (2004a) also reported data on monitoring behavior in TBI patients and controls. However, TBI patients did not show any strategic monitoring behavior prior to successfully perform prospective memory task showing a nearly flat monitoring behavior.

<sup>11</sup> These data have been calculated from the tables and figures included in the articles.



#### *2.9.2.5 Executive functions tasks*

We assessed inhibition and updating ability with the Stroop and n-back tasks, respectively. Apparatus and stimuli are the same previously reported in Study 1 (see pp. 43). We analysed the Stroop data in terms of reaction time (RT), and defined the Inhibition index as the difference between incongruent and congruent RT. N-back data were analysed in terms of number of errors (false alarms + omissions) and called Updating index.

### **2.9.3 Results**

#### *2.9.3.1 Time-based prospective memory*

##### *Prospective memory accuracy*

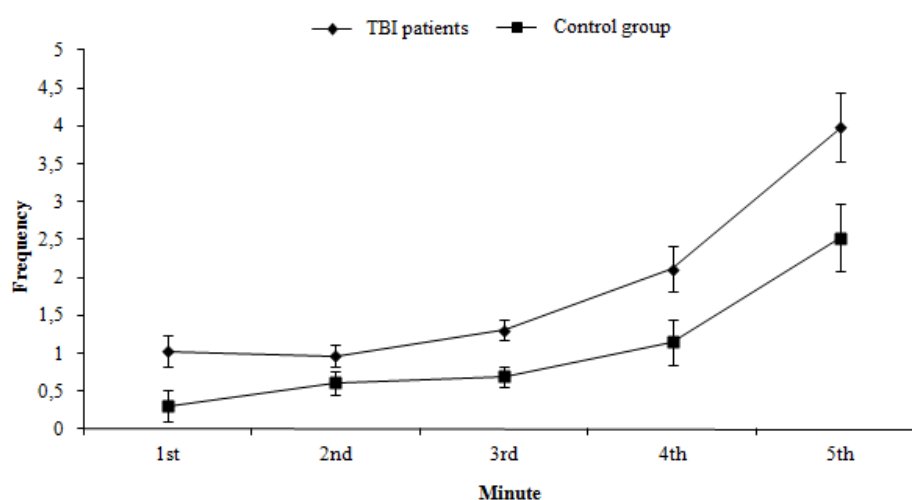
To assess prospective memory accuracy, we followed the methods of Einstein et al. (1995) and Shum et al., (1999) and computed latency responses. As such, participants' responses were categorized and assigned a score that ranged from 1 to 4 (1=from 0 to 2 sec; 2=from 3 to 5 sec; 3=from 6 to 8 sec and 4=9 sec or over) depending on latency of the response. The TBI group was significantly less accurate [ $t(33)=2.57$ ,  $p=.05$ , Cohen's  $d=.86$ ] and had lengthier latency response times relative to the healthy control group (4.05 vs. 1.61, respectively).

##### *Monitoring frequency*

We compared the groups regarding their monitoring behaviour, by analysing their monitoring frequency (e.g., number of clock checking) across 4 blocks (block 1=0-5 min; block 2=6-10 min; block 3=11-15 min and block 4=16-20 min; Mäntylä et al., 2007). To investigate learning effect across blocks a 2×4 ANOVA that included between-subject group (TBI, control) and the within-subject blocks (1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup>

block) was conducted. There was no effect for block [ $p=.21$ ,  $\eta^2_p=.044$ ], or interaction between group and block [ $p=.59$ ,  $\eta^2_p=.019$ ]. Therefore, each block was collapsed and analysed at each minute (see Figure 2.1). Data were subjected to a 2×5 ANOVA that included the between-subject group (TBI, control) and the within-subject minute (1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> minute). The results identified a main group effect [ $F(1,33)=7.28$ ,  $p<.01$ ], showing that TBI patients monitored more frequently than controls (1.88 vs. 1.05 times), and a main effect for minute [ $F(4,132)=64.22$ ,  $p<.0001$ ], consistent with increased time monitoring frequency at the target time deadline (1<sup>st</sup>=.66; 2<sup>nd</sup>=.89; 3<sup>rd</sup>=1; 4<sup>th</sup>=1.63 and 5<sup>th</sup>=3.25 times). The interaction between group and minute was also significant [ $F(4,132)=2.44$ ,  $p<.05$ ]. The TBI group significantly increased their monitoring starting from the 2<sup>nd</sup> minute, whereas the healthy control group increased their monitoring beginning at the 4<sup>th</sup> minute.

**Figure 2.9** Clock-checking frequency collapsed across 5-min task intervals and error bars for TBI patients and controls.



### *Ongoing task performance*

Data from ongoing task performance were also scored and the numbers of correct answers on the 10-item movie content questionnaire were included in the analysis. The groups showed similar performance regarding their recall of the movie content as demonstrated in their responses to the questionnaire [ $t(28)=-1.94$ ,  $p=.06$ , Cohen's  $d=-.71$ ; .50 vs. .64 for patients and controls, respectively].

#### *2.9.3.2 Time perception task*

Two separate ANOVAs were conducted on relative errors and CV. The between-subject factor was group (TBI, control) and the within-subject factor was duration (4, 9, and 14 sec). Analysis of relative errors revealed a significant main effect of duration [ $F(2,68)=36.29$ ,  $p<.001$ ,  $\eta^2_p=.516$ ]. Increasing durations produced more under-reproduction errors (.95, .83 and .72, respectively). No significant differences were found between groups ( $p=.989$ ,  $\eta^2_p=.001$ ): both groups equally under reproduced the durations (TBI=.83 and controls=.83). The interaction group and duration was also not significant ( $p=.978$ ,  $\eta^2_p=.001$ ).

The analysis of CV showed a group main effect [ $F(1,34)=5.77$ ,  $p<.001$ ,  $\eta^2_p=.145$ ]; TBI patients showed more variability in their performance than controls (.24 vs. .15). There was no main effect of duration ( $p=.284$ ,  $\eta^2_p=.036$ ), or interaction between group and duration ( $p=.727$ ,  $\eta^2_p=.009$ ).

### 2.9.3.3 Executive functions tasks

The results of the Inhibition index (Stroop task) revealed no significant differences between groups [ $t(34)=1.46$ ,  $p<.154$ ]. TBI and control participant were equally affected by the Stroop interference (184 vs. 136 msec). While, significant difference was found between groups on the Updating index (n-back task) [ $t(34)=2.57$ ,  $p<.015$ ] indicated that TBI patients produced more errors than controls (8.11 vs. 5.44).

### 2.9.3.4 Correlation analyses

We calculated specific indices to examine the relationship between time-based prospective memory, time perception and executive functions. The prospective memory accuracy (PM-accuracy) index was calculated using the accuracy at the target time and monitoring frequency indices (Min 1<sup>st</sup>, Min 2<sup>nd</sup>, Min 3<sup>rd</sup>, Min 4<sup>th</sup> and Min 5<sup>th</sup>) were calculated by adding participants' monitoring frequency at each minute. Time perception index was the mean of the participants' CV in the time reproduction conditions. For the executive functions, the Inhibition index of the Stroop was the difference between RTs in incongruent and congruent trials, and the Updating index was the number of produced errors in the n-back task. Two separate, one-tailed Pearson correlation analyses were performed for TBI patients and controls. Moreover, to better understand the differences between the TBI and healthy control groups, we compared the two correlation analyses (z Fisher).

#### *Correlation among time-based prospective memory and monitoring frequency*

No significant correlations were found between PM-accuracy and monitoring frequency indices in TBI patients. For controls, monitoring frequency in the 5<sup>th</sup> minute

correlated significantly with PM-accuracy ( $r=.398$ ). Controls with higher accuracy strategically increased their monitoring frequency closer to the target time.

*Correlation among time-based prospective memory, time perception and executive functions tasks*

In TBI group, correlation analysis revealed a significant negative correlation between PM-accuracy and Updating suggesting that patients who performed better on the prospective memory task made less error on the n-back task (Table 2.3). In addition, monitoring frequency at the 2<sup>nd</sup> and 5<sup>th</sup> minute significantly correlated with Inhibition indicating that TBI patients with higher numbers of clock-checking were less able to inhibit irrelevant information. For the control group, a significant negative correlation was found between PM-accuracy and Inhibition, suggesting that healthy controls with higher accuracy were less affected by interference. In addition, significant correlations were found between monitoring at the 1<sup>st</sup>, 2<sup>nd</sup> and 5<sup>th</sup> minute and Time perception: healthy control participants with higher monitoring frequency were more variable in time reproduction task. Significant negative correlation was also found between the 1<sup>st</sup> minute and the Updating index indicating that healthy controls with higher monitoring frequency at the 1<sup>st</sup> minute made less errors on the n-back task.

**Table 2.3** Pearson’s correlations between time-based prospective memory, time reproduction and executive functions tasks. PM-accuracy = accuracy at the target time; Min 1st, Min 2nd, Min 3rd, Min 4th and Min 5th = monitoring frequency; Time perception = mean of the participants’ CV in the time reproduction task; Inhibition = difference between the RTs in incongruent and congruent trials in the Stroop task; Updating = number of errors in the n-back task.

	TBI group			Control group		
	Time perception	Inhibition	Updating	Time perception	Inhibition	Updating
<b>PM-accuracy</b>	-.287	-.095	<b>-.431*</b>	-.328	<b>-.445*</b>	-.013
<b>Min 1<sup>st</sup></b>	.061	.375	-.256	<b>.621**</b>	.328	<b>-.483*</b>
<b>Min 2<sup>nd</sup></b>	.358	<b>.524*</b>	.028	<b>.563**</b>	.280	-.305
<b>Min 3<sup>rd</sup></b>	.145	.426	-.086	.387	.281	.015
<b>Min 4<sup>th</sup></b>	.032	.438	-.093	.210	.397	.015
<b>Min 5<sup>th</sup></b>	-.048	<b>.534*</b>	-.121	<b>.522*</b>	.355	-.054

\* $p < .05$ ; \*\* $p < .01$

Monitoring frequency at the 1<sup>st</sup> and 5<sup>th</sup> min differentially correlated with Time perception index in TBI patients and controls ( $z=1.82$ ,  $p < .01$  and  $z=1.45$ ,  $p < .01$ , respectively). In particular, the monitoring at the 1<sup>st</sup> and 5<sup>th</sup> min significantly correlated with time reproduction in the control group, while no significant correlations were found in the TBI group. Control participants with less monitoring frequency were also less variable in the time reproduction task.

*Correlation among time perception and executive functions tasks*

Significant positive correlation were found between Time perception and Updating in both groups (TBI  $r=.517$  and controls  $r=.439$ ). Participants that made more errors in n-back task were also more variable in time reproduction task.

*Correlation among time-based prospective memory and neuropsychological task in TBI patients*

We also have conducted correlation analysis within the TBI group between time-based prospective memory indices, time perception and tasks included in the neuropsychological evaluation (Table 2.4). Significant correlations were found between prospective memory accuracy, Action program, Go/No-go and WCST (global score). Patients with better executive abilities (Action program) of planning and executing that made less error in the Go/No-go task and had higher performance at the WCST task were more accurate at the target time; interesting significant correlations were also found between WCST and monitoring frequency at the 4<sup>th</sup> and 5<sup>th</sup> minute. Patients that had better performance at the WCST task increased their monitoring frequency closer to the target time. Finally, significant correlations were found between Time perception index, Action program, Go/No-go and Divided attention tasks. Patients with lower performance on those neuropsychological tasks were also more variable on time reproduction task indicating lower temporal abilities.

**Table 2.4** Pearson’s correlations between time-based prospective memory, time reproduction and neuropsychological tasks. PM-accuracy = accuracy at the target time; Min 1<sup>st</sup>, Min 2<sup>nd</sup>, Min 3<sup>rd</sup>, Min 4<sup>th</sup> and Min 5<sup>th</sup> = monitoring frequency; Time perception = mean of the participants’ CV in the time reproduction task; TMT=time to execute TMT part A; Action program and Zoo Map= refer to the performance at the two subtasks of BADS; Divided attention=refers to the number of errors at the subtask of TAP; WCST global score=refers at the performance on WCST task.

	<b>TMT</b> n=14	<b>Action program</b> n=12	<b>Zoo map</b> n=12	<b>Go/No-go</b> n=14	<b>Divided attention</b> n=14	<b>WCST global score</b> n=14
<b>PM accuracy</b>	-.134	<b>.540*</b>	.441	<b>-.494*</b>	-.295	<b>-.737**</b>
<b>Min 1st</b>	.092	.299	-.073	-.160	.069	-.063
<b>Min 2nd</b>	.338	.083	.196	.108	.197	-.400
<b>Min 3rd</b>	.266	.231	.184	-.056	-.025	-.403
<b>Min 4th</b>	.332	.037	.195	-.042	.240	<b>-.495*</b>
<b>Min 5th</b>	.462	-.066	-.092	-.237	.137	<b>-.550*</b>
<b>Time perception</b>	-.091	<b>-.545*</b>	-.203	<b>.711**</b>	<b>.574*</b>	.179

\* $p < .05$ ; \*\* $p < .01$

### 2.9.4 Discussion

The present study investigated time-based prospective memory in TBI patients and its relationship with time perception and executive functions. Compared to previous studies, where participants were required to engage in high-load concurrent activities (i.e. performing the time-based prospective memory task within a word verification task, Kinch and McDonald, 2001, or while answering a set of four-choice general-knowledge questions, Shum et al., 1999) our study asked participants to perform the time-based prospective memory task while watching a movie. Despite the low-load concurrent activity, TBI patients showed poorer performance than controls confirming the time-based prospective memory dysfunction in these patients.



The results suggested that healthy control participants performed significantly better than TBI patients, as they were more accurate in their responses closer to the target time. When the task was completed, participants were asked to repeat the instructions; all patients were able to recall the requirements confirming that the difficulties in the TBI group were related to performing the action at the target time rather than a failure to recall the task content. This might be because the cerebral areas commonly affected by TBI (i.e. frontal areas) are responsible for the processes involved in the prospective memory tasks (initiation and execution of plan action, updating and interruption of ongoing activity) (McFarland & Glisky, 2009).

Our study support previous data and confirm the involvement of executive functions on time-based prospective memory task (Kinch & McDonald, 2001; Kliegel, Eschen, & Thöne-Otto, 2004b; Mathias & Mansfield, 2005; Fleming et al., 2008). In particular, intact updating abilities were associated with better accuracy at target time in the TBI group (i.e., Carlesimo et al., 2004a; Maujean et al., 2003), while prospective memory accuracy was associated with inhibition abilities in the control group. Control participants who were more accurate at the target time were less affected by interference showing greater inhibition abilities (i.e., Gonneaud, Kalpouzos, Bon, Viader, Eustache, & Desgranges, 2011). A possible explanation is that TBI prospective memory accuracy is strongly influenced by working memory abilities, probably to keep constantly updating the prospective memory task (e.g., press the key at the target time), whereas controls participants, with better overall cognitive abilities, probably do not rely only on their working memory ability to constantly recall the task, but rather based their performance on inhibition of irrelevant task information.

In this study, monitoring behaviour has been discussed as a critical index to investigate time-based prospective memory because it is suitable to underlie differences between group performances (Einstein et al., 1995, Shum et al., 1999; Carlesimo et al., 2004a). Time-based prospective memory requires remembering the content of the future activity, inhibit the ongoing task, and strategically monitor the clock to accurately perform the prospective memory task. Deficits in inhibition and updating abilities could be compensated for increased monitoring frequency. Both groups increased their monitoring frequency as the target time approached and, in average, the TBI patients monitored more frequently than controls. TBI patients increased their monitoring frequency around the 2<sup>nd</sup> minute, whereas the control group significantly increased their monitoring frequency around the 4<sup>th</sup> minute. Patients with TBI may increase their monitoring frequency in order to compensate for executive and temporal dysfunction, and the healthy group may have not monitored as frequently due to their intact cognitive abilities. Despite the higher monitoring frequency TBI patients showed an inefficient monitoring strategy as they had lower prospective memory accuracy. Based on Einstein et al.'s (1995) results, it was expected that performance on the time-based task would be related to frequency of monitoring behaviour, especially in the period most proximal to the target time. This was confirmed in the control group, in fact, significant correlation was found between monitoring at the 5<sup>th</sup> minute and accuracy. As noted above, the control group showed a more efficient strategic monitoring pattern than TBI participants, which may have resulted in a higher accuracy performance.

Prior research has found contrasting data in the monitoring behaviour of patients with TBI, with some (Shum et al., 1999) indicating similar monitoring rates between TBI and healthy controls, and others (Carlesimo et al., 2004a) finding it to be less in

TBI groups. One possible explanation is that the studies used different time-based prospective memory tasks with different instructions. In the study by Shum et al. (1999), participants were asked to call the second experimenter every 5 minutes while engaged in a general-knowledge task, and they were instructed that they could press the ‘t’ key on the keyboard to check the clock. In Carlesimo et al. (2004a) study, participants performed eight triplets of actions at the occurrence of the target event or expiration of the established time, and they were not informed that they could reference a wall clock to benefit from a time cue. In our study, participants performed a training phase where they became familiar with the time monitoring task and they were instructed that they could use the keyboard to access a time cue. Previous studies have addressed the issue of task importance in prospective memory and have shown that the strategic allocation of attention improves prospective memory (Kliegel, Martin, McDaniel, & Einstein, 2001).

When engaged in a monitoring task (dual-task like paradigm), participants had to inhibit the irrelevant information to perform the prospective memory activity. Monitoring frequency was found to positively correlate with inhibition ability in both groups. Participants with low inhibition abilities checked the clock more frequently than did participants with more efficient inhibitory functions. Participants may have attempted to compensate for their difficulties in inhibition by relying on the external clock and monitor more frequently than did participants with more efficient inhibition functions. An interesting implication of this pattern of compensatory behavior is that increased monitoring should have direct effects on the prospective memory task performance. That is, high monitoring frequency should facilitate accurate prospective memory performance, but this was not the case for TBI patients. In fact, despite higher

monitoring frequency, TBI patients were less accurate than controls which further highlights their inefficient use of a compensatory strategy.

We have also conducted correlation analysis within the TBI patients between time-based indices and the tasks included in the neuropsychological evaluation. The limited number of data from the neuropsychological evaluation not allowed us to present clear conclusion however, some interesting considerations may be conducted. TBI patients with higher performance in the tasks included in the neuropsychological evaluation were also more accurate at the target time and increased their monitoring frequency closer to the target time indicating an adequate strategic behavior to perform the time-based prospective memory task.

Shum et al. (1999) proposed that differences in monitoring behaviour between TBI patients and controls may not be explained by differences in strategic monitoring alone, but also may be due to differences in time estimation, suggesting that the ability to accurately estimate the passage of time may be critical for successful time-based prospective memory performance. Particularly interesting is the positive correlation between monitoring frequency and time perception in the control group. Controls that frequently checked the clock were more variable in the time reproduction task, but TBI participants who did not have adequate temporal abilities needed to monitor the time more frequently. These results suggest that temporal abilities are involved in the performance of time-based prospective memory tasks, in particular, in monitoring behaviour.

In this study we also investigated time perception in TBI patients. According to the Attentional-Gate model (Block & Zakay, 2006) attentional and updating factors are critical to accurately perceive durations. Because attentional and updating dysfunctions

are often reported in TBI patients (Ponsford & Kinsella, 1992; Park, Moscovitch, & Robertson, 1998, Lezak et al., 2004; Stuss, 2011) we expected temporal impairment in patients. Both groups under-reproduced the durations confirming the influence of divided attention on time judgment (Zakay & Block, 1996). Particularly interesting are the findings on the variability index that showed greater variability in TBI patients than controls. This greater variability may be explained in terms of impaired updating and inhibition processes (Nichelli et al., 1995; Perbal et al., 2003). In time reproduction tasks, participants accumulate and store pulses during the presentation of the stimulus, retain the number of pulses in working memory while accumulating the new pulses corresponding to the current duration, and then compare the two numbers of pulses stored in working memory (Block et al., 1998). Variability in temporal perception could come from variable representations of the duration in working memory; TBI patients may have difficulty in maintaining a stable representation of duration due to updating dysfunctions. These data are further supported by the correlation analysis conducted on TBI patients between time perception and neuropsychological tasks. TBI patients with lower performance on the neuropsychological tasks were also more variable in the time reproduction task that indicated lower temporal abilities.

Strength of this study was the study of time perception and executive functions on time-based prospective memory tasks in TBI patients, which has received limited scientific investigation. The generalizability of our results may be limited by the sample size and by the tasks employed, particularly with regard to the domain of executive functions. Because executive functions are not a unitary system (Miyake et al., 2000), additional study is needed to examine if other executive functions (e.g., problem solving) are involved with prospective memory tasks. Future studies may also consider

enrolling patients based on the location of cortical lesions (e.g., frontal vs. non-frontal). Nevertheless our data are interesting and may have important implications for prospective memory rehabilitation. In fact, the results suggested that improving temporal abilities in TBI patients may improve TBI time-based prospective memory performance.

In conclusion, our results support the hypothesis that executive functions, particularly inhibition and updating abilities, are strongly related to time-based prospective memory (Cockburn, 1996; McDaniel et al., 1999; Kinch & McDonald, 2001) and provide additional information to their relative contribution to monitoring behaviour and performance on time-based prospective memory. Participants with better inhibition and updating abilities showed better performance on time-based prospective memory. Moreover, monitoring frequency was found to correlate with inhibition and time perception performance. TBI patients relied more on executive functions than temporal components, while control participants engaged both executive functions and temporal abilities. TBI patients with higher temporal variability may not feel confident with their temporal abilities and therefore, base their prospective memory performance on working memory and compensate by increasing their monitoring frequency. Controls were more confident with their temporal abilities and therefore could perform time-based prospective memory task also on the grounds of this additional cognitive component.

#### *2.9.4.1 A comprehensive model for monitoring behaviour in time-based prospective memory*

Following the interest of investigating how time perception and executive functions influence time-based prospective memory performance I will propose a preliminary model on time-based prospective memory in particular on monitoring behaviour. Despite the focus of this thesis is on time perception and prospective memory performance in TBI patients some generalization could be done.

Prospective memory performance relies on various frontally mediated cognitive processes. Previous studies have pointed out that prospective memory dysfunction present in TBI patients may be due to frontally mediate executive dysfunctions (Shum et al., 2011). In accordance with these findings, it has been observed that prospective memory dysfunctions increase with age (Park et al., 1997; Maylor et al., 2002; Park et al., 2004; see also Mäntyla & Nilsson, 1997) maybe due to age-related decay of prefrontal cortex functions (West, 1996; Glisky, 1996). Age-related functional and structural changes are often reported in adulthood (Salat, Kaye, & Janowsky, 2001) and it has been extensively observed that executive functions decline in old age (Crawford, Bryan, Luszcz, Obonsawin, & Stewart, 2000).

Interestingly, Kliegel et al. (2004b) tested healthy older adults, TBI patients and controls with a complex prospective memory task (Kliegel et al., 2000) to investigate the effect of executive dysfunction on prospective memory performance. Older adults and TBI patients, with retrospective memory abilities within normal limits, but executive functions impairments performed significantly lower than healthy controls on prospective memory tasks (Kliegel et al., 2004b).

Consistent with previous finding with TBI patients (Shum et al., 2011), with older adults (Mäntyla & Carelli, 2006) and with our finding from Study 3 frontally mediated executive functions are involved in time-based prospective memory performance. In particular, participants with better executive functions should have better performance in time-based prospective memory tasks. Our finding from Study 3 also suggested that time perception is involved in time-based prospective memory performance, in particular in monitoring behaviour. Healthy controls with better temporal abilities needed less clock check monitoring to accurately perform the time-based prospective memory task. In sum, we predict that both executive functions and time perception are involved in time-based prospective memory performance.

To confirm our hypothesis we employed structural equation model (SEMs) to predict which variables may appear as predictor for other variables, either directly or through other variables as intermediaries. This confirmatory method provide research with a comprehensive means for assessing and modifying theoretical models and is meant to represent causal relationships among the variables in the model (Baron & Kenny, 1986; Anderson & Gerbing, 1988).

## **Materials and procedure**

### *Participants*

One-hundred thirty one participants took part in the study (F=81 and M=50). They were all healthy adults ranging from 20 to 82 year old [mean age 44.85 years (SD=22.87); education 9.57 years (SD=2.82)].



### *Procedure*

Participants were tested in a quiet room at the University of Padova or in their own home (Padova or Cuneo). All participants performed a time-based prospective memory task (time monitoring), time perception task (time reproduction task) and executive functions tasks (Stroop and N-Back tasks).

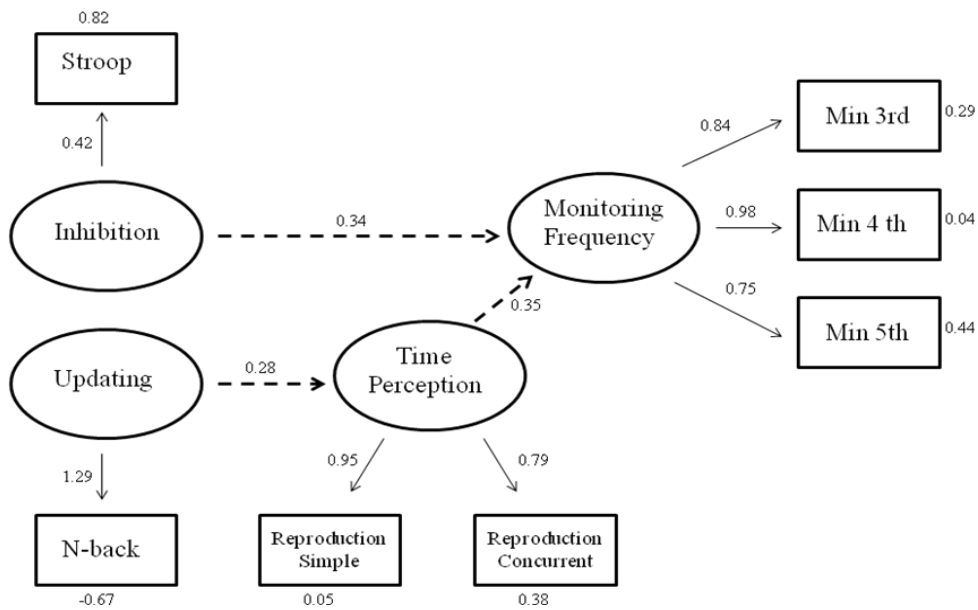
### *Materials*

To tap time-based prospective memory performance a time monitoring task was employed in which participants were required to watch a movie (ongoing task) and press a designed key every 5 min (time-based prospective memory task) (see pp. 76 for more procedural details). To tap temporal abilities participants were tested with a time reproduction task (4, 9 and 14 s) under simple and concurrent condition (see pp. 76 for more procedural details). Finally to tap executive abilities a Stroop (Inhibition) and N-back (Updating) tasks were employed (see pp. 77 for more procedural details).

### **Results and discussion**

The pattern of relationship between variables was investigated using structural equation model based on the hypothesis that both executive functions and time perception are involved in monitoring behaviour and computed via LISREL. The derived model is based on the covariance matrix between the observed variables (Figure 2.2). Stroop task measured the first latent variable “Inhibition”, while N-Back the observed variable measuring the first latent variable “Updating”. The other variables measured the latent variable monitoring frequency. The fitness indices were good, as the Root Mean Square Error of Approximation (RMSEA = 0.049) was lower than the usual critical value of 0.08 and the relationship between  $\chi^2$  and the degrees of freedom was

lower than the typical critical value of 2.5. The Normal Fit Index (NFI) and the Non-Normal Fit Index (NNFI) were also good (NFI=0.97 and NNFI=0.98). The goodness of the model was also supported by the residuals, which were uniformly low. Thus the model confirmed our assumption that inhibition and time perception, and updating via time perception affect monitoring behaviour in time-based prospective memory tasks.



**Figure 2.2** Relationship between variables included in the time-based prospective memory performance as emerging from the structural equation model (SEM).

The model we proposed clearly confirmed the involvement of inhibition and time perception in monitoring behaviour moreover, showed the involvement of updating via time perception on monitoring behaviour. In Study 3 we already pointed out the involvement of time perception in monitoring behaviour in controls and this models extend our previous finding through normal population. Healthy adults with adequate time perception, recruited temporal abilities to strategically monitor the clock while TBI with temporal dysfunctions relied only on executive abilities resulting in lower

strategically clock monitoring. These findings may have interesting implications in clinical settings, suggesting the importance of temporal abilities on performing time-based prospective memory tasks and suggesting the improvement of temporal abilities that may have implications on other cognitive processes.

## **2.10 Ecological tasks to investigate Prospective Memory**

Failure on prospective memory is one of the most common and disabling deficits after TBI (Cockburn, 1996; Kinsella et al., 1996; Shum et al., 1999; Groot, Wilson, Evans, & Watson, 2002; Schmitter-Edgecombe & Wright, 2004; Mathias & Mansfield, 2005; see also Shum et al., 2011 for a review). Prospective memory dysfunctions may constitute a significant barrier to return to independent living (Fleming et al., 2008) therefore a wide number of laboratory studies have been conducted to investigate prospective memory dysfunctions in TBI patients (Shum et al., 2011) and to investigate which attentional, memory and executive processes are relevant to successful prospective memory performance (Kinch & McDonald, 2001; Maujean et al., 2003; Schmitter-Edgecombe & Wright, 2004; Mathias & Mansfield, 2005; see also Einstein et al., 2005; Marsh, Hicks, & Cook, 2005 with older adults). However, for an adequate rehabilitation program and for adequate clinical assessment neuropsychologists need information about how a patient functions in the routines of everyday life, and laboratory-based measures may not always provide such information (Knight & Titov, 2009). In a recent review, Chaytor and Schmitter-Edgecombe (2003) found that the relationship between neuropsychological tests and measures of outcome is often limited and McDaniel and Einstein (2007) recently concluded that most prospective memory tasks lack reliability, with some tasks as low as 20%. As a consequence, it is often not possible to translate

test scores into either goals for rehabilitation or conclusions about the level of impairment; that is, many conventional tests of memory-related abilities lack any semblance of ecological validity (Burgess, Alderman, Forbes, Costello, Coates, Dawson, et al. 2006; Einstein & McDaniel, 2007; Knight & Titov, 2009).

To solve the discrepancy between performance at neuropsychological tests and performance in everyday life, researchers, using the growing development of computer programs, have developed tasks that can provide a bridge between conventional neuropsychological tests and behavioral observation. Virtual tasks, in fact, can simulate the activity of everyday life in a controlled setting (Knight & Titov, 2009). In this section I revise the main studies that have employed virtual tasks with ecological validity to investigate prospective memory performance in TBI patients and we also propose a new task: the Virtual Week (Rendell & Craik, 2000) to study and evaluate prospective memory dysfunction in TBI patients.

### **2.11 Prospective memory' ecological tasks and TBI**

To solve the little relationship between a patients' score on neuropsychological tests and their ability to function in the real world, recent line of research developed computer based tasks that simulated real life situations (Titov & Knight, 2000; Craik & Bialystok, 2006; Rendell & Henry, 2009) (Table 2.5 ). I have revised this literature separately from others studies on prospective memory because studies conducted with virtual tasks look more closely to everyday prospective memory performance and are more focused on filling the gap between performance on laboratory tasks and prospective memory performance on real life. The development of new technologies and new tasks is fundamental in a clinical setting to further investigate prospective memory

performance and create adequate assessment and rehabilitation projects. In fact, an emerging interest in clinical setting is the development of neuropsychological tasks with ecological validity (Sbordone, 1996).

**Table 6.5** Studies that used ecological tasks to investigate prospective memory performance on TBI patients. GCS= Glasgow Coma Scale; NPS assessment refers to the neuropsychological tasks included in the studies; NART=National Adults Reading Test; WCST=Wisconsin Card Sorting Test; LM=Logic Memory; COWAT=Controlled Oral Word Association Test; TMT=Trail Making Test; WMS=Wechsler Memory Scale; DEX=questionnaire from the Behavioural Assessment of Dyexecutive Syndrome; HVLTL=Hopkins Verbal Learning Test.

Study	Year	Sample	GCS	Time since injury (months)	NPS assessment <sup>12</sup>	Ecological Tasks
<b>Knight et al.</b>	2005	25 TBI and 20 controls	-	113.76 (75.13)	NART, WCST, LM, COWAT and TMT	Videotape: Performing activities when the cue appeared on the screen by saying to the experimenter the activities required
<b>Titov &amp; Knight</b>	2005	2 brain injury patients <sup>13</sup> and 3 controls	Patients SR GCS=3 and Patients TJ GCS=4	Patients SR 6 months; Patients TJ 3.5 months	WMS word list, Digit span, Stroop, WCST and NART	Virtual Street: Imagine walking on a street and performing 3 activities. The list of activities was either visible or hidden after instruction
<b>Knight et al.</b>	2006	20 TBI and 20 controls	-	160.2 (91.66)	DEX, Logical memory from WMS and Ruff 2&7 selective attention test	Virtual Street: Imagine being a street inspector and performing 3 activities under low and high distraction. Moreover performing 10 errands
<b>Kinsella et al.</b>	2009	16 TBI and 16 controls	8 or less	at least 3 month	HVLT, TMT and Digit span	The supermarket shopping trip: "buy" 8 items while watching a 8-min DVD of a supermarket trip

<sup>12</sup> References of neuropsychological tasks are not reported because the authors referred to different version of the tasks. Please refer to the specific articles for the appropriate references.

<sup>13</sup> The study includes 3 patients with brain injury: SR suffered a severe TBI as a result of assault, TJ suffered a TBI as a result of motor vehicle accident and RW suffered cerebellar and sub-arachnoid haemorrhages. Only information on patients SR and TJ were included because TBI patients.

The Prospective Remembering Video Procedure (PRVP, Titov & Knight, 2001) was designed to test prospective memory abilities in virtual street simulation. The task involves remembering to carry out a set of activities while watching a videotape filmed by a person walking slowly through a shopping complex. Participants virtually visited a shopping centre, with a set of event-based activities, each of which involved an action ('buy a record') and a cue ('from the record stand'). As each cue comes into view, the associated action must be recalled. The view that was presented focused mostly on the shop-front, although the footage also included views of passengers crossing the street. Studies conducted with health students and mix-brain injury patients, demonstrated that the PRVP procedure is reliable and easier to complete when the video is set in a familiar location. Moreover, it was found that the video-based task was correlated with performance on an equivalent real life memory task providing evidence for criterion validity (Titov & Knight, 2000, 2001, and 2005). Twenty severe TBI and 20 matched controls were tested with PRVP and completed the ongoing and prospective memory tasks while "walking" along the street. TBI patients performed the prospective memory tasks more poorly than controls and TBI patients were more affected by distractions (Knight et al., 2005).

Titov & Knight (2005) and Knight and colleagues (2006) confirmed and extended Knight et al. (2005) results with a Virtual Street task. In fact, Knight et al. (2006) showed that TBI patients performed more poorly than the controls group on prospective memory tasks but had similar performance on Logical Memory subtest of WMS-III. The authors discussed this result in favor of sensitivity of Virtual Street task to measure prospective memory performance. These results suggest that TBI patients may normally perform memory tests, particularly in a controlled and quiet testing

setting, but when memory performance is tested in a less controlled setting with distracters and with tasks that required more strategic process (like in real life conditions) real TBI dysfunctions may emerge.

Interesting, following the idea to create tasks more representative to real life situation, Kinsella et al., 2009 investigated additional methodological issue often discussed in prospective memory literature: the “generation effect” which refers to the effect of people demonstrating better memory for self-generated material than for experimenter-generated materials (Ellis & Kvavilashvili, 2001; Bertsch, Pesta, Wiscott, & McDaniel, 2007). Considering the instruction often presented in prospective memory setting to perform the action at a specific time or when a specific cue occurs, these tasks may allow control over the tasks but they do not produce the same level of motivation in participants compare to activities that have to be self-generated (Bertsch, et al., 2007). Kinsella et al. (2009) reasoned whether people with TBI are more likely to successfully remember prospective memory task if the task is self-generated as opposed to experimenter-generated. TBI patients were less accurate than control but the source of to-be-remembered item exerted minimal influence on prospective memory performance both in TBI and control. Additional analyses were conducted to further investigate the source of errors; it was found that both groups were able to recognize at post-test the shopping item that they had intended to buy, but TBI failed to activate their intention to buy the intended item at the appropriate time. Moreover, significant correlations were found between executive attention of working memory (attention-set shifting) and prospective memory performance giving further support to the notion that high cognitive functions (in particular working memory abilities) are necessary in prospective memory (Kliegel et al., 2004).

Although, the high reliability and the correspondence with real-life situation, the PRVP and the Virtual Street required participants to perform only event-based tasks, however, prospective memory performance should be investigated both with event- and time-based tasks. To investigate event- and time-based prospective memory performance with virtual tasks we used the Virtual Week task developed by Rendell & Craik (2000) and widely used with normal (Rendell & Craik, 2000; Rose et al., 2010; Abele et al., 2010) and clinical populations (Henry et al., 2007a b; Leitz et al., 2009; Paraskevaides, Morgan, Leitz, Bisby, Rendell, & Curran, 2010; Rendell et al., 2007a b; Rendell et al., 2009; see also Rendell & Henry, 2009 for a review). We have decided to use the Virtual Week to investigate prospective memory performance in TBI patients because (to the best of our knowledge) is the only virtual task that include event- and time-based tasks which are equally important and critical on prospective memory performance, moreover the Virtual Week gives additional information about performing routine or irregular activities. Like in real life, there are future activities that have to be performed every day at the same moment (i.e. picking up your son at school at 4 pm or taking medication every morning) or errant activities which are different every day (i.e. buying a present for your friend's birthday or attending to a work meeting at 11 am). The former activities are called "regular tasks" while the later ones are called "irregular tasks" (Rendell & Craik, 2000). Investigating the effect of regular and irregular activities on prospective memory performance has important clinical implications; imagine the situation in which patients have to take medications regularly every day, do they have the abilities to perform regular activities? Repeating the same activities might improve their prospective memory performance? Previous studies confirmed this hypothesis with older adults, showing that task regularity tend to reduce age-related



differences on prospective memory performance. It has been hypothesised that prospective memory cues that occur more regularly may be more likely to spontaneously trigger intention retrieval, while irregular cues may involve more strategic monitoring (Rendell & Craik, 2000; Kvavilashvili & Fisher, 2007; Henry et al., 2004; McDaniel & Einstein, 2007). We expect to have similar results with TBI patients.

## **2.12 The Virtual Week: Characteristics and assessment in clinical population**

The Virtual Week (see Figure 2.3) was developed as a laboratory prospective memory task that closely represent prospective memory tasks in everyday life in which each circuit of the game around the board represents 1 day. Participants move around the board with the roll of a die. At the center of the board is presented a virtual clock which represent the time of the virtual day. Every virtual day start at 7 am and it ends at 10 pm. The time of the virtual day moves according to the number obtained on the die: 15 minute every 2 squares. The second clock presented on the board is a stop-clock that starts from 0:00 at the beginning of every new virtual day and shows the real time to execute the virtual day. The demands of rolling the die, moving the token around the board and making decisions about the activities, serve as the ongoing activity for the prospective memory tasks. Every time which participants stop or pass through the green square labeled “E” are required to click on the green card “EVENT”.

The Event card describes specific activities normally required during a day, starting from breakfast in the morning concluding with after dinner at the end of the virtual day. Moreover, in every Event card, soon after the image, that describes the moment of the day, participants are required to select one of the three options relevant to the virtual time of day (Figure 2.4A). The three option presented are not related to the

prospective activity, but prescribed the number that must be rolled before continuing on with the day (Figure 2.4B).

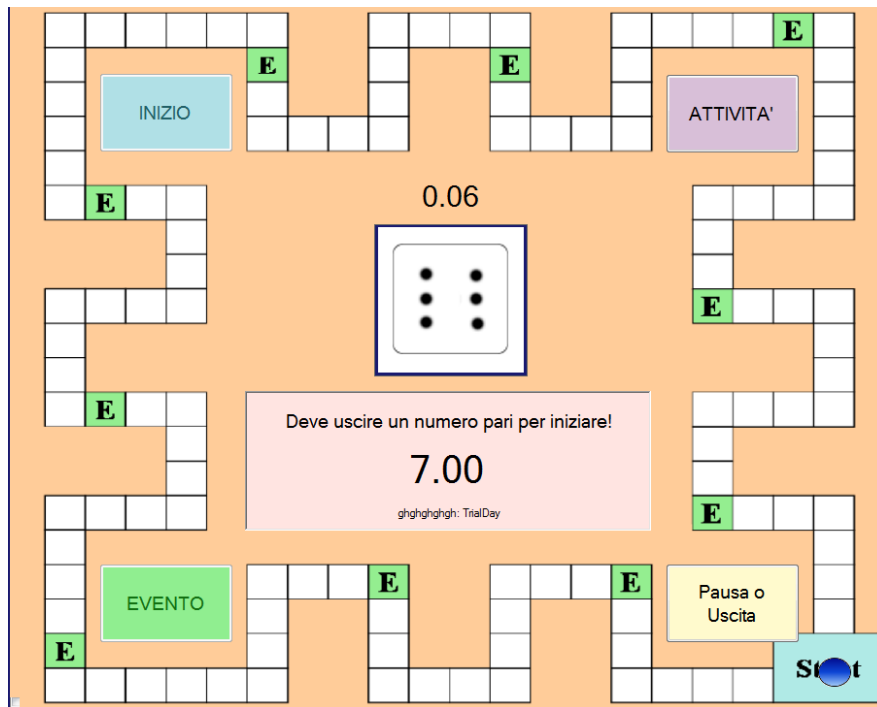


Figure 2.3 The Virtual Week: computer screen display in the Italian version.

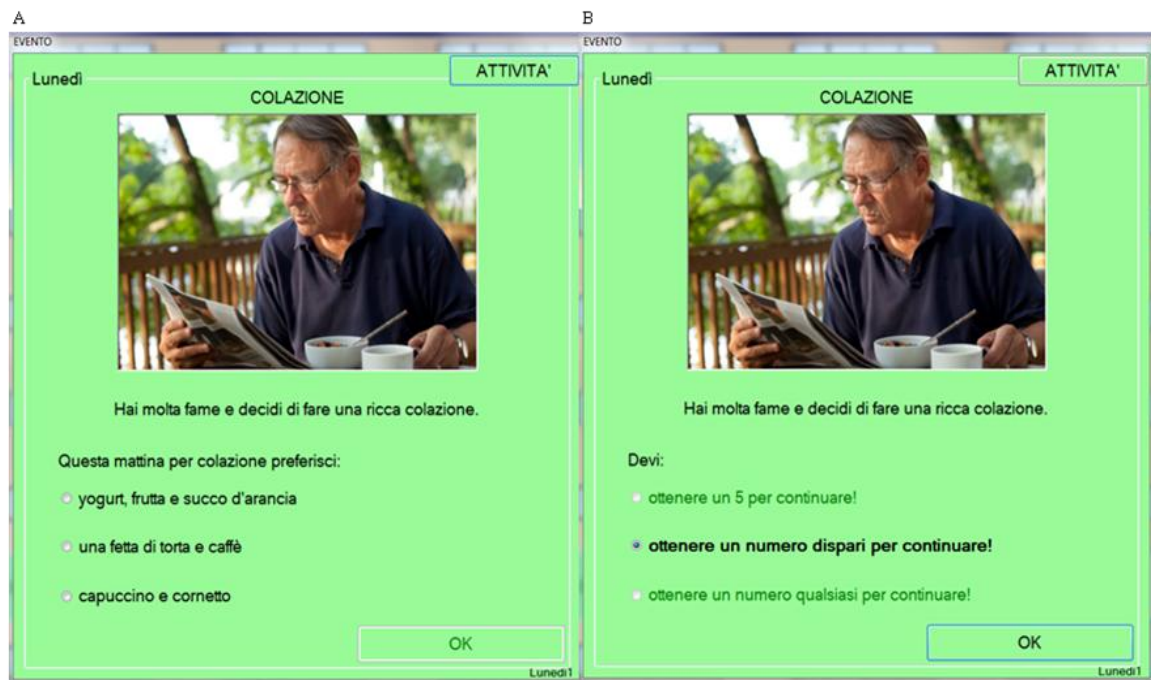


Figure 2.4 Examples of Event Card in the Italian version.

Each virtual day of the Virtual Week includes 10 prospective memory tasks (four regular, four irregular, and two time-checks). Participants do not physically carry out each prospective memory task, but are required to remember and virtually perform them by selecting the required activity from a list that appeared clicking on the “PERFORM” button (ATTIVITA’). The four regular prospective memory tasks represent the kinds of regular tasks that one perform every day with regularity, in the Virtual Week participants are instructed to imagine to be sick and that the doctor have prescribed them to take medication regularly every day.



**Figure 2.5** Examples of regular event-based (A) and time-based (B) tasks included in the Italian version.

Two of which are event-based (i.e., triggered by some information shown on an Event Card; Figure 2.5A), and two are time-based (i.e., triggered by the virtual time of day; Figure 2.5B). The event-based tasks are “take antibiotics at breakfast and dinner” (triggered by event cards featuring breakfast and dinner), and the time-based “take asthma medication at 11 a.m. and 9 p.m.” (triggered by time displayed in the central clock). The two time-check tasks require the participant to do a lung test on two

occasions, at 2 min and at 4 min and where related to the stop-clock placed in the top part of the board.

Prior to start the game, participants are required to click on the “START” (INIZIO) card and learn about the irregular activities that have to be performed. The four irregular prospective memory tasks simulate the kinds of occasional tasks that occur in everyday life; again, two of these tasks are event-based (Figure 2.6A) and two are time-based (see Figure 2.6B). Two irregular tasks are presented in the Start Card (one time-based and one event-based) and two irregular tasks are presented during the Virtual Day (one time-based and one event-based). All the activities presented have to be performed within the Virtual Day.



**Figure 2.6** Examples of irregular event-based (A) and time-based (B) tasks included in the Italian version.

The Virtual Week is a promising task to investigate prospective memory performance in TBI patients and it has been extensively used with normal aging (Rendell & Craik, 2000; Rose et al., 2010; Abele et al., 2010; Rendell, Phillips, Hendy, Brumby-Rendell, & de la Piedad Garcia, Altgassen & Kliegel, 2011) and different clinical population: Abnormal aging (Ozgis et al., 2009; Will et al., 2009); Multiple

Sclerosis (Rendell et al., 2007a; West et al., 2007); Schizophrenia (Henry et al., 2007b); Substance users (Rendell et al., 2007b; Rendell et al., 2009; Leits, Morgen, Bisby, Rendell, & Curran, 2009; Paraskevaides, Morgen, Leitz, Bisby, & Rendell, & Curran, 2010). Interestingly, Kim et al (2011) tested 12 stroke patients with lesions mainly in frontal areas and 12 healthy controls. Stroke patients with anterior lesions should show deficits in tasks requiring self-initiated processing, planning and executive abilities like TBI patients (Burgess & Shallice, 1996). Results showed lower performance prospective memory dysfunction in TBI patients and participants were more accurate on the regular than on the irregular tasks (Kim, Craik, Luo, & Ween, 2010).

Compared to prospective memory tasks that included fewer number of observation (McDaniel & Einstein, 2007) the Virtual Week incorporates 50 prospective memory task observations (4 regular, 4 irregular and 2 stop-clock activities every day) over 5 virtual days (from Monday to Friday). Moreover, allow the investigation of some of the main theoretical issues included in the prospective memory literature likewise the differences between time- and event-based tasks, the effect of cue focality and the effect of regularity (McDaniel & Einstein, 2000). Regarding the effect of cue focality, prospective memory tasks cued with event cards are hypothesized to involve more focal processing than tasks cued by the time on the board, and therefore, the authors predicted that performance would be better when cued by event cards than by time on the board. Regarding the effect of task regularity, repeatedly performing the same prospective memory task on each day of the Virtual Week is expected to result in performance becoming more habitual and therefore, improving over the course of the Virtual Week. Moreover, performances can be compared according to event- or time-based activities. In particular time-based activities are triggered by virtual time (the clock at the center of

the board) and by the stop-clock, including both clocks authors can investigate time-based performance under both “virtual” and “real” time.

Another important strength of Virtual Week lies in its psychometric properties. The reliability of Virtual Week was investigated by Rose and colleagues (2010) in a study involving 61 younger (age 18-22 years) and 45 older adults (age 61-87 years). Across the entire sample, reliability estimates ranged from .84 to .94 for the regular, irregular and time-check tasks.

### **2.13 Translation and adaptation to the Italian population**

The Virtual Week has been developed for English speaking population and this is the first study with Italian speaking population. Prior testing TBI patients the Virtual Weeks has been translated and adapted. We tried to maintain the same number of words, length of the sentences and activities to perform. However, some changes have been required adapting the Virtual Week to the Italian population and to TBI patient’s necessities.

Specifically:

- 1- We have reduced the number of activities related to University. The original Australian version was created for older participants that were tested mainly at University (Table 2.6A), therefore for older Australian is not so unusual going to the University to participate in experimental studies or to follow courses at the University of Third Age. Because this situation is not common in Italy we have changed some activities related to University with new activities (Table 2.6B).

2- We have also simplified the presentation of the instructions to avoid distractions in TBI patients. The presentation of instructions comes through pop-up messages that appeared when necessary during the training day. Previous studies have demonstrated that TBI patients have attentional dysfunctions and are easily distracted for these reasons we reduced the number of pop-up instructions without changing the way to present the task.

Pilot studies have been conducted with University students to verify the efficacy of the Italian virtual week. Students filled a questionnaire concluded the task to report considerations and suggestions.

**Table 2.6** Event tasks in the Australian (A) and Italian (B) Virtual Week tasks. In colour the activities that we have changed.

A

	<b>Monday</b>	<b>Tuesday</b>	<b>Wednesday</b>	<b>Thursday</b>	<b>Friday</b>
Event Card (1) 7.50am	Breakfast	Breakfast	Breakfast	Breakfast	Breakfast
Event Card (2) 9.20am	Phone Call	Phone Call	Session at University	Repairman Visits	Yellow pages
Event Card (3) 10.50am	Visit from Neighbour	Go to Library	Problem with an Assignment	Go to Doctor	Go to Office Works
Event Card (4) 12.20pm	Lunch	Lunch	Lunch	Lunch	Lunch
Event Card (5) 1.50pm	Shopping	Session at University	Session at University	University Session	University Session
Event Card (6) 3.20pm	Library	After the Session at the University	Library	Afternoon tea	Go to see Movie
Event Card (7) 4.50 pm	Send Congratulations	Swimming Pool	Shopping	Before dinner	After Movie
Event Card (8) 6.20 pm	Dinner	Dinner	Dinner	Dinner	Dinner
Event Card (9) 7.50 pm	After Dinner	Phone Call	Dessert at Restaurant	Wash Clothes	Before Going Out
Event Card (10) 9.20 pm	Watch Television	Prepare for Early Night	After Dessert	Phone Call	Go Out

B

	<b>Monday</b>	<b>Tuesday</b>	<b>Wednesday</b>	<b>Thursday</b>	<b>Friday</b>
Event Card (1) 7.50am	Breakfast	Breakfast	Breakfast	Breakfast	Breakfast
Event Card (2) 9.20am	Cleaning home	Phone Call	Flower market	Repairman Visits	Yellow pages
Event Card (3) 10.50am	Visit from Neighbour	Go to Library	Dancing class	Go to Doctor	Go to Office Works
Event Card (4) 12.20pm	Lunch	Lunch	Lunch	Lunch	Lunch
Event Card (5) 1.50pm	Shopping	Session at University	Session at University	Travel agency	Post office
Event Card (6) 3.20pm	Library	After the Session at the University	Music store	Afternoon tea	Go to see Movie
Event Card (7) 4.50 pm	Send Congratulations	Swimming Pool	Shopping	Before dinner	After Movie
Event Card (8) 6.20 pm	Dinner	Dinner	Dinner	Dinner	Dinner
Event Card (9) 7.50 pm	After Dinner	Phone Call	Dessert at Restaurant	Wash Clothes	Before Going Out
Event Card (10) 9.20 pm	Watch Television	Prepare for Early Night	After Dessert	Phone Call	Go Out

## 2.14 Study 4

### 2.14.1 Introduction

Fundamental in clinical activity is developing laboratory tasks that have ecological validity to have correspondence between prospective memory performance in laboratory setting and prospective memory performance in real life. Despite the growing interest on prospective memory performance in TBI patients less study have been conducted with tasks that had ecological validity (Table 2.5) and prospective memory is still faced with the difficulty of finding appropriate measures that tap real-life prospective memory performance in clinical setting while also being experimentally reliable (Groot et al., 2002; Uttil, 2008).

One of the first tests proposed and widely used in clinical setting is the Rivermead Behavioral Memory Test (RBMT, Wilson, Cockburn, & Baddeley, 1991).



This test includes three tasks that assess prospective memory: Remembering where a belonging is hidden and asking for it to be returned, asking for the next appointment time when an alarm sounds, and delivering a message. Although these tests from the RBMT have been used in several neuropsychological studies of prospective memory (Cockburn, 1995, 1996; Kinsella, Murtagh, & Landry, 1996; Mathias & Mansfield, 2005), they provide only a limited range of scores and are unlikely to be sensitive to deficits in less impaired patients. More recently Wilson and co-workers developed the Cambridge Behavioral Prospective Memory Test (CAMPROMPT, Wilson, Emslie, Foley, Shiel, Watson, Hawkins, Groot, & Evans, 2005) in which participants are asked to carry out time-based and event-based at different times, while performing a filler activity, using both verbal and written instructions. Although, the CAMPROMPT provide higher number of scores and is theoretically conformed to the distinction between event- and time-based prospective memory types of tasks, it doesn't adequately represent prospective memory dysfunction in real life situation. The developing of new technologies gives the opportunity to reduce the gap between prospective memory performance in laboratory setting and prospective memory performance in real life. Moreover, sensible instrument to evaluate prospective memory performance in clinical setting need to be create.

In this study we have tested TBI patients and healthy controls with the Virtual Week (Rendell & Craik, 2000). We hypothesized prospective memory dysfunctions in TBI patients, particularly for those tasks that are more demanding in monitoring (irregular tasks). In regular tasks the cue are presented in a consistent routine and might provide a richer set for retrieving (Kvavilashvili & Fisher, 2007). Task regularity has been demonstrated to reduce age-related differences in prospective memory

performance, consistent with the hypothesis that prospective memory cue that occur more regularly may be more likely to spontaneously trigger intention retrieval (Henry et al., 2004; McDaniel & Einstein, 2007; Kligel et al., 2008; Rose et al., 2010). Moreover, we predict lower performance in time-based tasks compare to event-based tasks consistent with the hypothesis that time-based tasks are more demanding than event-based tasks because they required more self-initiated retrieval (Einstein & McDaniel, 1990; Kvavilashvili & Ellis, 1996). With regards with the Virtual Week tasks, event-based task are hypothesized to involve more focal processing than time-based tasks in which participants have to monitor the time at the centre of the board. We expect better performance when the activity is cues by the event card than when is time-related.

Participants in the study also performed tasks to evaluate executive and attentional functions that might be involved on prospective memory performance. We hypothesized that participants with lower attentional and executive abilities would have lower prospective memory performance.

## ***2.14.2 Materials and methods***

### ***2.14.2.1 Participants***

TBI sample included 18 patients (M=13 and F=5) that referred to Modulo di Neuropsicologia Riabilitativa (Azienda Ospedaliero-Universitaria Ferrara, Italy) (Table 2.7). The average age was 31.72 years (SD=10.05) the mean number of years of education was 12.22 years (SD=3.07). TBI patients were tested at least 6 months post their injury. TBI patients had suffered a severe head injury as indexed by the Glasgow Coma Scale (Teasdale & Jennett, 1974). The Level of Cognitive Functioning (LCF; Hagen et al., 1979) and the Functional Independence Measure and Functional

Assessment Measure (FIM/FAM; Hall et al., 1993) scales were employed to identify cognitive recovery after brain injury. TBI patients also performed a neuropsychological evaluation. To tap attentional ability three tasks were administered: the Visual Search (Spinnler & Tognoni, 1987); the Divided Attention and Go-Nogo subtasks from TAP battery (Zimmerman & Finn, 2002). The working memory was evaluated using the WAIS-R Digit Span Forward and Backward (Wechsler, 1981) and the Corsi task (Spinnler & Tognoni, 1987). Moreover, the Behavioural Assessment of the Dysexecutive Syndrome (BADS, Wilson, Alderman, Burgess, Emslie, & Evans, 2003) to evaluate perseverative tendencies, problem solving and planning. According to the clinical records, they were not densely amnesic or aphasic and had no past or current history of psychiatric disturbance. All patients had CT or MRI scans, showed damage in a wide variety of locations in the brain, with the majority having frontal lesions. Patients included in the study were all right handed and had no significant motor deficits that would have affected the performance.

Control group included 18 participants (M=7 and F=11) all right handed, who never suffered from a TBI. Participants were recruited from Padova University and matched to the TBI patients on the basis of age and education. The average age was 32 years (SD=10.10) and the mean number of years of education was 12.39 (SD=3.31). TBI patients and control group did not show significant differences with respect to age [ $t(34)=-.083$ ,  $p=.935$ ] or level of education [ $t(34)=-.156$ ,  $p=.877$ ]. All participants were physically and mentally able to understand and complete the experiment.

**Table 2.7** Demographic and clinical features of TBI patients. Cause referred to the cause of accident; MB=moto-bike; TPI=Time Post Injury (month); Injury site referred to the prevalent site of injury: F = Frontal; F-T = Fronto-Temporal; F-P = Fronto-Parietal; TPI = Time Post Injury (months); GCS = Glasgow Coma Scale; PTA = Post Traumatic Amnesia (weeks); LCF = Level of Cognitive Functioning (Hagen et al., 1979); FIM/FAM = Functional Independence Measure/Functional Assessment Measure.

	Gender	Age	Education	Injury site	TPI	GCS	PTA	LCF	FIM/FAM
1	M	25	13	F	30	3	4	7	75
2	M	35	8	F	212	3	-	7	92
3	F	43	8	F	32	5	5	7	83
4	M	32	8	F	120	6	5	6	93
5	M	28	13	F-T	6	6	6	7	95
6	M	20	10	F-T	12	6	12	6	82
7	M	33	18	F-T	11	-	-	7	94
8	M	42	13	F-T	11	4	-	6	81
9	F	28	13	F	6	5	3	6	93
10	M	23	15	F	20	-	7	7	87
11	F	41	13	F-T	228	-	-	7	88
12	M	19	10	F-T	7	-	6	6	81
13	M	25	18	F-P	14	3	7	7	91
14	M	26	8	F-T	13	-	25	6	57
15	M	53	13	F	45	6	-	8	85
16	F	26	13	F-P	60	-	7	7	98
17	F	49	13	F	336	-	4	7	90
18	M	23	13	F	42	3	2	7	85
	M (SD)	31.72 (10.05)	12.22 (3.08)	50% F	66.94 (95.22)	4.54 (1.37)	7.15 (5.90)	6.72 (0.57)	86.11 (9.42)

#### 2.14.2.2 Procedure

TBI patients were tested in a quiet room at Modulo di Neuropsicologia Riabilitativa (Azienda Ospedaliero-Universitaria Ferrara, Italy) and controls were tested at University of Padova. The prospective memory tasks (Virtual Week) was presented on a 15inch computer screen and participants were from a distance of approximately 60 cm to the computer screen. Patients were tested in two experimental sessions; in the first session they undertake the executive functions tasks (approximately 50 min); in the

second session they performed the Virtual Week (approximately 70 min). Control participant were tested in one experimental session (approximately 90 min) that included the Virtual Week and the executive functions tasks.

#### 2.14.2.3 *Prospective memory task*

The computer version of *Virtual Week* was used as laboratory measure of prospective memory performance (Rendell & Craik, 2000; Rendell & Henry, 2009). Participants are required to click on a virtual-dice and move the token around the board and to make choices about daily activities and remember to carry out lifelike activities (prospective memory tasks). Each day contained 4 regular tasks and 4 irregular tasks (in this study we did not included the time-check tasks). The regular tasks are presented at the beginning of every day and are the same during the entire game (i.e. taking antibiotics at breakfast). They can be either event-based (two activities triggered by information on the event card) or time-based (two activities triggered by the virtual time of day shown on the 24-h clock). The irregular tasks changed every day; two irregular task are presented on the start card after the regular tasks (one time- based and one event-based), the two remain irregular activities (one event-based and one time-based) are presented during the virtual day. Participants performed three days from Monday to Wednesday. A practice phase was included before the test session in which participants performed one virtual day. Responses on Virtual Week were scored as correct if the target item was remembered before the next roll of the dice. We also analysed the characteristics of the errors separately for number of missing, little late and lot late responses considering when the response occurred after the expected time (little late or lot late) or if the participants completely forgot to perform the activity (missing).

#### 2.14.2.4 Executive functions tasks

*Phonemic and Semantic Verbal Fluency tasks* are used to evaluate executive functions and cognitive functioning following neurological damage. In this study we used a phonemic fluency task (F, P, and L) (Novelli, Papagno, Capitani, Laiacona, Vallar & Cappa, 1986) and a semantic fluency task (Colours, Animals, Fruits and Cities) (Spinnler & Tognoni, 1987). Participants were asked to produce as many words as possible in 1 minute in the phonemic verbal fluency task, while had 2 minute in the semantic verbal fluency task. Performance was scored as numbers of correct responses separately for the two tasks.

*Trial Making Test (TMT)* is used to measure the cognitive domains of attention, processing speed, mental flexibility and visual–motor skills. In part A, participants are required to connect a series of 25 numbers in numerical order. In part B, participants connected 25 numbers and letters in numerical and alphabetical order, alternating between the numbers and letters. The primary variables of interest are the total time to completion for parts A and B (Bowie & Harvey, 2006).

*Wisconsin Card Sorting Test (WCST)* (Laicon, Inzaghi, De Tanti, & Capitani, 2000) is the measure most frequently used to tap set-shifting, and also provides an index of perseveration. The WCST involved the presentation of 120 cards that contain symbols that vary among three dimensions (shape, colour and number). In the present study we calculated and analyzed the following indices: a) Global score, which estimates how many cards the subject actually used in excess of the minimum necessary to achieve the six categories; b) Perseverative responses, which quantifies the perseverative behaviour; c) Non-perseverative errors, which quantifies the lack of

strategies and the tendency to give responses that do not match the any of the sorting criteria.

### **2.14.3 Results**

#### *2.14.3.1 Prospective memory task*

The time required to complete each virtual day was analysed and included into 2 × 3 mixed ANOVA with the between variable of group (TBI, controls) and the within variables day (Monday, Tuesday and Wednesday). The results revealed that TBI patients were significantly slower to complete each virtual day than controls [ $F(2,68)=4.50$ ,  $p<.01$ ,  $\eta^2_p=.117$ ; TBI=10.85 min (SD=3.50) and Controls=6.25 min (SD=1.02)]. Moreover, a significant effect of day was found, in particular participants got faster as they played the game [ $F(1,34)=395.09$ ,  $p<.001$ ,  $\eta^2_p=.457$ ]; the mean time to play Monday was 9.14 min (SD=3.35), Tuesday was 9.08 min (SD=4.02) and Wednesday was 7.45 min (SD=3.97). The results also showed no group differences over the three days ( $p=.21$ ,  $\eta^2_p=.045$ ).

Participants' performance was analyzed in terms of proportions of correct responses. Data were analyzed with a 2 × 2 × 2 mixed ANOVA with the between variable of group (TBI, controls) and the within variables of prospective memory task (regular, irregular) and prospective memory target (event-based, time-based). TBI patients were significantly less accurate than controls [ $F(1,34)=15.68$ ,  $p<.001$ ,  $\eta^2_p=.316$ ; TBI=.53 and controls=.77]. Prospective memory task [ $F(1,34)=19.61$ ,  $p<.001$ ,  $\eta^2_p=.366$ ] and prospective memory target [ $F(1,34)=110.05$ ,  $p<.001$ ,  $\eta^2_p=.764$ ] were also significant. Participant were more accurate when the prospective memory task was

regular than irregular and they were more accurate when the prospective memory target was event-based than time-based. Moreover, significant interaction prospective memory task  $\times$  prospective memory target [ $F(1,34)=4.40, p<.05, \eta^2_p=.114$ ] was also found. No significant interactions with group were found. To further evaluate the effect of prospective memory task and prospective memory target on prospective memory performance, *post-hoc t-test* was performed to test group differences in each task (Table 2.8). The results showed that the group differences were significant in all variables included, in particular in Irregular-Time tasks.

**Table 2.8** Mean and standard deviations for prospective memory tasks (regular, irregular) and targets (event, time) of the TBI and control groups. T test and Cohen's *d* were also reported.

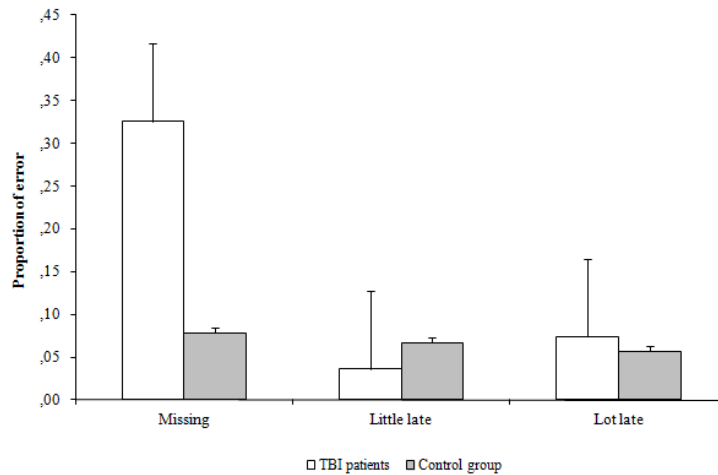
	TBI patients	Control group		
	M (SD)	M (SD)	<i>t</i>	<i>d</i>
Regular Event	.74 (.25)	.96 (.09)	3.44*	1.17
Regular Time	.44 (.28)	.67 (.20)	2.81*	.94
Irregular Event	.70 (.28)	.89 (.09)	2.68*	.91
Irregular Time	.24 (.24)	.56 (.29)	3.54*	1.20

\*  $p<.01$

Prospective memory performance was also analyzed on type of errors. In particular we consider the proportion of missing, the proportion of little late responses and the proportion of lot late responses. A  $2 \times 3$  mixed ANOVA was conducted with the between variable of group (TBI, controls) and within variable of type of error (missing, little late, lot late responses). Type of error was significant [ $F(2,68)=21.21, p<.001$ ,



$\eta^2_p=.384$ ] and significantly interact with group [ $F(2,68)=16.90, p<.001, \eta^2_p=.332$ ] (Figure 2.7).



**Figure 2.7** Proportion of missing, little late and lot late responses in TBI and controls.

To further investigate prospective memory performance in TBI patients separate analysis were conducted within the TBI patients between patients with LCF=6 and patients with LCF=7. The LCF scale used to assess cognitive functioning in post-coma patients and classifying of outcome levels. Use of the scale generates a classification of the patient in one of eight levels; Level=6 means Confused-Appropriate: patient gives context appropriate responses in familiar context. Memory problems persist; Level=7 means Automatic-Appropriate: patient behaves appropriately in familiar settings, performs daily routines automatically. Patient initiates social interactions.

Participants' performance was analyzed in terms of proportions of correct responses. Data were analyzed with a  $2 \times 2 \times 2$  mixed ANOVA with the between variable of TBI group (LCF 6, LCF 7) and the within variables of prospective memory task (regular, irregular) and prospective memory target (event-based, time-based). Significant difference was found between patients with LCF=6 and LCF=7

[ $F(1,16)=4.79$ ,  $p<.05$ ,  $\eta^2_p=.231$ ]. TBI patients with LCF=6 were less accurate than patients with LCF=7 (.32 vs. 60%). Significant effect of prospective memory task [ $F(1,16)=13.57$ ,  $p<.01$ ,  $\eta^2_p=.459$ ] and prospective memory target [ $F(1,16)=59.61$ ,  $p<.001$ ,  $\eta^2_p=.788$ ] were also found. TBI patients were less accurate when the activity was irregular (.43 vs. .55) and time-based (.31 vs. .68).

The numbers of errors were also analysed. A  $2 \times 3$  mixed ANOVA was conducted with the between variable of group (TBI, controls) and within variable of type of error (missing, little late, lot late responses). Significant effect of group was found [ $F(1,16)=4.79$ ,  $p<.05$ ,  $\eta^2_p=.231$ ]; patients with LCF=6 made more errors than patients with LCF=7 (.19 vs. .12). Moreover, a significant effect of type of error was also found [ $F(1,16)=23.38$ ,  $p<.001$ ,  $\eta^2_p=.594$ ]; TBI patients made more missing errors than little late or lot late errors (.34, .03 and .08, respectively).

#### *2.14.3.2 Executive functions tasks*

Descriptive statistics (mean and standard deviation),  $t$ -test and Cohen's  $d$  results for the executive functions measures are reported in Table 2.9. TBI patients were significantly less accurate than controls in all executive functions tasks. In particular TBI patients produced less number of words on both verbal fluency tasks and they were slower than controls on TMT tasks. Concerning the WCST task TBI patients achieved less number of categories (global score), made more perseverative and non-perseverative errors than controls.

**Table 2.9** Mean and standard deviations for the Executive functions tasks of the TBI and control groups. T test and Cohen's d were also reported.

	TBI patients	Control group	<i>t</i>	<i>d</i>
	M (SD)	M (SD)		
Phonemic Fluency	18.34 (9.51)	53.50 (8.59)	4.88**	3.88
Semantic Fluency	9.06 (4.44)	19.34 (4.77)	5.94**	.73
TMT A (sec)	67.41 (17.58)	34.53 (9,73)	6.90**	2.31
TMT B (sec)	164.06 (56.12)	80.17 (24.89)	5.74**	1.93
WCST Global score	56.28 (34.46)	29.48 (12.45)	3.09*	1.03
WCST Perseverative	21.52 (13.76)	12.09 (5.43)	2.68*	.90
WCST Non-perseverative	18.99 (12.29)	8.68 (4.09)	3.36*	1.12

\*  $p < .01$ ; \*\*  $p < .001$

#### 2.14.3.3 Correlation analysis between prospective memory and executive functions

Two separate, two-tailed Pearson correlation analyses were performed for TBI patients and controls between prospective memory and executive functions tasks (Table 2.10). Significant correlations were found between Semantic fluency and time-based tasks both in the regular and in the irregular tasks. TMTa significantly correlate with irregular time-based tasks both in TBI patients and in the control group. Moreover, in the control group significant correlations were also found between TMTb and irregular tasks both event- and time-based.

**Table 2.10** Correlations between prospective memory task and executive functions.

	TBI patients				Control group			
	Regular Event	Regular Time	Irregular Event	Irregular Time	Regular Event	Regular Time	Irregular Event	Irregular Time
Phonemic Fluency	.369	.024	.257	-.202	-.152	.266	-.250	.070
Semantic Fluency	.462	<b>.572*</b>	.305	<b>.587*</b>	.013	.441	.029	.360
TMT A (sec)	.103	.360	.232	<b>.510*</b>	-.188	.222	.164	<b>.585*</b>
TMT B (sec)	.058	.095	.035	.083	-.168	.302	<b>.554*</b>	<b>.635**</b>
WCST Global score	-.155	-.007	.065	-.216	-.083	.162	.060	-.135
WCST Perseverative	.156	.124	-.106	-.032	-.224	.140	.356	.192
WCST Non-perseverative	-.271	-.121	.091	-.286	.026	.335	.159	-.069

\*  $p < .05$ ; \*\*  $p < .001$

Setting aside significant levels, which is maybe affected by sample size, Cohen (1992) equates a correlation of .30 with a medium effect and .50 with a large effect size. Using these criteria there were no strong correlation but there were a number of medium level relationships. In the TBI patients between prospective memory accuracy and prospective memory errors and TMT part A; while in the control group between prospective memory accuracy, prospective memory errors, Semantic fluency and TMT part A.

#### 2.14.3.4 *Correlations between prospective memory, clinical features and neuropsychological tasks in TBI patients*

To further investigate prospective memory performance in TBI patients additional correlations were conducted between prospective memory performance,

clinical features and neuropsychological tasks (Table 2.11). Significant correlations were found between regular event-based tasks and LCF index. Moreover, the Corsi task significantly correlates with the time-based task both in the regular and in the irregular condition. Likewise, in the previous correlation analyses, a number of medium level relationships were found (e.g. prospective memory performance and FIM/FAM index, Go/Nogo and BADS).

**Table 2.11** Correlations between prospective memory task, clinical features and neuropsychological tasks in TBI patients.

	<b>Regular Event</b>	<b>Regular Time</b>	<b>Irregular Event</b>	<b>Irregular Time</b>
<i>Clinical features</i>				
LCF	<b>.546*</b>	.381	.359	.365
PTA	-.440	-.067	-.250	-.092
GCS	-.120	.345	-.129	.424
FIM/FAM	.453	.299	.064	.363
<i>Neuropsychological tasks</i>				
Visual search (errors)	-.185	-.199	-.010	-.394
Divided Attention (errors)	-.304	-.078	-.183	-.197
Go/Nogo (errors)	-.442	-.480	-.513	-.300
Digit Span Forward (accuracy)	.316	.178	.078	.210
Digit Span Backward (accuracy)	.178	-.054	-.126	.025
Corsi task (accuracy)	.264	<b>.578*</b>	.245	<b>.531*</b>
BADS	.062	.370	.566	.482

\*  $p < .05$

#### **2.14.4 Discussion**

This study investigated prospective memory performance in TBI patients with the Virtual Week, which is a new ecological task to investigate prospective memory performance. We hypothesised an effect of prospective memory performance task and prospective memory performance target on prospective memory performance, in particular we expected better performance when participants were engaged with regular tasks compared to irregular tasks because prospective memory performance cues that occur more regularly may be more likely to spontaneously trigger intention retrieval, while irregular cues may involve more strategic monitoring (Kvavilashvili & Fisher, 2007; Henry et al., 2004; McDaniel & Einstein, 2007). Moreover, we expected lower performance when participants were engaged with time-based tasks compared to event-based tasks because time-based tasks are more demanding than event-based tasks because they required more self-initiated retrieval (Einstein & McDaniel, 1990; Kvavilashvili & Ellis, 1996).

TBI patients were less accurate compared to controls when required to perform time-based tasks. When participants are required to perform time-based tasks they have to break out the ongoing activity induced by the Virtual Week and self-initiated the decision to check the virtual clock at the centre of the board. TBI patients were also less accurate when performed event-based tasks; despite the fact that event-based tasks should be easier than time-based task, because are triggered by the Event card, TBI patients performed lower than controls showing a consisted prospective memory performance deficit.

When TBI and controls prospective memory performance performances were compared with respect to the regularity of the prospective memory performance task,

TBI patients performed lower than controls both on regular and irregular tasks. Irregular tasks are expected to be more difficult because they are different every virtual day and are associated with increasing demand to constantly update the intended activity. These results confirmed previous data in which stroke patients suffered a deficit on irregular tasks (Will et al., 2010). With respects to Will et al. (2010) study in which stroke patients made as many correct responses as controls in regular tasks, in our study TBI patients were always less accurate than controls even when tested with regular tasks.

It should be noted that, both groups had better performance on regular tasks compare to irregular tasks. This result is particularly interesting for TBI patients in particular in rehabilitation prospective. Despite consistent prospective memory performance dysfunction in TBI patients, they were able to benefit from the environmental support provided by reoccurrence and explicit cue in the regular tasks.

### ***2.15 General discussion***

Prospective memory performance, defined as the ability to perform an intended action sometime in the future, has been reported to be one of the most commonly occurring memory errors of everyday life (Einstein & McDaniel, 2004; Kliegel & Martin, 2003). Many researchers investigating prospective memory have begun to use models of prefrontal function and associated working memory, attention and executive function as cognitive abilities involved on prospective memory performance (Burgess, Quayle, & Frith, 2001; Fleming et al., 2008; Logie et al., 2004; McDaniel & Einstein, 2000; Martin et al., 2003). The expectation is that high cognitive functions are necessary for forming the intention to remember and activating the intention at the appropriate time. Clearly, disruption to either of the major cognitive systems will compromise

adequate prospective memory performance in both event- and time-based tasks (Einstein et al., 1999; Shum et al., 2011).

Prospective memory dysfunctions are frequently encountered in TBI patients and represent a considerable challenge to their successful return to independent living in the community (Fleming et al., 2005; Shum et al., 2011). Prospective memory dysfunctions observed in TBI patients are maybe due to sustain diffuse damage in frontal brain regions suspected of being involvement in high cognitive processes involved on prospective memory performance (Shallice & Burgess, 1991; McDaniel & Einstein, 2000; Burgess, Quayle, & Frith, 2001). Our Study 3 also confirmed previous finding that pointed out the involvement of high cognitive functions on prospective memory performance (Kinch & McDonald, 2001; Maujean et al., 2003; Schmitter-Edgecombe & Wright 2003; Mathias & Mansfield, 2005). In our study TBI patients had lower prospective memory performance than controls and inhibition and updating abilities were differently involved on TBI patients and controls on prospective memory performance. prospective memory accuracy in TBI patients significantly correlates with updating; this result indicates that TBI patients required additional updating abilities to retrain the prospective intention. Medium and large effect have been found between inhibition and monitoring frequency, indicating that participants that frequently monitored were less able to inhibit irrelevant information in the Stroop task. Strength of our study was the hypothesis that additional temporal abilities may be involved in prospective memory performance in particular when participants are engaged with time-based prospective memory tasks. We predicted that adequate temporal abilities are required on monitoring behavior more than on prospective memory accuracy. TBI patients were more variable than controls on time reproduction task indicating that TBI



patients had difficulties on maintaining a stable representation of the duration in working memory due to updating dysfunctions. This greater variability may be explained in terms of impaired updating and inhibition processes (Nichelli et al., 1995; Perbal et al., 2003). Executive and temporal dysfunction in TBI patients may be responsible of lower prospective memory performance observed in TBI patients; in particular despite TBI patients monitored more than controls, they did not show strategic monitoring which is critical to accurately perform the time-based prospective memory task.

Prospective memory dysfunctions were also found on Study 4 in which TBI patients were tested with the Virtual Week (Rendell & Craik, 2000) which is a computer task that simulate real life activities. This was the first study that employed the Virtual Week with TBI patients and we have selected it for clinical and theoretical reasons. With respect to the clinical reason, the Virtual Week is a promising task to fill the observed discrepancy between performance on laboratory task and performance on real life situation (Chaytor & Schmitter-Edgecombe; 2003; Burgess et al., 2006; McDaniel & Einstein; 2007). A growing body of research developed virtual tasks which simulate real life activities to test prospective memory performance and pointed out the importance of using tasks that better recreate real life activities (Knight et al., 2005, 2006; Titov & Knight, 2006; Kinsella et al., 2009). The Virtual Week required performing activities through virtual days like remembering to pick up the laundry when shopping or calling the plumber at 5 pm. The Virtual Week also demonstrated adequate levels of reliability (Henry, et al., 2007b; Rose et al., 2010). With respect to the theoretical reasons the Virtual Week includes, within the same task, both event and time-based tasks which allowed researchers to investigate the effect of cue focality and

self-initiated retrieval. Moreover, the Virtual Week includes regular and irregular tasks which allowed researchers to investigate effect of routinely (regular tasks) on prospective memory performance; it has been expected that task regularity tend to reduce differences on prospective memory performance (Henry et al., 2004; Kvavilashvili & Fisher, 2007; McDaniel & Einstein, 2007).

Prospective memory dysfunction was observed in TBI patients when tested with the Virtual Week confirming the reliability of the Virtual Week to evaluate prospective memory performance. TBI patients had lower performance both on event- and time-based tasks and both on regular and irregular tasks. However, within groups higher performances were observed on event-based tasks compared to time-based tasks confirming the difficulty of time-based tasks maybe due to more self-initiated processes (McDaniel & Einstein, 2000), and on regular tasks compared to irregular tasks confirming that repeating the same activities improved prospective memory performance (Henry et al., 2004; Kvavilashvili & Fisher, 2007; McDaniel & Einstein, 2007). In sum, Study 3 and Study 4 confirmed prospective memory dysfunction on TBI patients and introduced new line of research. In Study 3 we have pointed out that prospective memory performance is not only related with executive functions but also required a high degree of temporal abilities in particular in strategic monitoring. In Study 4 we have presented a new prospective memory task to investigate prospective memory performance in TBI patients, which also has promising employment in rehabilitation.

## **GENERAL CONCLUSION AND FUTURE DIRECTIONS**

This thesis was conducted to investigate time perception and prospective memory performance in TBI patients. Often TBI Patients report dysfunction on time perception and temporal order of events likewise TBI patients often report dysfunctions on remembering and executing future intention. Rehabilitation of impaired temporal and prospective memory process is fundamental to improve the independence of TBI patients and to reduce the rely on caregivers for prompting their life.

I have presented four studies that investigated temporal and prospective memory abilities in TBI patients but also investigated which cognitive abilities are critical to accurately perceived time or perform future actions. Specifically, Study 1 was conducted to extend the knowledge on temporal abilities on TBI patients with a time discrimination task and investigate if different cognitive process are engaged when discriminating duration above and below 1 s. TBI patients were less accurate than controls in particular when discriminating duration below 1 s (500 ms). Interesting, both groups showed a greater tendency to respond “brief” with the 500 ms standard duration and “long” with the 1300 ms standard duration, but this effect was greater for TBI patients; showing a greater response bias in TBI patients. Study 2 was conducted to investigate temporal abilities with different methodologies. Different temporal tasks may be used to investigate time perception, each of which required different cognitive resources and reveal different characteristics of time perception (Allan, 1979; Zakay, 1990, 1993; Nichelli, 1996; Mangels & Ivry, 2000). Participants were tested with time reproduction, time production and time discrimination tasks and performed executive functions tasks. Results showed significant differences between groups when

reproducing and producing long durations (4, 9 and 14 s.), but no differences when tested with briefer durations (.5, 1 and 1.5 s). Although, significant differences were found with brief duration in time discrimination task, showing that time discrimination task is a better method to investigate temporal differences with brief duration. Interesting significant correlations were found between temporal tasks indicating that these tasks shared similar temporal processes.

Future studies on time perception in TBI patients might focus on further investigate response bias present in TBI patients when tested with time discrimination task as index of impulsivity and not strategic behaviour. TBI patients presented temporal dysfunctions however we expected consistently lower performance in patients, instead TBI patients performed lower than controls in most on temporal task but also presented comparable performance showing that same temporal abilities may be kept even after the trauma. Clinical studies should consider training programs to improve residual temporal abilities which may have important implication also in other activities likewise prospective memory performance.

Moreover, more studies need to be conducted to investigate the involvement of high cognitive functions on time perception. The results from our studies and from previous researches extensively pointed out the involvement of inhibition and updating abilities, however other attentional abilities may be involved (i.e. sustained attention) in relation to the methodology and temporal duration employed.

Studies 3 and 4 focused on prospective memory performance in TBI patients. Study 3 was conducted to investigate time-based prospective memory performance and the involvement of temporal and executive abilities. Results showed time-based prospective memory dysfunction in TBI patients: TBI patients were less accurate and

presented a less strategic monitoring behaviour. Moreover, TBI patients presented lower temporal and executive abilities that are maybe responsible for lower time-based prospective memory performances. Study 4 investigated prospective memory performance with the Virtual Week and showed prospective memory dysfunctions in TBI patients both on event- and time based tasks. Moreover, TBI patients were less accurate than controls both on regular and irregular tasks, but analyzing performances within groups, TBI and controls had higher performances on regular tasks compared to irregular tasks, indicating that repeating activities improved prospective memory performance (Henry et al., 2004; Kvavilashvili & Fisher, 2007; McDaniel & Einstein, 2007).

Further studies need to be conducted to investigate clinical and psychological variables on prospective memory performance in particular for those patients who are tested within the recovery or experienced a long hospitalization. In fact, previous studies showed that patients that experienced long recovery may present altered psychological state that could influence their performance on neuropsychological tasks likewise depression or anxiety. Moreover, very few studies have been conducted to investigate metacognitive variable on prospective memory performance (Fleming et al., 2008). Interestingly, Knight et al. (2001) also investigated the likelihood of recalling items and objective prospective memory performance. TBI and controls did not differ on their likelihood of recalling items but TBI prospective memory performance was significantly reduced. TBI are less self aware of memory problems and often over estimating their abilities (Kinsella et al., 1996; Knight et al., 2005; Roche, Fleming, & Shum, 2002; Kinsella et al., 2009). Moreover, following the latest review by Shum and colleagues (2010) on prospective memory dysfunction in TBI patients emerged that only one study

was conducted with mild TBI. More studies need to be conducted on mild TBI patients to prevent long term dysfunctions maybe not evident during the first test session.

Regarding the potential rehabilitation implication we have found that time perception seems to be involved on time-based prospective memory tasks in particular in the monitoring behaviour. Healthy controls with better temporal abilities checked the clock less frequently than TBI patients and their monitoring behaviour was more strategic and achieved better performance. Note that a strategic monitoring behaviour is critical to accurately perform time-based prospective memory tasks but participants need to balance between the costs of monitoring against the cost of having inaccurate information about the environment (Einstein et al., 1995; Einstein & McDaniel, 1995). A rehabilitation project that increases temporal abilities in TBI patients may have potential implications on time-based prospective memory performance in particular on monitoring behaviour.

## REFERENCES

- Abele, I., Rendell, P. G., Rose, N. S., McDaniel, M. A., & Kliegel, M. (2010). The age prospective paradox: young adults may not give their best outside of the lab. *Developmental Psychology, 46*, 1444-1453.
- Adam, N., Rosner, B. S., Hosick, E. C., & Clark, D. L. (1971). Effect of anesthetic drugs on time production and alpha rhythm. *Perception & Psychophysics, 10*, 133-136.
- AharonPeretz, J., & Tomer, R. (2007). Traumatic brain injury. In B.L. Miller and J.L. Cummings (Eds.), *The human frontal lobes: Functions and disorders* (2nd ed.). New York, NY, US: Guilford Press; US, 540-551.
- Allan, L. G. (1979). The perception of time. *Perception & Psychophysics, 26*, 340-354.
- Altgassen, M., Williams, T.I., Bölte, S., & Kliegel, M. (2009). Time-based prospective memory performance in children with autism spectrum disorders. *Brain Impairment, 10*, 52-58.
- Altgassen, M., Phillips, L. H., Henry, J. D., Rendell, P. G., & Kliegel, M. (2010). Emotional target cues eliminate age differences in prospective memory. *Quarterly Journal of Experimental Psychology, 63* (6), 1057-1064.
- Anderson, J. C. & Gerbing, D. W. (1988). Structural equation modelling in practice: A review and recommended two-step approach. *Psychological Bulletin, 103*, 411-423.
- Anderson, J. W. & Schmitter-Edgecombe, M. (2009). Predictions of episodic memory following moderate to severe traumatic brain injury during inpatient rehabilitation. *Journal of Clinical and Experimental Neuropsychology, 31*, 425–438.

- Anderson, J. W. & Schmitter-Edgecombe, M. (2011). Recovery of time estimation following moderate to severe traumatic brain injury. *Neuropsychology*, 25, 36–44.
- Andrzejewski, S. J., Moore, C. M., Corvette, M., & Herrman, D. (1991). Prospective memory skill. *Bulletin of Psychonomic Society*, 29, 304-306.
- Angrilli, A., Cherubini, P., Pavese, A., & Manfredini, S. (2007). The influence of affective factors on time perception. *Perception & Psychophysics*, 59, 972-982.
- Arshavsky, Y. I., Deliagina, T. G., & Orlovsky, G.N. (1997). Pattern generation. *Current Opinion in Neurobiology*, 7, 781-789.
- Arushanyan, E. B., Baida, O. A., Mastiyagin, S. S., Popova, A. P., & Shikina, I.B., (2003). Influence of caffeine on the subjective perception of time by healthy subjects in dependence on various factors. *Human Psychology*, 29, 433-436,
- Atkin, M. S., & Cohen, P. R. (1996). Monitoring strategies for embedded agents: experiment and analysis. *Journal of Adaptive Behaviour*, 4, 125-172.
- Azouvi, P. (2000). Neuroimaging correlates of cognitive and functional outcome after traumatic brain injury. *Current Opinion in Neurology*, 13, 665–669.
- Baddeley, A. D. (1992). Working memory. *Science*, 255, 556-559.
- Baddeley, A. D., & Wilkins, A. J. (1983). Taking memory out of the laboratory. In J. E. Harris & P. E. Morris (Eds.), *Everyday memory, actions, and absentmindedness* (pp. 1-17). New York: Academic Press.
- Barkley, R. A., Koplwitz, S., Anderson, T., & McMurray, M. B. (1997). Sense of time in children with ADHD: Effects of duration, distraction, and stimulant medication. *Journal of the International Neuropsychological Society*, 3, 359-369.



- Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology, 51*, 1173-1182.
- Baudouin, A., Vanneste, S., Isingrini, M., & Pouthas, V. (2006a). Different involvement of internal clock and working memory in the production and the reproduction of duration: A study on older adults. *Acta Psychologica, 121*, 285-296.
- Baudouin, A., Vanneste, S., Pouthas, V., & Isingrini, M. (2006b). Age-related changes in duration reproduction: Involvements of working memory processes. *Brain and Cognition, 62*, 17-23.
- Bertsch, S., Pesta, B. J., Wiscott, R., & McDaniel, M. A. (2007). The generation effect: A meta-analysis review. *Memory & Cognition, 35*, 201-210.
- Bigler, E. D. (2001). The lesion(s) in traumatic brain injury: Implication for clinical neuropsychology. *Archives of Clinical Neuropsychology, 16*, 95-131.
- Bigler, E. D. (2007). Anterior and middle cranial fossa in traumatic brain injury: Relevant neuroanatomy and neuropathology in the study of neuropsychological outcome. *Neuropsychology, 21* (5), 515-531.
- Binkofski, F., & Block, R. A. (1996). Accelerate time experience after left frontal cortex lesion. *Neurocase, 2*, 485-493.
- Bisiacchi, P. S. (1996). The neuropsychological approach in the study of prospective memory. In M. Brandimonte, G. O. Einstein, & M. A. McDaniel (Eds.), *Prospective memory: Theory and applications* (pp. 297-317). Mahwah, NJ: Lawrence Erlbaum Associates, Inc.
- Block, R. A., George, E. J., & Reed, M. A. (1980). A watched pot sometimes boils: A study of duration experience. *Acta Psychologica, 46*, 81-94.

- Block, R. A. (1986). Remembered duration: Imagery processes and contextual encoding. *Acta Psychologica*, 62, 103-122.
- Block, R. A. (1989). Experiencing and remembering time: Affordances, context, and cognition. In I. Levin, & D. Zakay (Eds.), *Time and Human cognition: A life span perspective* (pp. 333-363). Amsterdam: North-Holland.
- Block, R. A. (1990). Models of psychological time. In R.A. Block (Eds.), *Cognitive models of psychological time* (pp. 1-35). Hillsdale, NJ: Lawrence Erlbaum Associates Inc.
- Block, R. A. (Ed.). (1990). *Cognitive models of psychological time*. Hillsdale , NJ : Lawrence Erlbaum Associates.
- Block, R. A. (1992). Prospective and retrospective duration judgment: The role of information processing and memory. In Macar, F., Pouthas, V., & Friedman, W.J. (Eds.) *Time, Action and Cognition: Towards Bridging the Gap*. (pp. 141-152). Dordrecht, Netherlands Kluwer Academic.
- Block, R. A., & Zakay, D. (1996). Models of psychological time revised. In Helfrich H (Eds.), *Time and Mind* (pp. 171-195). Kirkland, Hogrefe and Huber.
- Block, R. A. & Zakay, D. (1997). Prospective and retrospective duration judgments: A meta-analytic review. *Psychonomic, Bulletin & Review*, 4, 184-197.
- Block, R. A. Zakay, D., & Hancock, P.A. (1998). Human Aging and Duration Judgments: A Meta-Analytic Review. *Psychology and Aging*, 13, 584-596.
- Block, R. A. (2003). Psychological timing without a timer: The roles of attention and memory. In H. Helfrich (Ed.), *Time and mind II* (pp. 41- 60). Göttingen: Hogrefe & Huber.

- Block, R. A., & Zakay, D. (2006). Prospective remembering involves time estimation and memory processes. In Glickson J, and Myslobodsky M (Eds.), *Timing the Future: The Case of Time-based Prospective Memory* (pp. 25-49). New York: World Scientific Publishing.
- Block, R. A., & Zakay, D. (2008). Timing and remembering the past, the present, and the future. In S. Grondin (Ed.), *Psychology of time* (pp. 367-394). Bingley, England: Emerald.
- Boelen, D. H. E, Spikman, J. M, Rietveld, A. C. M, & Fasotti, L. (2009). Executive dysfunction in chronic brain injured patients: Assessment in outpatient rehabilitation. *Neuropsychological Rehabilitation, 19* (5), 625–644.
- Bowie, C. R. & Harvey, P. D. (2006). Administration and interpretation of the Trail Making Test. *Nature Protocols, 1*, 2277-2281.
- Brandimonte, M. A., Einstein, G. O., & McDaniel, M. A. (Eds.). (1996). *Prospective memory: Theory and applications*. Mahwah, NJ: Lawrence Erlbaum Associates, Inc.
- Brendimonte, M. A., Ferrante, D., Feresin, C., & Delbello, R. (2001). Dissociating prospective memory from vigilance process. *Psicologia, 22*, 97-113.
- Brown, S. W. & West, A. N. (1990). Multiple timing and the allocation of attention. *Acta Psychologica, 75*, 103-121.
- Brown, S. W., Stubbs, D. A., & West, A. N. (1992). Attention, multiple timing, and psychophysical scaling of temporal judgments. In F. Macar, V. Pouthas, & W. Friedman (Eds.), *Time, action, cognition: Towards bridging the gap* (pp 129-140). Dordrecht, The Netherlands: Kluwer.

- Brown, S. W. (2006). Timing and executive function: Bidirectional interference between concurrent temporal production and randomization tasks. *Memory and Cognition*, *34*, 1464-1471.
- Bueti, D., Walsh, V., Frith, C., & Rees, G. (2008). Different brain circuits underlie motor and perceptual representation of temporal intervals. *Journal of Cognitive Neuroscience*, *20*, 204-214.
- Buonomano, D. V. (2007). The biology of time across different scales. *Nature Chemical Biology*, *3*, 594-597.
- Burgess, P. W. & Shallice, T. (1996). Response suppression, initiation and strategy use following frontal lobe lesions. *Neuropsychologia*, *34*, 263-288.
- Burgess, P. W. & Shallice, T. (1997). The relationship between prospective and retrospective memory: Neuropsychological evidence. In M. A. Conway (Eds.), *Cognitive models of memory*, (pp. 247-272). MIT Press: Cambridge, MA.
- Burgess, P. W., Veith, E., de Lacy Costello, A., & Shallice, T. (2000). The cognitive and neuroanatomical correlates of multi-tasking. *Neuropsychologia*, *38*, 848-863.
- Burgess, P. W., Quayle, A., & Frith, C. D. (2001). Brain regions involved in prospective memory as determined by positron emission tomography. *Neuropsychologia*, *39*, 545-555.
- Burgess, P.W., Alderman, N., Forbes, C., Costello, A., Coates, L.M., Dawson, D.R., et al. (2006). The case for the development and use of 'ecologically valid' measures of executive function in experimental and clinical neuropsychology. *Journal of the International Neuropsychological Society*, *12*, 194-209.

- Buhusi, C. V. & Meck, W. H. (2005). What makes us stick? Functional and neural mechanisms of interval timing. *Neuroscience*, 6, 755, 765.
- Cahoon, D., & Edmonds, E. M. (1980). The watched pot still won't boil: Expectancy as a variable in estimating the passage of time. *Bulletin of the Psychonomic Society*, 16, 115-116.
- Carelli, M. G., Forman, E., & Mäntylä, T. (2007). Sense of time and executive functioning in children and adults . *Child Neuropsychology*, 1, 1–15, 2007.
- Carlesimo, G. A., Formisano, R., Bivona, U., Barba, L., & Caltagirone, C. (2004a). Prospective memory in patients with severe closed-head injury: Role of concurrent activity and encoding instructions. *Behavioral Neurology*, 22, 101-110.
- Carlesimo, G. A., Casadio, P., & Caltagirone, C. (2004b). Prospective and retrospective components in the memory for actions to be performed in patients with severe closed-head injury. *Journal of the International Neuropsychological Society*, 10, 679–688.
- Casini, L. & Macar, F. (1997). Effects of attention manipulation on judgments of duration and on intensity in the visual modality. *Memory & Cognition*, 25, 812-818.
- Casini, L., & Ivry, R. (1999). Effects of divided attention on temporal processing in patients with lesions of cerebellum or frontal lobe. *Neuropsychologia*, 13, 10-21.
- Ceci, S. J. & Bronfenbrenner, U. (1985). "Don't Forget to Take the Cupcakes out of the Oven": Prospective Memory, Strategic Time-Monitoring, and Context. *Child Development*, 56, 152-164.

- Christensen, B. K., Colella, B., Inness, E., Hebert, D., Monette, G., Bayley, M., & Green, R. E. (2008). Recovery of cognitive function after traumatic brain injury: A multilevel modelling analysis of Canadian outcomes. *Archives of Physical Medicine and Rehabilitation, 89*, 3–15.
- Chambon, M., Gil, S., Niedenthal, P. M., & Droit-Volet, S. (2005). Psychologie sociale et perception du temps: l'estimation temporelle des stimuli sociaux et émotionnels [Social psychology and time perception: The temporal estimation of social and emotional stimuli]. *Psychologie Française, 50*, 167-180.
- Chan, R. C. K., Wang, Y., Ma, Z., Hong, Y-H., Yuan, Y., Yu, X., Li, Z., Shum, D., & Gong, Q-J. (2008). Objective measures of prospective memory do not correlate with subjective complaints in schizophrenia. *Schizophrenia Research, 103*, 229–239.
- Chaytor, N., & Schmitter-Edgecombe, M. (2003). The ecological validity of neuropsychological tests. *Neuropsychology Review, 13*, 181–197.
- Church, R. M. (1984). Properties of the internal Clock. *Annals New York Academy of Sciences, 566-582*.
- Cockburn J. (1995). Task interruption in prospective memory: A frontal lobe function? *Cortex, 31*, 87-97.
- Cockburn, J. (1996). Failure of prospective memory after acquired brain damage: Preliminary investigation and suggestions for future directions. *Journal of Clinical and Experimental Psychology, 18*, 304–309.
- Cockburn, J. (2006). The neurology and neuropsychology of time-based prospective memory. In Glickson J, and Myslobodsky M (Eds.), *Timing the Future: The*

*Case of Time-based Prospective Memory* (pp. 239-262). New York: World Scientific Publishing.

Cohen, J. (1992). Quantitative methods in psychology. *Psychological Bulletin*, *112*, 155-159.

Cohen, P. R., Atkin, M. S., & Hansen, E. A. (1994). The interval reduction strategy for monitoring cupcake problems. *Proceedings of the Third International Conference on the Simulation of Adaptive Behaviour*, 82-90.

Cohen, J. D., & O'Reilly, R. C. (1996). A preliminary theory of the interactions between prefrontal cortex and hippocampus that contribute to planning and prospective memory. In M. Brandimonte, G. O. Einstein, & M. A. McDaniel (Eds.), *Prospective memory: Theory and applications* (pp. 267–296). Mahwah, NJ: Lawrence Erlbaum Associates, Inc.

Cooke, D. L., & Kausler, D. H. (1995). Content memory and temporal memory for actions in survivors of traumatic brain Injury. *Journal of Clinical and Experimental Neuropsychology*, *17*, 90–99.

Coull, J. T., Vidal, F., Nazarian, B., & Macar, F. (2004). Functional anatomy of the attentional modulation of time estimation. *Science*, *303*, 1506-1508.

Conway, M. A. (1992). A structural model of autobiographical memory. In M. A. Conway, D. C. Rubin, H. Spinnler, & W. A. Wagenaar (Eds.), *Theoretical prospective on autobiographical memory* (pp. 167-194). Dordrecht, The Netherlands: Kluwer Academic Publishers.

Cooke, D. L., & Kausler, D. H. (1995). Content memory and temporal memory for actions in survivors of traumatic brain Injury. *Journal of Clinical and Experimental Neuropsychology*, *17*, 90–99.

- Costa, A., Peppe, A., Caltagirone, C., & Carlesimo, G. A. (2008). Prospective memory impairment in individual with parkinson's disease. *Neuropsychology*, 22, 283-292.
- Craik, F. I. M. (1977). Age differences in human memory. In J. E. Birren & K. W. Schaie (Eds.), *Handbook of the psychology of aging* (pp. 384-420). New York: Van Nostrand Reinhold.
- Craik, F. I. M., & Byrd, M. (1982). Aging and cognitive deficits: The role of attentional resources. In F. I. M. Craik & S. Trehub (Eds.), *Aging and cognitive processes* (pp. 191-211). New York: Plenum.
- Craik, F. I. M. (1986). A functional account of age differences in memory. In F. Klix & H. Hagendorf (Eds.), *Human memory and cognitive capabilities: Mechanisms and performances* (pp. 409-422). North Holland: Elsevier.
- Craik F. I. M. & Kerr, S. (1996). Prospective memory, aging, and lapses of intention. In M. Brandimonte, G. O. Einstein, & M. A. McDaniel (Eds.), *Prospective memory: Theory and applications* (pp. 227-237). Mahwah, NJ: Lawrence Erlbaum Associates, Inc.
- Craik, F. I. M. & Hay, J. F. (1999). Aging and judgments of duration: Effects of task complexity and method of estimation. *Perception & Psychophysics*, 61, 549-560.
- Craik, F. I. M. & Bialystok, E. (2006). Planning and task management in older adults: Cooking breakfast. *Memory & Cognition*, 34, 1236-1249.
- Crawford, J. R., Bryan, J., Luszcz, M. A., Obonsawin, M. C., & Stewart, L. (2000). The executive decline hypothesis of cognitive aging: Do executive deficits quality as differential deficits and do they mediate age-related memory decline? *Aging, Neuropsychology, and Cognition*, 7, 9-31.



- Crawford, J. R. & Henry, J. D. (2005). Assessment of executive deficits. In P. W. Halligan & N. Wade (Eds.), *The effectiveness of rehabilitation for cognitive deficits* (pp. 233-246). London: Oxford University Press.
- Creelman, C. D. (1962). Human discrimination of auditory duration. *Journal of the Acoustical Society of America*, *34*, 582-593.
- Curtis, G., Vanderploeg, R. D., Spencer, J. et al. (2001). Patterns of verbal learning and memory in traumatic brain injury. *Journal of the International Neuropsychology Society*, *7*, 574-585.
- Cuttler, C. & Graf, P. (2009). Checking-in on the memory deficit and meta-memory deficit theories of compulsive checking. *Clinical Psychology Review* *29*, 393–409
- Del Missier, F., Mäntylä, T., & Bruine de Bruin, W. (2010). Executive functions in decision making: An individual differences approach. *Thinking & Reasoning*, *16*, 69–97.
- Dobbs, A. R., & Rule, B. G. (1987). Prospective memory and self-reports of memory abilities in older adults. *Canadian Journal of Psychology*, *41*, 209-222.
- Dreher, J. C. & Grafman, J. (2002). The roles of the cerebellum and basal ganglia in timing and error prediction. *European Journal of Neuroscience*, *16*, 1609-1619.
- Droit-Volet, S., Brunot, S., & Niedenthal, P. M. (2004). Perception of the duration of emotional events. *Cognition & Emotion*, *18*, 849-858.
- Ebbinghaus H. 1964. *Memory: A Contribution to Experimental Psychology*. Dover: (New York original work published 1885; translated 1913).
- Einstein, G. O., & McDaniel, M. A. (1990). Normal aging and prospective memory. *Journal of Experimental Psychology: Learning, Memory and Cognition*, *16*,

717-726.

- Einstein, G. O., Holland, L. J., McDaneil, M. A. & Guynn, M. J. (1992). Age-related deficits in prospective memory: The influence of task complexity. *Psychology and Aging, 7*, 471-478.
- Einstein, G. O., McDaniel, M. A., Richardson, S. L., Guynn, M. J., & Cufer, A. R. (1995). Aging and prospective memory: Examining the influence of self-initiated retrieval. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 21*, 996-1007.
- Einstein, G. O. & McDaniel, M. A. (1996). Retrieval Processes in prospective memory: Theoretical approaches and some new empirical findings. In M. Brandimonte, G. O. Einstein, & M. A. McDaniel (Eds.), *Prospective memory: Theory and applications* (pp. 115–141). Mahwah, NJ: Lawrence Erlbaum Associates, Inc.
- Einstein, G. O., Smith, R. E., McDaniel, M. A., & Shaw, P. (1997). Aging and prospective memory: The influence of increased task demands at encoding and retrieval. *Psychology and Aging, 12*, 479-488.
- Einstein, G. O., McDaneil, M. A., Smith, R. E., & Shaw, P. (1998). Habitual prospective memory and aging: Remembering intentions and forgetting actions. *Psychological Science, 9*, 284-288.
- Einstein, G. O., McDaniel, M. A., Marzi, M., Cochran, B., & Baker, M. (2000). Prospective memory and aging: Forgetting intentions over short delay. *Psychology and Aging, 15*, 671-683.
- Einstein, G. O., McDaniel, M. A., Thomas, R., Mayfield, S., Shanck, H., Morisette, N. et al. (2005). Multiple processing in prospective memory retrieval: Factors determining monitoring versus spontaneous retrieval. *Journal of Experimental*

*Psychology: General, 134, 327-342.*

- Einstein, G. O. & McDaniel, M. A. (2007). Monitoring in prospective memory (Chapter 2). In G. O. Einstein and M. A. McDaniel (Eds.) *Prospective memory: An overview and synthesis of an emerging field*. Sage Publications, Inc.
- Eisler, H., Eisler, A. D., & Hellström, Å. (2008). Psychophysical issues in the study of time perception. In S. Grondin (Ed.), *Psychology of time* (pp. 75-110). Bingley, U.K.: Emerald Group.
- Ellis, J. A. (1996). Prospective memory or the realization of delayed intentions: A conceptual framework for research. In M. Brandimonte, G. O. Einstein, & M. A. McDaniel (Eds.), *Prospective memory: Theory and applications* (pp. 1–22). Mahwah, NJ: Lawrence Erlbaum Associates, Inc.
- Ellis, J., & Kvavilashvili, L. (2001). Prospective memory in 2000: Past, present and future directions. *Applied Cognitive Psychology, 14*, 1-9.
- Ellis, J. & Freeman, J. E. (2008). Ten years of realizing delayed intentions. In M. Kliegel, M. A. McDaneil, & G. O. Einstein (Eds.) *Prospective memory: Cognitive, neuroscience, developmental, and applied perspective*. (pp. 1-22) Mahwah, NJ: Erlbaum.
- Fleming, J. M., Shum, D., Strong, J., & Lighthouse, S. (2005). Prospective memory rehabilitation for adults with traumatic brain injury: A compensatory training program. *Brain Injury, 19*, 1-13.
- Fleming, J., Riley, L., Gill, H., Gullo, M. J., Strong, J., & Shum, D. 2008. Predictors of prospective memory in adults with traumatic brain injury. *Journal of the International Neuropsychological Society, 14*, 823–831.
- Folstein, M. F., Folstein, S., & McHugh, P. (1975). “Mini-Mental State”: A practical

- method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12, 189–198.
- Fraisse, P. (1984). Perception and estimation of time. *Annual Review of Psychology*, 35, 1-36.
- Frazier, P. A., Tix, P., & Barron, K. E. (2004). Testing moderator and mediator effects in counseling psychology research. *Journal of Counseling Psychology*, 51, 115\_134.
- Friedman, W. J. (1990). *About time: Inventing the fourth dimension*. Cambridge, MA: MIT Press.
- Fuster, J. M. (2001). The prefrontal cortex—An update: time is of the essence. *Neuron*, 30, 319-333.
- Gibbon, J., Church, R. M., & Meck, W. (1984). *Scalar timing in memory* (Eds.) (Vol. 423; pp. 52-77).
- Gibbon, J., Malapani, C., Dale, C. L., & Gallistel, C. R. (1997). Toward a neurobiology of temporal cognition: Advances and challenger. *Current Opinion in Neuropsychology*, 7, 170-184.
- Gil, S., Niedenthal, P. M., & Droit-Volet, S. (2007). Anger and time perception in children. *Emotion*, 7, 219-225.
- Glisky, E. L., & Delaney, S. M. (1996). Implicit memory and new semantic learning in posttraumatic amnesia. *Journal of Head Trauma Rehabilitation*, 1, 31-42.
- Glisky, E. L. (1997). Rehabilitation of memory dysfunction. In T. E. Feinberg & M. J. Farah (Eds.), *Behavioral neurology and neuropsychology* (pp. 491-495). New York.
- Glisky, E. L., & Glisky, M. L. (2002). Learning and memory impairments. In P. J.

- Eslinger (Ed.), *Neuropsychological interventions*, (pp. 137-162). New York: Guilford Press.
- Glickson J., & Myslobodsky M. (2006). *Timing the future: The case of time-based prospective memory*. New York: World Scientific Publishing.
- Goldstone, S., & Kirkham, J. E. (1968). The effects of secobarbital and dextroamphetamine upon time judgment: Intersensory factors. *Psychopharmacologia*, *13*, 65-73.
- Gollwitzer, O. M. (1999). Implementation intentions: Strong effects of simple plan. *American Psychologist*, *54*, 493-503.
- Gonneaud, J., Kalpouzos, G., Bon, L., Viader, F., Eustache, F., & Desgranges, B. (2011). Distinct and shared cognitive functions mediate event- and time-based prospective memory impairment in normal ageing. *Memory*, *19*, 360-377.
- Gontier, E., Le Dantec, C., Leleu, A., Pauli, I., Charvin, H., Bernarda, C., Lalonde, R., & Rebaï, M. (2007). Frontal and parietal ERPs associated with duration discriminations with or without task interference. *Brain Research*, *1170*, 79-89.
- Gontier, E., Paul, I., Le Dantec, C., Pouthas, V., Jean-Marie, G., Berbard, C., Lalonde, R., & Rebaï, M. (2009). ERPs in anterior and posterior regions associated with duration and size discriminations. *Neuropsychology*, *23*, 668-678.
- Goscheke, T. & Kuhl, J. (1993). Representation of intention: Persisting activation in memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *19*, 1211-1226.
- Goschke, T. & Kuhl, J. (1996). Remembering what to do: Explicit and implicit for intentions. In M. Brandimonte, G.O. Einstein. & M.A. McDaniel (Eds.), *Prospective memory: Theory and applications* (pp. 53-91). USA: LEA.

- Grondin, S. & Macar, F. (1992). Dividing attention between temporal and nontemporal tasks: A performance operating characteristics – POC – analysis. In F. Macar, V. Pouthas, & W. Friedman (Eds.), *Time, action, cognition: Towards bridging the gap* (pp. 119-128). Dordrecht, The Netherlands: Kluwer.
- Grondin, S. (1993). Duration discrimination of empty and filled intervals marked by auditory and visual signals. *Perception & Psychophysics*, *54*, 383-394.
- Grondin, S., Meilleur-Wells, G., & Lachance, R. (1999). When to start explicit counting in time-intervals discrimination task: A critical point in the timing process of humans. *Journal of Experimental Psychology: Human Perception and Performance*, *25*, 993-1004.
- Grondin, S. (2003). Sensory modalities and temporal processing. In H. Helfrich (Ed.), *Time and mind II* (pp. 61-77). Göttingen: Hogrefe & Huber.
- Grondin, S. & Rammsayer, T. (2003). Variable foreperiods and duration discrimination. *Quarterly Journal of Experimental Psychology*, *56A*, 702-765.
- Grondin, S., Ouellet, B., & Roussel, M.-E. (2004). Benefits and limits of explicit counting for discriminating temporal intervals. *Canadian Journal of Experimental Psychology*, *58*, 1-12.
- Grondin, S., Roussel, M.-E., Gamache, P.-L., Roy, M., & Ouellet, B. (2005). The structure of sensory events and the accuracy of time judgments. *Perception*, *34*, 45-58.
- Grondin, S. (2008). Methods for studying psychological time. In S. Grondin (Eds.), *Psychology of time* (pp 51-74), Bingley, UK: Emerald Group.
- Grondin, S. (Ed.) (2008). *Psychology of time*. Bingley, U.K.: Emerald Group.

- Grondin, S., & McAuley, J. D. (2009). Duration discrimination in crossmodal sequences. *Perception*, *38*, 1542-1559.
- Grondin, S. (2010). Timing and time perception: A review of recent behaviour and neuroscience findings and theoretical directions. *Attention, Perception, & Psychophysics*, *72*, 561-582.
- Gronwall D, & Wrightson P. (1981). Memory and information processing capacity after closed head injury. *Journal of Neurology, Neurosurgery, and Psychiatry*, *44*, 889–895.
- Groot, Y. C. T., Wilson, B. A., Evans, J., & Watson, P. (2002). Prospective memory functioning in people with and without brain injury. *Journal of the International Neuropsychological Society*, *8*, 645–654.
- Gruber, R. P., & Block, R. A. (2003). Effects of caffeine on prospective and retrospective duration judgments. *Human Psychopharmacology*, *18*, 351-359.
- Guynn, M. J., McDaneil, M. A., & Einstein, G. O. (1998). Prospective memory: When memories fail. *Memory and Cognition*, *26*, 287-298.
- Guynn, M. J., McDaniel, M. A., & Einstein, G. O. (2001). Remembering to perform actions: A different type of memory? In H. D. Zimmer, R. L. Cohen, M. J. Guynn, J. Engelkamp, R., Kormi-Nouri & M., A., Foley (Eds.), *Memory for Action: A distinct form of episodic memory* (pp. ),
- Guynn, M. J. (2003). Two process model of monitoring in event-based prospective memory: Activation/retrieval mode and checking. *International Journal of Psychology*, *38*, 245-256.
- Guynn, M. J., & McDaniel, M. A. (2007). Target pre-exposure eliminates the effect of distraction on event-based prospective memory. *Psychonomic Bulletin &*

*Review, 14*, 484-488.

- Guynn, M. J. (2008). Theory of monitoring in prospective memory: Instantiating a retrieval mode and periodic target checking. In M. Kliegel, M. A. McDaniel, & G. O. Einstein (Eds.) *Prospective memory: Cognitive, neuroscience, developmental, and applied perspective*. (pp. 53-75) Mahwah, NJ: Erlbaum.
- Hagen, C., Malkmus, D., Durham, P., & Bowman, K. (1979). Level of cognitive functioning. In *Rehabilitation of head injured adult. Comprehensive physical management*. Downey, CA: Professional Staff Association of Rancho Los Amigos Hospital.
- Hall, K. M., Hamilton, B. B., Gordon, W. A., & Zasler, N. D. (1993). Characteristic and comparison of functional assessment indices: Disability Rating Scale, Functional Independence Measure and Functional Assessment Measure. *Journal of Head Trauma Rehabilitation, 8*, 60-74.
- Hannay, H. J., Levin, H. S., & Grossman, R. G. (1979). Impaired recognition memory after mild head injury. *Cortex, 15*, 269-283.
- Hannon, R., Gipson, M. T., Rebmann, M., Keneipp, J., Sattler, J., Lonero, P., Day, C. L., & Bolter, J. F. (1990). *Self-rating of prospective memory by normal, brain-injured and alcoholic individuals*. Paper presented at the meeting of the National Academy of Neuropsychology, Reno, NV.
- Hannon, R., Adams, P., Harrington, S., Fries-Dias, C., & Gibson, M. T. (1995). Effects of brain injury and age on prospective memory self-rating and performance. *Rehabilitation Psychology, 40*, 289-297.
- Harris, H. E. & Wilkins, A. J. (1982). Remembering to do things: A theoretical framework and an illustrative experiment. *Human Learning, 1*, 123-136.



- Harrington, D. L., Haaland, K. Y., & Knight, R. T. (1998). Cortical networks underlying mechanisms of time perception. *The Journal of Neuroscience*, *18* (3), 1035-1095.
- Harrington, D. L., Haaland, K. Y., Hermanowics, N. (1998b). Temporal processing in the basal ganglia. *Neuropsychology*, *12*, 3-12.
- Harrington, D. L. & Haaland, K. Y. (1999). Neural underpinnings of temporal processing: A review of focal lesion, pharmacology, and functional imaging research. *Review in the Neurosciences*, *10*, 91-116.
- Harrington, D. L., Lee, R. R., Boyd, L. A., Rapcsak, S. Z., & Knight, R. T. (2004). Does the representation of time depend on the cerebellum? Effect of cerebellar stroke. *Brain* *127*, 561-574.
- Hartikainen K. M., Waljas M., Isoviita T., Dastidar P., Liimatainen S., Solbakk A. K., Ogawa K. H., Soimakallio S., Ylinen A., Ohman J. (2010). Persistent symptoms in mild to moderate traumatic brain injury associated with executive dysfunction. *Journal of Clinical Experimental Neuropsychology*, *32*, 767-774.
- Heffernan, T. M. & Ling, J. (2001). The impact of Eysenck's extraversion-introversion personality dimension on prospective memory. *Scandinavian Journal of Psychology*, *42*, 321-325.
- Hellström, Å. (1985). The Time-Order Error and its relatives. Mirrors of cognitive processes in comparing. *Psychological Bulletin*, *97*, 35-61.
- Hellström, Å., & Rammsayer, T. H. (2004). Effects of time-order, interstimulus interval, and feedback in duration discrimination of noise bursts in the 50- and 1000-ms ranges. *Acta Psychologica*, *116*, 1-20.

- Henry, J. D., MacLeod, M. S., Phillips, L. H., & Crawford, J. R. (2004). A meta-analytic review of prospective memory and aging. *Psychology and Aging, 19*, 27-39.
- Henry, J. D., Phillips, L. H., Crawford, J. R., Kliegel, M., Theodorou, G., & Summers, F. (2007a). Traumatic brain injury and prospective memory: Influence of task complexity. *Journal of Clinical and Experimental Neuropsychology, 1*, 1-10.
- Henry, J. D., Rendell, P. G., Kliegel, M., & Altgassen, M. (2007b). Prospective memory in schizophrenia: Primary or secondary impairment? *Schizophrenia Research, 95*, 179–185.
- Herman, D. J. & Neisser, U. (1978). An inventory of everyday memory experience. In M. M. Gruneberg, P.E., P. E. Morris & R. N. Sykes (Eds.), *Practical aspects of memory*. New York: Academic Press.
- Hicks, R. E., Miller, G. W., & Kinsbourne, M. (1976). Prospective and retrospective judgments of time as a function of amount of information processing. *American Journal of Psychology, 89*, 719-730.
- Hicks, R. E., Gualtieri, C. T., Mayo, J. P., Jr., & Perez-Reyes, M. (1984). Cannabis, atropine and temporal information processing. *Neuropsychobiology, 12*, 229-237.
- Hinton, S. C., & Meck, W. H. (2004). Frontal–striatal circuitry activated by human peak-interval timing in the supra-seconds range. *Cognitive Brain Research, 21*, 171-182.
- Ivry, R. B., Keele, S. W., Diener, H. C. (1988). Dissociation of the lateral and medial cerebellum in movement timing and movement execution. *Experimental Brain Research, 73*, 167-180.
- Ivry, R. B. & Keele, S. W. (1989). Timing functions of the cerebellum. *Journal of*

*Cognitive Neuropsychology, 1*, 136-152.

James, W. (1890). *The principles of psychology*. New York: Holt.

Janowsky, J. S., Shimamura, A. P., Squire, L. R. (1989). Memory and metamemory: Comparisons between patients with frontal lobe lesions and amnesic patients. *Psychobiology, 17*, 3-1.

Jones, C. R. G., Rosenkranz, K., Rothwell, J. C., & Jahanshahi, M. (2004). The right dorsolateral prefrontal cortex is essential in time reproduction: An investigation with repetitive transcranial magnetic stimulation. *Experimental Brain Research, 158*, 366-372.

Jones, M. R. & Boltz, M. (1989). Dynamic attending and responses to time. *Psychological Review, 96*, 459-491.

Jones, M. R. (2006). Dynamic attending and prospective memory for time. In Glickson J, and Myslobodsky M (Eds.), *Timing the Future: The Case of Time-based Prospective Memory* (pp. 51-85). New York: World Scientific Publishing.

Jones, S., Livner, A., & Bäckman, L. (2006). Patterns of prospective and retrospective memory impairment in preclinical Alzheimer's disease. *Neuropsychology, 2*, 144–152.

Joubert, C. E. (1983). Subjective acceleration of time: Death anxiety and sex differences. *Perceptual & Motor Skills, 57*, 49-50.

Jueptner, M., Rijntjes, M., Weller, C., Faiss, J. H., Timman, D., Mueller, S., & Diener, H. C. (1995). Localization of a cerebellar timing process using PET. *Neurology, 45*, 1540-1545.

Katai, S., Maruyama, T., Hashimoto, T., & Ikeda, S. (2003). Event based and time based prospective memory in Parkinson's disease. *Journal of Neurology, Neurosurgery,*

*and Psychiatry, 74, 704–709.*

- Kerns, K.A. (2000). The Cyber Cruiser: An investigation of development of prospective memory in children. *Journal of the International Neuropsychological Society, 6,* 62-70.
- Kerns, K. A. & Price, K. J. (2001). An Investigation of Prospective Memory in Children With ADHD. *Children Neuropsychology, 7,* 162-171.
- Kidder, D. P., Park, D. C., Hertzong, C., & Morrel, R. W. (1997). Prospective memory and aging: The effects of working memory and prospective memory task load. *Aging, Neuropsychology, and Cognition, 4,* 93-112.
- Kim, H. J., Craik, F. I. M., Luo, L., & Ween, J. E. (2010). Impairment in prospective and retyrospective memory following stroke. *Neurocase, 15,* 145-156.
- Kinch, J., & McDonald, S. (2001). Traumatic brain injury and prospective memory: An examination of the influence of executive functioning and retrospective memory. *Brain Impairment, 2,* 119-130.
- Kinsella, G., Murtagh, D., Landry, A., Homfray, K, Hammond, M., O’Beirne, L., Dwyver, L., Lamont, M., & Ponsford, J. (1996). Everyday memory following traumatic brain injury. *Brain Injury, 10,* 499-507.
- Kinsella, G. J., (1999). Assessment of Attention Following Traumatic Brain Injury: A Review. *Neuropsychological rehabilitation, 8,* 351–375.
- Kinsella, G. J., Ong, B., & Tucker, J. (2009). Traumatic brain injury and prospective memory in a virtual shopping trip task: Does it matter who generates the prospective memory target? *Brain Impairment, 10,* 45–51.
- Kliegel, M., McDaniel, M. A., & Einstein, G. O. (2000). Plan formation, retention, and execution in prospective memory: A new approach and age-related effects.

*Memory & Cognition*, 28, 1041-1049.

Kliegel, M., Martin, M., McDaniel, M. A., & Einstein, G. O. (2001). Varying the importance of a prospective memory task: Differential effects across time- and event-based prospective memory. *Memory*, 9, 1-11.

Kliegel, M., Martin, M., McDaniel, M. A., & Einstein, G. O. (2002). Complex prospective memory and executive control of working memory: A process model. *Psychologische Beiträge*, 44, 303–318.

Kliegel, M., Martin, M., McDaniel, M. A., & Einstein, G. O. (2004a). Importance effects on performance in event-based prospective memory tasks. *Memory*, 12, 553-561.

Kliegel, M., Eschen, A., & Thöne-Otto, A. I. T. (2004b). Planning and realization of complex intentions in traumatic brain injury and normal aging. *Brain and Cognition*, 56, 43–54.

Kliegel, M., Phillips, L. H., Lemke, U., & Kopp, U. A. (2005). Planning and realisation of complex intentions in patients with Parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*, 76, 1501–1505.

Kliegel, M., McDaniel, M. A., & Einstein, G. O. (Eds.). (2008). *Prospective memory: Cognitive, neuroscience, developmental, and applied perspective*. Mahwah, NJ: Erlbaum.

Kliegel, M., Jäger, T., Altgassen, M., & Shum, D. (2008a). Clinical neuropsychology of prospective memory. In M. Kliegel, M. A. McDaneil, & G. O. Einstein (Eds.) *Prospective memory: Cognitive, neuroscience, developmental, and applied perspective*. (pp. 283-308) Mahwah, NJ: Erlbaum.

Kliegel, M., Mackinlay, R., & Jäger, T. (2008b). Complex prospective memory: Development across the lifespan and the role of task interruption. *Developmental*

*Psychology, 44*, 612–617.

Kliegel, M., Jäger, T., & Phillips, L. H. (2008c). Adult age differences in event-based prospective memory: A meta-analysis on the role of focal versus nonfocal cues.

*Psychology and Age, 23*, 203-208.

Kliegel, M., Atgassen, M., Hering, A., & Rose, N. S. (2011). A process-model based approach to prospective memory impairment in Parkinson's disease.

*Neuropsychologia, 49*, 2166-2177.

Knight, R. G., Harnett, M., & Titov, N. (2005). The effects of traumatic brain injury on the predicted and actual performance of a test of prospective remembering. *Brain Injury, 19*, 27–38.

*Injury, 19*, 27–38.

Knight, G. G., Titov, N., & Crawford, M. (2006). The effects of distraction on prospective memory remembering following traumatic brain injury assessed in a simulated naturalistic environment. *Journal of the International Neuropsychology Society, 12*, 8-16.

*Neuropsychology Society, 12*, 8-16.

Knight, R. G., & Titov, N. (2009). Use of virtual reality tasks to assess prospective memory: Applicability and evidence. *Brain Impairment, 10*, 3–13.

Kock, G., Olivieri, M., Torriero, S., Salerno, S., Lo Gerfo, E., & Caltagirone, C. (2007).

Ripetitive TMS of cerebellum interferens with millisecond time processing.

*Experimental Brain research, 179*, 291-299.

Kopp, U. A., & Thöne-Otto, A. I. T. (2003). Disentangling executive function and memory processes in event-based prospective remembering after brain damage:

A neuropsychological study. *International Journal of Psychology, 38*, 229-235.

Kvavilashvili, L. (1987). Remembering intention as a distinct form of memory. *British*

*Journal of Psychology, 78*, 507-518.

- Kvavilishvili, L. (1992). Remembering intention: A critical review of existing experimental paradigms. *Applied Cognitive Psychology, 6*, 507-524.
- Kvavilashvili, L. & Ellis, J. (1996). Varieties of intentions: Some distinctions and classifications. In M. Brandimonte, G. O. Einstein, & M. A. McDaniel (Eds.), *Prospective memory: Theory and applications* (pp. 23-51). Mahwah, NJ: Lawrence Erlbaum Associates, Inc.
- Kvavilashvili, L., & Fisher, L. (2007). Is time-based prospective remembering mediated by self-initiated rehearsals? Role of cues, ongoing activity, age and motivation. *Journal of Experimental Psychology: General, 136*, 112–132.
- Laicono, M., Inzaghi, M. G., De Tanti, A., & Capitani, E. (2000). Wisconsin card sorting test: a new global score, with Italian norms, and its relationship with the Weigl sorting test. *Neurological Science, 21*, 279-291.
- Labelle, M. A., Graf, P., Grondin, S., & Gagné-Roy, L. (2009). Time-related processes in time-based prospective memory and in time-interval production. *European Journal of Cognitive Psychology, 21*, 501-521.
- Lapid, E., Ulrich, R., & Rammsayer, T. (2008). On estimating the difference limen in duration discrimination tasks: A comparison of the 2AFC and the reminder tasks. *Perception & Psychophysics, 70*, 291-305.
- LeDantec, C., Grondin, E., Paoul, I., Charvin, H., Bernard, C., Lalonde, R., & Rebaï, M. (2007). ERPs associated with visual duration discriminations in prefrontal and parietal cortex. *Acta Psychologica, 125*, 85-98.
- Leclercq, M., Couillet, J., Azouvi, P., Marlier, N., Martin, Y., Strypstein, E., & Rousseaux, M. (2000). Dual task performance after severe diffuse traumatic

- brain injury or vascular prefrontal damage. *Journal of Clinical and Experimental Neuropsychology*, 22, 339–350.
- Lee, K. H., Eagleston, P. N., Brown, W. H., Gregory, A. N., Barker, A. T., & Woodruff, P. W. R. (2007). The role of the cerebellum in the subsecond time perception: Evidence from repetitive transcranial magnetic stimulation. *Journal of Cognitive Neuroscience*, 19, 147-157.
- Leitz, J. R., Morgan, C. J. A., Bisby, J. A., Rendell, P. G., & Curran, H. V., (2009). Global impairments of prospective memory following acute alcohol. *Psychopharmacology*, 205, 379-387.
- Levin, H. S., O'Donnell, V. M. & Grossman, R. G. (1979). The Galveston orientation and amnesia test: A practical scale to assess cognition after head injury. *The Journal of Nervous and Mental Disease*, 167, 675-684.
- Levin, H. S. (1991). Memory impairment after closed head injury. In F. Boller & J. Grafman (Eds.), *Handbook of neuropsychology* (Vol. 6) (pp. 183-207). Amsterdam: Elsevier.
- Levin, H. S., Greenberg, H. M., & Benton, A. L. (1991). *Frontal lobe function and dysfunction*. New York: Oxford University Press.
- Levin, H. S. & Krauss, M. F. (1994). The frontal lobes and traumatic brain injury. *Journal of Neuropsychiatry and Clinical Neuroscience*, 6, 433-454.
- Lewis, P. A., & Miall, R. (2002). Brain activity during non-automatic motor production of discrete multi-second intervals. *Neuroreport*, 13, 1731-1735.
- Lewis, P. A., & Miall, R. (2003a). Distinct system from automatic and cognitively controlled time measurement: Evidence from neuroimaging. *Current Opinion in Neurobiology*, 13, 1-6.



- Lewis, P. A. & Miall, R. (2003b). Brain activation patterns during measurement of sub- and supra-second intervals. *Neuropsychologia*, *41*, 1583-1592.
- Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological Assessment, 4<sup>th</sup> Edition*. Oxford University Press.
- Light, L. L. (1991). Memory and aging: Four hypotheses in search of data. *Annual Review of Psychology*, *42*, 333-376.
- Logie, R. H., Maylor, E. A., DellaSala, S., & Smith, G. (2004). Working memory in event- and time-based prospective memory tasks: Effects of secondary demand and age. *European Journal of Cognitive Psychology*, *16*, 441-456.
- Ling, J., Heffernan, T. M., Buchanan, T., Rodgers, J., Scholey, A. B., & Parrott, A. C. (2003). Effects of alcohol on subjective ratings of prospective and everyday memory deficits. *Alcoholism: Clinical and Experimental Research*, *27*, 970-974.
- Maatter, C. A., Sohlberg, M. M. & Crinean, J. (1987). Focus on clinical research: Perceptions of memory function in individuals with closed-head injury. *Journal of Head Trauma Rehabilitation*, *2*, 74-84.
- Macmillan, N. A., & Creelman, C. D. (1991). *Detection theory: A user's guide*. New York: Cambridge University Press.
- Macar, F., Lejeune, H., Bonnet, M., Ferrara, A., Pouthas, V., Vidal, F., & Maquet, P. (2002). Activation of the supplementary motor area and of attentional networks during temporal processing. *Experimental Brain Research*, *142*, 475-485.
- Mackinlay, R. J., Kliegel, M., & Mäntylä, T. (2009). Predictors of time-based prospective memory in children. *Journal of Experimental Child Psychology*, *102*, 251-264.

- Malapani, C., Rakitin, B., Levy, R., Meck, W. H., Deweer, B., Dubois, B., & Gibbon, J. (1998). Coupled temporal memories in Parkinson's disease: A dopamine-related dysfunction. *Journal of Cognitive Neuroscience*, 10, 316–331.
- Malapani, C., Deweer, B., & Gibbon, J. (2002). Separating storage from retrieval dysfunction of temporal memory in Parkinson's disease. *Journal of Cognitive Neuroscience*, 14, 31–322.
- Mangels, J. A., Ivry, R. B., & Shimizu, N. (1998). Dissociable contributions of the prefrontal and neocerebellar cortex to time perception. *Cognitive and Research*, 7, 15-39.
- Mangels, J. A. & Ivry, R. B. (2000). Time perception. In B. Rapp (Eds.). *The handbook of cognitive neuropsychology: What deficits reveal about the human mind* (pp. 467-493). Psychology Press.
- Mäntylä, T. (1996). Activating actions and interrupting intentions: Mechanisms of retrieval sensitization in prospective memory. In M. A. Brandimonte, G. O., Einstein, & M. A., McDaniel, (Eds.), *Prospective memory: Theory and applications*. (pp. 93-113) Mahwah, NJ: Lawrence Erlbaum Associates, Inc.
- Mäntylä, T., & Carelli, M. G. (2006). Time monitoring and executive functioning: Individual and developmental differences. In Glickson J., and Myslobodsky M. (Eds.), *Timing the Future: The Case of Time-based Prospective Memory* (pp. 191-211). New York: World Scientific Publishing.
- Mäntylä, T., Carelli, M. G., & Forman, H. (2007). Time monitoring and executive functioning in children and adults. *Journal of Experimental Child Psychology*, 96, 1-19.

- Mäntylä, T. & Nilsson, L. G. (2009). Remembering to remember in adulthood: A population based study on aging and prospective memory. *Aging, Neuropsychology, and Cognition*, *4*, 81-91.
- Mäntylä, T., Del Missier, F., & Nilsson, L. G. (2009). Age differences in multiple outcome measures of time-based prospective memory. *Aging, Neuropsychology, and Cognition*, *1*, 1–13, 2009.
- Maquet, P., Lejeune, H., Pouthas, V., Bonnet, M., Casini, L., Macar, F., Timsit-Berthier, M., Vidal, F., Ferrara, A., Degueldre, C., Quaglia, L., Delfiore, G., Luxen, A., Woods, R., Mazziotta, J. C., & Comar, D. (1996). Brain activation induced by estimation of duration: A PET study. *NeuroImage*, *3*, 119-126.
- Marsh, R. L., Hicks, J. L., Hancock, T. W., & Munsayac, K. (2002). Investigating the output monitoring component of event-based prospective memory performance. *Memory and Cognition*, *30*, 302-311.
- Marsh, R. L., Hicks, J. L., & Cook, G. I. (2005). On the relationship between effort toward an ongoing task and cue detection in event-based prospective memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *31*, 68-75.
- Martin, M., Kliegel, M., & McDaniel, M. A., (2003). The involvement of executive functions in prospective memory performance of adults. *International Journal of Psychology*, *38*, 195-206.
- Mathias, J. L., & Mansfield, K. M. (2005). Prospective and declarative memory problems following moderate and severe traumatic brain injury. *Brain Injury*, *4*, 271–282.
- Mathias, J. L. & Wheaton, P. (2007). Changes in attention and information processing

- speed following severe traumatic brain injury: A meta-analytic review. *Neuropsychology*, *21*, 212-223.
- Matsuzaka, Y., Aizawa, H., & Tanji, J. (1992). A motor area rostral to the supplementary motor area (presupplementary motor area) in the monkey: neuronal activity during a learned motor task. *Journal of Neurophysiology*, *68*, 653-662.
- Maujean, A., Shum, D., & McQueen, R. (2003). Effect of cognitive demand on prospective memory in individuals with traumatic brain injury. *Brain Impairment*, *4*, 135-145.
- Maylor, E. A. (1990). Age and prospective memory. *The Quarterly Journal of Experimental Psychology*, *42*, 471-493.
- Maylor, E. A. (1996). Age-related impairment in an event-based prospective memory task. *Psychology and Aging*, *11*, 74-78.
- Maylor, E. A., Smith, G., DellaSala, S., & Logie, R. H. (2002). Prospective and retrospective memory in normal aging and dementia: An experimental study. *Memory and Cognition*, *20*, 871-884.
- McAllister, T. W., Saykin, A. J., Flashman, L. A., Sparling, M. B., Johnson, S. C., Guerin, S. J., Manounà, A. C., Weaver, J. B., & Yanofsky, N. (1999). Brain activation during working memory 1 month after mild traumatic brain injury. A functional MRI study. *Neurology*, *53*, 1300-1308.
- McDaniel, M. A., & Einstein, G. O. (1993). The importance of cue familiarity and the cue distinctiveness in prospective memory. *Memory*, *1*, 23-41.
- McDaniel, M. A., Robinson-Riegler, B., & Einstein, G. O. (1998). Prospective remembering: Perceptually driven or conceptually driven processes? *Memory and Cognition*, *26*, 121-134.

- McDaniel, M. A., Guynn, M. J., Glisky, E. L., Rubin, S. R., & Routhieaux, B.C. (1999). Prospective memory: A neuropsychological study. *Neuropsychology, 13*, 103-110.
- McDaniel, M. A. & Einstein, G. O. (2000). Strategic and automatic processes in prospective memory retrieval: a multiprocess framework. *Applied Cognitive Psychology, 14*, 127-144.
- McDaniel, M. A., Guynn, M. J., Einstein, G. O., & Breneiser, J. (2004). Cue-focused and reflexive-associative processes in prospective memory retrieval. *Journal of Experimental Psychology: Learning, Memory, & Cognition, 30*, 605-614.
- McDaniel, M. A., & Einstein, G. O. (2007). *Prospective memory: An overview and synthesis of an emerging field*. Thousand Oaks, CA: Sage.
- McDaniel, M. A., Einstein, G. O., & Rendell, P. G. (2008). The puzzle of inconsistent age-related declines in prospective memory: A multiprocess explanation. In M. Kliegel, M. A. McDaniel, & G. O. Einstein (2008), *Prospective memory: Cognitive, neuroscience, developmental, and applied perspectives* (pp. 141–160). Mahwah, NJ: Erlbaum.
- McDowd, J. M., & Craik, F. I. M. (1988). Effects of aging and task difficulty on divided attention performance. *Journal of Experimental Psychology: Human Perception & Performance, 14*, 267-280.
- McFarland, C.P., & Glisky, E. I. (2009). Frontal lobe involvement in a task of time-based prospective memory. *Neuropsychologia, 47*, 1660-1669.
- Meacham, J. A. & Leiman, B. (1982). Remembering to perform future actions. In U. Neisser (Eds.) *Memory observed: Remembering in Natural Contexts*. (pp. 327-336) San Francisco: W.H. Freeman.

- Meck, W. H. (1996). Neuropharmacology of timing and time perception. *Cognitive Brain Research*, 3, 227-242.
- Meck, W. H. (2005). Neuropsychology of timing and time perception. *Brain and Cognition*, 58, 1-8.
- Meyers, C. A., & Levin, H. S. (1992). Temporal perception following closed head injury: Relationship of orientation and attention span. *Neuropsychiatry, Neuropsychology, and Behavioural Neurology*, 1, 28-32.
- Miller, E. K. (2000). The prefrontal cortex and cognitive control. *Nature Reviews Neuroscience*, 1, 59–65.
- Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience*, 24, 167–202.
- Mimura, M., Kinsbourne, M., & O'Connor, M. (2000). Time estimation by patients with frontal lesions and by Korsakoff amnesia. *Journal of the International Neuropsychology Society*, 6, 517-528.
- Miyake, A., Friedman, N. P., Emerson, M.J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex “Frontal Lobe” tasks: A latent variable analysis. *Cognitive Psychology*, 41, 49–100.
- Moscovitch, M. (1994). Models of consciousness and memory. In M.S. Gazzaniga (Eds.), *The Cognitive Neuroscience*, MIT Press, Cambridge, MA, (pp 1341-1356).
- Nichelli, P., Clark, K., Hollnagel, C., & Grafman, J. (1995). Duration processing after frontal lobe lesions. *Annals of the New York Academic of Science*, 769, 183-190.

- Nichelli, P. (1996). Time perception measurements in neuropsychology. In M.A. Pastor & J. Artieda (Eds.), *Time, internal clocks and movement* (Vol. 115, pp. 187-204). Amsterdam: Elsevier.
- Nichelli, P., Always, D., & Grafman, J. (1996). Perceptual timing in cerebellar degeneration. *Neuropsychologia*, *34*, 863-871.
- Novelli G., Papagno C., Capitani E., Laiacona N., Vallar G. and Cappa S. F. (1986). Tre test clinici di ricerca e produzione lessicale: taratura su soggetti normali. *Archivio di Psicologia, Neurologia e Psichiatria*, *47*, 477-506.
- Ogden, R. S., Wearden, J. H., & Jones, L. A. (2010). Are memories for duration modality specific? *The Quarterly Journal of Experimental Psychology*, *63*, 65-80.
- Oshio, K. I., Chiba, A., & Inase, M. (2006). Delay period activity of monkey prefrontal neurons during duration-discrimination task. *European Journal of Neurosciences*, *23*, 2779–2790.
- Owen, A.M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-Back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. *Human Brain Mapping*, *25*, 46–59.
- Ozgis, S., Rendell, P. G., & Henry, J. D. (2009). Spaced retrieval significantly improves prospective memory performance of cognitively impaired older adults. *Gerontology*, *55*, 229-232.
- Paraskevaides, T., Morgan, C. J. A., Leitz, J. R., Bisby, J. A., Rendell, P. G., & Curran, H. V. (2010). Drinking and future thinking: acute effects of alcohol on prospective memory and future simulation, *Psychopharmacology*, *208*, 301–308.

- Park, D. C., Hertzong, C., Kidder, D. P., Morrell, R. W., & Mayhorn, C. B. (1997). Effect of age on event-based and time-based prospective memory. *Psychology and Aging, 12*, 314-327.
- Park, N. W., Moscovitch, M., & Robertson, I. H. (1998). Divided attention impairments after traumatic brain injury. *Neuropsychologia, 37*, 1119–1133.
- Pastor, M. A., Artieda, J., Jahanshahi, M., & Obeso, J. A. (1992). Time estimation and reproduction is abnormal in Parkinson's disease. *Brain, 115*, 211-225.
- Paul, I., Le Dantec, C., Bernard, C., Lalonde, R., & Rebai, M. (2003). Frontal lobe event related potentials in a visual duration discrimination task. *Journal of Clinical Neurophysiology, 20*, 351–360.
- Penney, T. B., Gibbon, J., & Meck, W. H. (2000). Differential effects of auditory and visual signals on clock speed and temporal memory. *Journal of Experimental Psychology: Human Perception & Performance, 26*, 1770-1787.
- Penney, T. B., Gibbon, J., & Meck, W. H. (2008). Categorical scaling of duration bisection in pigeons (*Columba livia*), mice (*Mus musculus*), and humans (*Homo sapiens*). *Psychological Science, 19*, 1103-1109.
- Penney, T. B., & Vaitilingam, L. (2008). Imaging time. In S. Grondin (Ed.), *Psychology of time* (pp. 261-294). Bingley, U.K.: Emerald Group.
- Perbal, S., Droit-Voler, S., Isingrini, M., Pouthas, V. (2002). Relationships between age-related changes in time estimation and age-related changes in processing speed, attention, and memory. *Aging Neuropsychology and Cognition, 9*, 201-216.
- Perbal, S., Couillet, J., Azouzi, P., & Pouthas, V. (2003). Relationship between time estimation, memory, attention, and processing speed in patients with severe traumatic brain injury. *Neuropsychologia, 41*, 1599-1610.



- Petrušić, W. (1984). Explicit counting and the time-order errors in discrimination. In J. Gibbon & L. G. Allan (Eds.), *Annals of the New York Academy of Sciences: Vol. 423, Timing and time perception* (pp. 630-633). New York Academy of Science.
- Picton, T.W., Stuss, D. T., Shallice, T., Alexander, M. P., & Gillingham, S. (2006). Keeping time: Effects of focal lesions. *Neuropsychologia*, *44*, 1195-1209.
- Ponsford, J., & Kinsella, G. (1992). Attentional deficits following severe closed head injury. *Journal of Clinical and Experimental Neuropsychology*, *14*, 822–838.
- Ponsford, J. Sloan, S., & Snow, P. (1995). Traumatic brain injury: Rehabilitation for everyday adaptive living. Hove, UK: Lawrence Erlbaum.
- Pöppel, E. (1972). Oscillations as possible basis for time perception. In J. T. Fraser, F.C. Haber, & G. H. Müller (Eds.), *The study of time* (pp. 219-241). Berlin: Springer-Verlag.
- Pöppel, E. (2004). Lost in time: a historical frame, elementary processing units and the 3-second window. *Acta Neurobiologiae Experimentalis*, *64*, 295-301.
- Pouthas, V., George, N., Poline, J.-B., Pfeuty, M., VandeMoortele, P.-F., Hugueville, L., et al. (2005). Neural network involved in time perception: An fMRI study comparing long and short interval estimation. *Human Brain Mapping*, *25*, 433-441.
- Prigatano, G. P., Glisky, E. L., & Klonoff, P. (1996). Cognitive rehabilitation after traumatic brain injury. In P. W. Corrigan & S. C. Yudofsky (Eds.), *Cognitive rehabilitation and neuropsychiatric disorders* (pp. 223-242). American Psychiatric Press.
- Rakitina, B. C., Sterna, Y., & Malapani, C. (2005). The effects of aging on time reproduction in delayed free-recall. *Brain and Cognition*, *58*, 17-34.

- Rammsayer, T. H. (1999). Neuropharmacological evidence for different timing mechanisms in humans. *The Quarterly of Experimental Psychology*, *52*, 273-286.
- Rammsayer, T. H. (2001). Ageing and temporal processing of durations within the psychological present. *European Journal of Cognitive Psychology*, *13*, 549-565.
- Rammsayer, T. H., & Ulrich, R. (2001). Counting models of temporal discrimination. *Psychonomic Bulletin & Review*, *8*, 270-277.
- Rao, S. M., Mayer, A. R., & Harrington, D. L. (2001). The evolution of brain activation during temporal processing. *Nature Neuroscience*, *4*, 317-323.
- Raskin, S. A., Woods, S. P., Poquette, A. J., McTaggart, A. B., Sethma, J., Williams, R. C., & Tröster, A. I. (2011). A differential deficit in time- versus event-based prospective memory in Parkinson's disease. *Neuropsychology*, *25*, 201-209.
- Rendell, P. G., & Craik, F. I. M. (2000). Virtual and actual week: Age-related differences in prospective memory. *Applied Cognitive Psychology. Special Issue: New Perspective in Prospective Memory*. *14*, S43-S62
- Rendell, P. G., Jensen, F., & Henry, J. D. (2007a). Prospective memory in multiple sclerosis. *Journal of the International Neuropsychological Society*. *13*, 410-416.
- Rendell, P. G., Gray, T. J., Henry, J. D., & Tolan, A. (2007b). Prospective memory impairment in 'ecstasy' (MDMA) users. *Psychopharmacology*. *194*, 497-504.
- Rendell, P. G., McDaniel, M. A., Forbes, R. D., & Einstein, G. O. (2007c). Age-related effects in prospective memory are modulated by ongoing task complexity and relation to target cue. *Aging, Neuropsychology, and Cognition*, *14*, 236-256.
- Rendell, P. G., Mazur, M., & Henry, J. D. (2009). Prospective memory impairment in former users of methamphetamine. *Psychopharmacology*, *203*, 609-616.

- Rendell, P. G., & Henry, J. D. (2009). A review of Virtual Week for prospective memory assessment: Clinical implications. *Brain Impairment, 10*, 14-22.
- Rendell, P. G., Phillips, L. H., Hendy, J. D., Brumby-Rendell, T., de la Piedad Garcia, X., Altgassen, M., & Kliegel, M. (2011). Prospective memory, emotional valence and aging. *Cognition and Emotion, 25*, 916-925.
- Rose, N. S., Rendell, P. G., McDaniel, m. A., Abele, I., & Kliegel, M. (2010). Age and individual differences in prospective memory during a “Virtual Week”: The role of working memory, task regularity and cue focality. *Psychology and Aging, 25*, 595-605.
- Rubia, K., Taylor, A., Taylor, E., & Sergeant, J. A. (1999). Synchronization, anticipation, and consistency in motor timing in children with dimensionality defined attention deficit hyperactivity behaviour. *Perceptual and Motor Skills, 89*, 1237-1258.
- Rubia, K., & Smith, A. (2004). The neural correlates of cognitive time management: A review. *Acta Neurobiologiae Experimentalis, 64*, 329-340.
- Rubia, K. (2006). The neural correlates of timing functions. In Glickson J, and Myslobodsky M (Eds.), *Timing the Future: The Case of Time-based Prospective Memory* (pp. 213-238). New York: World Scientific Publishing.
- Salat, D. H., Kaye, J. A., & Janowsky, J. S. (2001). Selective preservation and degeneration within the prefrontal cortex in aging and Alzheimer’s disease. *Archives of Neurology, 58*, 1403-1408.
- Salthouse, T. A., Rogan, J. D., & Prill, K. A. (1984). Division of attention: Age differences on a visually presented memory task. *Memory & Cognition, 12*, 613-620.

- Salthouse, T. A. (1994). How many causes are there for aging-related decrements in cognitive functioning? *Development Review, 14*, 413-437.
- Salthouse, T. A. (1996). Constraints of theories of cognitive aging. *Psychonomic Bulletin & Review, 3*, 287-299.
- Sbordone, R. J. (1996). Ecological validity: Some critical issues for the neuropsychologist. In R. J. Sbordone, & C. J. Long (Eds.), *Ecological validity of neuropsychological testing*. Florida, CA: GR Press (pp. 15-41).
- Schmitter-Edgecombe, M., & Wright, M. J. (2004). Event-based prospective memory following severe closed-head injury. *Neuropsychology, 18*, 353–361.
- Schmitter-Edgecombe, M., & Anderson, J. W. (2007). Feeling of knowing in episodic memory following moderate to severe closed-head injury. *Neuropsychology, 21*, 224–234.
- Schmitter-Edgecombe, M. & Rueda, A. D. (2008). Time estimation and episodic memory following traumatic brain injury. *Journal of Clinical and Experimental Neuropsychology, 30* (2), 212-223.
- Schroots, J. J. F., & Birren, J. E. (1990). *Concepts of time and aging in science*. In J.E. Birren & K.W. Schaie (Eds.), *Handbook of the psychology of aging* (pp. 45-64). San Diego, CA: Academic Press.
- Searleman, A. (1996). Personality variables and prospective memory performance. In D. J. Herrmann, C. McEvoy, C. Hertzog, P. Hertel, & M.K. Johnson. (Eds.). *Basic and Applied Memory Research Practical Applications*. Vol. 2. USA: LEA.
- Sgaramella, T. M., Zettin, M., Bisiacchi, P. S., Vernè, D., & Rago, R. (1993). *Retrospective memory and planning components in prospective remembering*.

- Evidence from a neuropsychological study.* Paper presented at the workshop on Memory and Mental Representation, Roma, Italy.
- Shallice, T., & Burgess, P.W. (1991) Deficits in strategy application following frontal lobe damage in man. *Brain, 114*, 727-41
- Shimamura, A. P. (1994). Memory and frontal lobe function. In M.S. Gazzaniga (Eds.), *The Cognitive Neuroscience*, MIT Press, Cambridge, MA, (pp 803-814).
- Shum, D., Sweeper, S., & Murray, R. (1996). Performance on verbal implicit and explicit memory tasks following traumatic brain injury. *The Journal of Head Trauma Rehabilitation, 11*, 43-53.
- Shum, D., Valentine, M., & Cutmore, T. (1999). Performance of individuals with severe long-term traumatic brain injury on time-, event-, and activity-based prospective memory tasks. *Journal of Clinical and Experimental Neuropsychology, 21*, 49-58.
- Shum, D., Harris, D., & O’Gorman, J., G. (2000). Effects of severe traumatic brain injury on visual memory. *Journal of Clinical and Experimental Neuropsychology, 22*, 25-39.
- Shum, D., Ungvari, G. S., Tang, W., & Leung, J. P., 2004. Performance of schizophrenia patients on time-, event-, and activity-based prospective memory tasks. *Schizophrenia Bulletin. 30*, 693–701.
- Shum, D., Levin, H., & Chan, R. C. K. (2011). Prospective memory in patients with closed head injury: A review. *Neuropsychologia. 49*, 2156-2165.
- Smith, E. E., & Jonides, J. (1999). Storage and executive processes in the frontal lobes. *Science, 283*, 1657-1661.
- Smith, G., Della Sala, S., Logie, R. H., & Maylor, E. A. (2000). Prospective and

- retrospective memory in normal ageing and dementia: A questionnaire study. *Memory*, 8, 311–321.
- Smith, R. E. (2003). The cost of remembering to remember in event-based prospective memory: investigating the capacity demands of delayed intention performance. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 29, 347-361.
- Smith, A. Taylor, E. Lidzba, K., & Rubia, K. (2003). A right hemispheric frontocerebellar network for time discrimination of several hundreds of milliseconds. *NeuroImage*, 20, 344-350.
- Smith, R. E., & Bayen, U. J. (2004). A multinomial model of event-based prospective memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 30, 756–777.
- Smith, R. E. & Bayen, U. J. (2004). A multinomial model of event-based prospective memory. *Journal of Experimental Psychology: Learning, Memory and Cognition*, 30, 756-777.
- Spinnler, H. & Tognoni, G. (1987) (Eds). *Standardizzazione e taratura italiana di test neuropsicologici*. Masson Italia Periodici, Milano.
- Spreen, O., & Strauss, E. (1998). *A compendium of neuropsychological tests* (2nd ed.). New York: Oxford University Press.
- Stuss, D. T. & Benson, D. F. (1987). The frontal lobe in the control of cognition and memory. In E. Perecman (Eds.), *The frontal lobes revised* (pp. 141-158), Hillsdale, NJ: Lawrence Erlbaum Associates Inc.
- Stuss, D. T. (2011). Traumatic brain injury: relation to executive dysfunction and the frontal lobes. *Current Opinion in Neurology*, 24, 584–589.

- Szelag, E., Dreszer, J., Lewandowska, M., & Szymaszek, A. (2008). Neural representation of time and timing processes. In E. Kraft, B. Gyulas, & E. Pöppel (Eds.), *Neural Correlates of thinking* (pp. 2-15). Springer Verlag, Berlin.
- Tay, S. Y., Ang, B. T., Lau, X. Y., Meyyappan, A., & Collinson, S. L. (2010). Chronic impairment of prospective memory after mild traumatic brain injury. *Journal of Head Trauma, 27*, 77–83.
- Tinklenberg, J. R., Roth, W. T., & Koppell, B. S. (1976). Marijuana and ethanol: Differential effects on time perception, heart rate, and subjective response. *Psychopharmacology, 49*, 275-279.
- Titov, N. & Knight, R. G. (2000). A procedure for testing prospective remembering in persons with neurological impairment. *Brain Injury, 14*, 877-886.
- Titov, N. & Knight, R. G. (2001). A video-based procedure for the assessment of prospective memory. *Applied Cognitive Psychology, 15*, 61-83.
- Titov, N. & Knight, R. G. (2005). A computer-based procedure for assessing functional cognitive skills in patients with neurological injury: The virtual street. *Brain Injury, 19*, 315-322.
- Teasdale, G. & Jennett, B. (1974). Assessment of coma and impaired consciousness. A practical scale. *Lancet, 13*, 81-84.
- Terry, D., Dumas, S., Desai, S., & Wing, J. (2009). Dissociations between motor timing, motor coordination, and time perception after the administration of alcohol or caffeine. *Psychopharmacology*.
- Thomas, E. A. C. & Cantor, N. E. (1975). On the duality of simultaneous time and size perception. *Perception & Psychophysics, 18*, 44-48.

- Thompson, C., Henry, J. D., Rendell, P. G., Withall, A., & Brodaty, H. (2010). Prospective memory functions in mild cognitive impairment and early dementia. *Journal of the International Neuropsychological Society, 16*, 318-325.
- Tracy, J. I., Faro, S. H., Mohamed, F. B., Pinski, M., & Pinus, A. (2000). Functional location of a “time keeper” function separate from attentional resources and task strategy. *NeuroImage, 11*, 228-242.
- Tragellas, J. R., Davalos, D. B., & Rojas, D. C. (2006). Effect of task difficulty on the functional anatomy of temporal processing. *NeuroImage, 32*, 307-315.
- Treisman, M. (1963). Temporal discrimination and the indifference interval: Implications for a model of the “internal clock.” *Psychological Monographs, 77*(Whole no. 576).
- Tsal, Y., Shalev, L., & Mvorach, C. (2005). The diversity of attention deficits in ADHD: The prevalence of four cognitive factors in ADHD versus controls. *Journal of Learning Disabilities, 38*, 142-157.
- Vakil, E., Sherf, R., Hoffman, M., & Stern, M. (1998). Direct and indirect memory measures of temporal order and spatial location: Control versus closed-head injury participants. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology, 11*, 212–217.
- Vallesi, A., Binns, M. A., & Shallice, T. (2008). An effect of spatial–temporal association of response codes: Understanding the cognitive representations of time. *Cognition, 107*, 501-527.
- Vanneste, S., & Pouthas, V. (1999). Timing in aging: The role of attention. *Experimental and Aging Research, 25*, 49- 67.



- Wahl, O. F., & Sieg, D. (1980). Time-estimation among schizophrenics. *Perceptual and Motor Skills*, 50, 535–541.
- Wearden, J. H., Edwards, H., Fakhiri, M., & Percival, A. (1998). Why “sounds are judged longer than lights”: Application of a model of the internal clock in humans. *Quarterly Journal of Experimental Psychology*, 51B, 97-120.
- Wearden, J. H., Norton, R., Martin, S., & Montford-Bebb, O. (2007). Internal clock processes and the filled-duration illusion. *Journal of Experimental Psychology: Human Perception & Performance*, 33, 716-729.
- Wechsler, D. (1981), WAIS-R. Scala d'Intelligenza Wechsler per Adulti-Riveduta. Tr. it. O.S. Organizzazioni Speciali, Firenze 1997.
- West, R. L. (1988). Prospective memory and aging. In M. M. Gruneberg, P. E. Morris, & R. N. Sykes (Eds.), *Practical aspects of memory* (Vol. 2, pp. 119-125). Chichester, England: Wiley.
- West, R. L. (1996). An application of prefrontal cortex function theory to cognitive aging. *Psychological Bulletin*, 120, 272-292.
- West, R., McNerney, M. W., & Krauss, I. (2007). Impaired strategies monitoring as the locus of a focal prospective memory deficit. *Neurocase*, 13, 115-126.
- Wiener, M., Turkeltaub, P. E., & Coslett, H. B. (2009). Implicit timing activates the left inferior parietal cortex. *Neuropsychologia*, 48, 3967-3971.
- Will, C. M., Rendell, P. G., Ozgis, S., Pierson, J. M., Ong, B., & Henry, J. D. (2009). Cognitively impaired older adults exhibit comparable difficulties on naturalistic and laboratory prospective memory tasks. *Applied Cognitive Psychology*, 23, 804-812.

- Willcutt, E. G., Doyle, A. E., Nigg, J. T., Faraone, S. V., & Pennington, B. F. (2005). A meta-analytic review of the executive function theory of ADHD. *Biological Psychiatry*, *57*, 1336-1346.
- Wilkins, A. J. & Baddeley, A. D. (1978). Remembering to recall in everyday life: An approach to absent-mindedness. In M.M. Gruneberg, P.E. Morris & R. N. Sykes (Eds.), *Practical aspects of memory*. New York: Academy Press.
- Wilson, B.A., Cockburn, J.M. & Baddeley, A.D. (1985). *The Rivermead Behavioural Memory Test*. Bury St Edmunds: Thames Valley Test Co.
- Wilson, B. A., Cockburn, J., & Baddley, A. (1991). *The Rivermead Behavioural Memory Test* (2<sup>nd</sup> Eds.) Bury St Edmonds, UK: Thames Valley Test Company.
- Wilson, B. A., Cockburn, J., & Baddley, A. (1995). *The Rivermead Behavioural Memory Test*. Titchfield, UK: Thames Valley Test Co.
- Wilson, B. A., Alderman, N., Burgess, P. W., Emslie, H., & Evans, J. J. (1996). *Behavioural Assessment of the Dysexecutive Syndrome (BADS)*. Published by Thames Valley Test Company, 1996.
- Wilson, B. A., Emslie, H., Foley, J., Shiel, A., Watson, P., Hawkins, K., Groot, Y., & Evans, J. (2005). *The Cambridge Prospective Memory Test*, London: Harcourt.
- Winograd, E. (1988). Some observation of prospective remembering. In M. M. Gruneberg, P. M. Morris, & R. N. Skeys (Eds). *Practical aspects of memory* (Vol 1, pp. 348-353). Wiley: Chichester.
- Zakay, D. (1990). The evasive art of subjective time measurement: Some methodological dilemmas. In R.A. Block (Eds.), *Cognitive models of psychological time* (pp. 59-84). Hillsdale, NJ: Lawrence Erlbaum Associates Inc.
- Zakay, D. (1993). Time estimation methods - do they influence prospective duration

estimates? *Perception*, 22, 91-101.

Zakay, D., & Block, R.A. (1996). The role of attention in time estimation processes. In Pastor M. A., & Artieda J. (Eds.), *Time, Internal Clocks and Movement* (pp.143-164). Amsterdam: Elsevier/North Holland.

Zakay, D. & Block, R. A. (1997). Temporal cognition. *Current Directions in Psychological Science*, 6, 12-16.

Zakay, D. (1998). Attention allocation policy influences prospective timing. *Psychonomic Bulletin & Review*, 5, 114-118.

Zakay, D. & Block, R. A. (2004). Prospective and retrospective duration judgements: An executive controls perspective. *Acta Neurobiologiae Experimentalis*, 64, 319-328.

Zakay, D. & Diamant, I. (2011). The role of attentional functions in prospective timing. The 27<sup>th</sup> Annual Meeting of the International Society for Psychophysics, Raanana, Israel.

Zimmermann, P., & Fimm, B. (2002). Batteria di Test per l'esame dell'attenzione (TEA). Italian adaptation by: L. Pizzamiglio; P. Zoccolotti; P.A. Pittau. V. Fimm, Psychologische Testsysteme.