

Functional neuroimaging of dual task interference and divided attention

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Stockholm, 2002

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Abstract

It is known that human subjects cannot perform two reaction time (RT) tasks as efficiently as they would perform the constituent tasks individually. Increments of reaction times or error rates that occur when two RT tasks are performed nearly simultaneously is known as interference. The Neurophysiological mechanism or mechanisms behind this phenomenon has remained largely unexplored.

This thesis describes a series of experiments designed to investigate psychophysical and neurophysiological aspects of interference.

We psychophysically studied mechanisms behind how simple reaction times are prolonged when they are performed for stimuli presented with short inter-stimulus intervals. These psychophysical experiments were later examined with functional neuroimaging for putative neurophysiological mechanisms of interference, namely, occupancy of motor structures by a task, division of attention between sensory modalities, and effector assignment strategies. Thus, our findings are presented in a neurobiological framework to explain interference, in contrast to the previously existed psychological models.

We found that simple reaction time tasks, when performed in close succession, produce interference of several different patterns. Firstly, the reaction time to the second of a pair of stimuli increases linearly as a function of the inter-stimulus interval when it is below 400 ms. This RT increase is psychophysically separable from the increment of RT to the first of the stimuli pair, which occurs only when subjects divide attention between two sensory modalities. The increment in RT to the second stimulus could be due to strategies that the nervous system uses to specify effectors, in that when the effector can only be specified *a posteriori* to stimuli, there is a longer increment of RT than when the effector is specified *a priori*.

Corresponding to these psychophysical findings, we found that the motor tasks activate a nearly identical spatial extent in motor structures that include the primary motor cortex, supplementary and cingulate motor areas, basal ganglia and the ventral lateral and ventral anterior thalamic nuclei. When two reaction time tasks requiring motor control of two effectors must be near simultaneously controlled by a large proportion of neurons in these structures, this cannot be done, because the control of the effector to the first stimulus appears to occupy these neuronal populations for a finite length of time. When this happens, the response to the second stimulus is delayed, which is the behavioral outcome that indicates interference. We have demonstrated that the occupancy of motor structures lead to the activation of an additional cortical area located in the right inferior frontal gyrus, and that this activity is strongly correlated to the delay in the RT to the second stimulus (i. e., interference).

In addition, we found that division of attention prolongs the RT to the first stimulus and that this activates a set of brain regions that are located in the caudal superior frontal areas and intra-parietal areas bilaterally. These areas are anatomically dissociable from the activity in the motor structures.

The findings of these experiments have raised the need to reconcile the notion of computational parallel processing in the brain with the interference phenomena that occur under concurrent multitasking situations. Investigating these phenomena with specific neurophysiological hypotheses would, on the one hand, allow us to elucidate why the human brain is limited in certain aspects of its information processing capabilities, and on the other, provide organizing principles to understand how the brain works.

Preface

This thesis, like most doctoral theses, is the outcome of a decision that was made after many months of deliberation. And yet, over the past several years, I have not really been able to resolve whether I contemplated enough, before I embarked on this journey. In a sense however, the decision to come in to neuroscience research was an act of defiance, because I wanted an education beyond factual knowledge and rote learning. Perhaps then, long after I have forgotten everything that I learned, the inexorable test of time will indicate whether I acquired any education here as a doctoral student.

And so, I came here to Stockholm, half way across the world, and was plunged right in to the complicated business of mapping the human brain, without much assistance and supervision. In retrospect, I can see that this turned out to be a blessing. I learned mostly on my own. Along the way, I hope that have produced some new knowledge. Some of it is written in this thesis. It is my fervent hope that the work described here will serve the functions of a direction finder as well as that of a lighthouse. The former will hopefully help find new ways to further investigate the questions that I have attempted to investigate here. The latter will help avoid making the same mistakes -conceptual and otherwise- that I may have made during my formative years as a scientist. What the impact of the work that I have described here is difficult to say. Hopefully, it will generate more questions than the number of answers that it has provided.

I thank Prof. Per Roland for taking me under his wing as a graduate student. Through many an amorphous and seemingly meandering discussions, I have learned a great deal from him. It has been a great privilege and an honor to be one of his students.

A heartfelt 'thank you' is owed to all my subjects who patiently underwent all the extensive, tedious, and what they called 'extremely boring' experiments with and without the scanner. Without them, this work would not have come to be.

Several others helped my work over the years. Jeremy Young -my colleague, favorite Aussie, and fellow, but reluctant cigar-aficionado- deserves a special mentioning here, because he was the epitome of the best collaborator and colleague that I could ever have hoped for. The other fellow graduate students in the laboratory often helped me with sharp and engaging criticisms and fruitful discussions that occasionally helped formulate my thoughts. Grants from the Volvo Foundation of Sweden, and QLG 1999 00677, which is an EU project for the advancement of neuroinformatics, supported parts of the work described in this thesis.

Paul Manger, PhD, carefully proofread the manuscript of the part A of this thesis. Any remaining errors -both omissions and commissions- however, are mine alone.

I also wish to thank my parents for all the hardships that they underwent, all the sacrifices that they made in order to provide for my education. As I write this, I realize that they, along with all my former teachers, in many ways deserve my gratitude for the long journey that had taken me here.

Finally, I think that without Sagarika, my wife, friend and my life's companion, I could and would not ever have found the courage to complete this work. Life of a doctoral student, which is relentlessly involving and often endlessly protracted, inevitably takes its toll on those who are close to them. I am grateful to her for encouraging and supporting me over the many bleak years; holding me when I was down and ready to quit; and for loving me for what I am, despite all my faults. This work is a tribute to her love and is therefore fondly dedicated to her.

Priyantha Herath
Stockholm, May 2002.

On Learning...

“Do not believe in anything (simply) because you have heard it. Do not believe in traditions because they have been handed down for many generations.

Do not believe in anything because it is spoken and rumored by many.

Do not believe in anything (simply) because it is found written in your books.

Do not believe in anything merely on the authority of your teachers and elders.

But after observation and analysis when you find that anything agrees with reason and is conducive to the good and benefit of one and all then accept it and live up to it...”

-Buddha-

(Anguttara Nikaya, p. 188-193 P.T.S. Ed.)

Organization of the thesis

This thesis has two parts. Part A is a general introduction to the concepts and work described in the thesis, including comments on methodological issues. Part A also contains a discussion of the findings of work described in Part B that consists of papers and manuscripts that form the basis of the thesis. These include the following.

- Paper I Psychophysical outcomes of dual reaction time tasks leading to different neurophysiological hypotheses: investigating dual task interference (2002) Priyantha Herath, Per Roland (manuscript)
- Paper II Psychophysical outcomes of dual reaction time tasks leading to different neurophysiological hypotheses: investigating dual task interference (2001). Priyantha Herath, Torkel Klingberg, Jeremy Young, Katrin Amunts, Per Roland. *Cerebral Cortex* 11: 796-805
- Paper III Two mechanisms of protracted reaction times mediated by dissociable cortical networks (2002) Priyantha Herath, Jeremy Young, Per Roland (manuscript)
- Paper IV Visual Recognition: Evidence for Two Distinctive Mechanisms from a PET Study (2001) Priyantha Herath, Shigeo Kinomura, Per E. Roland. *Hum Brain Mapping* 12: 110-119

List of Abbreviations

ACC	Anterior cingulate cortex
BA	Broadmann Area
BOLD	Blood oxygen level dependant
CFH	Cortical Field Hypothesis
CMA	Cingulate motor area
DTI	Dual task interference
EEG	Electroencephalography
fMRI	Functional magnetic resonance imaging
ILTN	Intra-laminar thalamic nuclei
IPA	Intra-parietal area
IPS	Intra-parietal sulcus
ISI	Inter-stimulus interval
MBRF	Midbrain reticular formation
MRI	Magnetic resonance imaging
PET	Positron emission tomography
PRP	Psychological refractory period
rCBF	Regional cerebral blood flow
RIFG	Right inferior frontal gyrus
ROC	Receiver operating characteristic
RT1	Reaction time to the first stimulus of a pair
RT2	Reaction time to the second stimulus of a pair
SI	Primary somatosensory cortex
SII	Secondary somatosensory cortex
SMA	Supplementary motor area
Som	Somatosensory (stimuli)
S-R	Stimulus-response
STM	Short term memory
STMCOLDISTR	Short term memory task with color distractors
STMLTMDISTR	Short term memory task with long-term memory distractors
Vis	Visual (stimuli)
V-S ONE EFF	Vis/Som stimuli, both responded with same effector
V-S TWO EFF	Vis/Som stimuli, each responded with different effectors
WM	Working memory

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Part A

General Introduction

Over the course of the 3,800 million years since life began on earth, an incredible number of marvelous life forms have evolved. Most have vanished without a trace, but some continue to evolve to date. One such life form, the latter day *Homo sapiens*, claims that he has conquered the earth, although hominids have been in existence for only less than 4.3 million years. Be that as it is, humans have evolved in to something that other life forms apparently have not been able to. We are sentient beings. Although the question whether other living beings are sentient has been asked, at present we have no idea whether they are or not. All we know is that we are. How would evolution achieve this feat? In the case of *Homo sapiens*, the answer is a self-organizing assembly of cells. This is the human brain. In many ways it is very similar to many of the primate brains. It has some 100 billion cells, each cell signaling to as many as 10,000 others, giving combinatorial possibilities of gargantuan proportions. Yet, this collection of interconnected cell mass appears to have given rise to all the major differences between humans and the rest of the animal kingdom.

What does the brain do? The simple answer is that it processes information. How does the brain do this? At present, there is no exacting answer to this question. However, in the last century, particularly the last few decades, we have achieved a rudimentary understanding of how the brain does what it does. Someday, when we know how the brain processes information, it will in one way or the other answer nearly all questions about how we behave, how we think, how we feel, and how we judge and reason; and therefore who we are. Hence, it comes as no surprise that so many of us are trying to study the brain from a myriad of perspectives.

Given the complexity of the number of different kinds of tasks that can be performed by the brain, it is easier to study these tasks or functions separately, at least at the beginning, until we have some idea about how things work. To this end, numerous methods have been developed and adopted. At one end of the scheme of things, we study the molecules as well as the basic electrical properties of the neurons that are involved in signaling between neurons. At the other end of the spectrum, we use systems level connectivity studies, structural and functional imaging, and theoretical studies using computers that simulate different models of neuronal interactions. This whole scheme of studying the brain piece by piece using different methods has been likened to a blind man sampling an elephant.

Fortunately, this analogy is beginning to lose some of its validity, as the progress in science has achieved a remarkable degree of sophistication in our understanding of some elementary aspects of the brain in action. Meanwhile, human brain appears to be far more complex than we understand at present, and this will keep many more generations of human inquisitiveness deeply engaged in our own selves.

COGNITIVE SCIENCE AND THE BRAIN

Until the early 19th century, the study of the mind was almost exclusively confined to philosophical debates and introspection. The 19th century saw some of the most remarkable advances in the study of human behavior, and therefore, by extension, the brain. These changes came slowly, and were mostly subtle and conceptual in nature. By 1834, Weber had already worked out the basic principle behind what was later christened as the Weber's law of just noticeable difference, which describes the minimum amount by which stimulus intensity must be changed in order to produce a noticeable variation in sensory experience (Murray, 1978). By 1850, Helmholtz had written his treatise on physiological optics (Southall, 1925), and by 1860, the discipline of Psychophysics had been introduced (Fechner, 1860). Thus, by the time the American psychologist William James wrote in perhaps the most widely cited textbook in the history of psychology, that "psychology is the science of mental life, both of its phenomena and their conditions" (James, 1890), the emphasis of psychology in studying phenomena as the science of mental life had already shifted to being a science of studying overt actions. By the 20th century, the objective study of human behavior had come to stay, and in 1906, Jennings wrote that the "conscious aspect of behavior is undoubtedly the most interesting" (Jennings, 1906). In the same treatise, Jennings asserted that introspective investigations of acts themselves are an unworkable methodology for objective science. That assertion remains valid to date. The objective alternative to the introspective study of mind became the study of behavior, and has been called behaviorism. Although this way of studying the functions of the brain has provided a large body of knowledge, until recently, such knowledge has remained in the domain of psychology, confined to the development of metaphorical descriptions and abstract constructs to explain behaviors. This is in contrast to another branch of the natural sciences that was rapidly emerging in the last century, which is the study of the physiology of the cells that comprise the nervous system. It is only recently that these two disparate branches of the study of the brain and mind have made serious attempts to merge. The resultant discipline is now called cognitive science. The main purpose of this branch of science is and ought to be, to answer the fundamental philosophical questions about the nature of knowledge through empirical means, and to find functional correlates (logically, as in 'when A occurs, B occurs' or vice versa) of these within the confines of the hundred billion neurons that constitute the human brain. Thus, it can be said that cognitive science is the science of the mind, encompassing any and all domains that will allow us to understand how the brain processes information. This trend has been extolled recently as "progress beyond mindless neuroscience and brainless psychology" (Bunge, 1980).

INFORMATION PROCESSING

What is information? To a first approximation, it appears to have a complicated meaning. Often, information can be thought of as that which forms within, but perhaps more adequately, the equivalent of or the capacity of something to perform organizational work. Similarly, it could be intuitively understood as the difference between two forms of organization or between two states of uncertainty before and after a message has been received. However, information may be more formally clarified as the degree to which one variable of a system depends on, or is constrained by another (Wilson and Keil, 1999). Many examples illustrate this concept: DNA carries genetic “information” inasmuch as it organizes or controls the orderly growth of a living organism. A message carries “information” inasmuch as it conveys something not already known by the recipient. The answer to a question carries information to the extent that it reduces the questioner’s uncertainty. A fiber optic cable carries information only when the signals sent correlate with those received. Since information is linked to certain changes, differences or dependencies, it is desirable to refer to these and distinguish between information stored, information carried, information transmitted, information required, etc. Clearly therefore, reference to pure and unqualified information is an unwarranted abstraction. These ideas were formally introduced in 1948 by Claude Shannon, when he introduced what is now called “information theory” (Shannon, 1948). This branch of scientific study of information allows measurement of quantities of all kinds of information in terms of bits, and describes the fundamental relationship between input and output with respect to information exchange. Information theory therefore also formally defines the properties of carriers of information (symbols). The larger the uncertainty removed by a message, the stronger the correlation between the input and output of a communication channel, the more detailed particular instructions are, and the more information transmitted. However, it must be noted that even the information theory itself, with all its aesthetic beauty and the forceful formal definitions, have not been entirely capable of dealing with the elusive end product of communication – information (Abramson, 1963).

What happens to the information when it is transmitted? It is clear that there must be an input and an output. What happens at the transition? What are the physical phenomena that occur at the interface where the input is transformed in to the output by removing some degree of uncertainty of the input? For many years, questions about the input-output information transformation went unasked, a tradition that has been somewhat accentuated by references to the brain as a computer (Rumelhart et al., 1986).

Computers, which are mechanical devices for drawing conclusions from typically elaborate premises. They are used, among many other purposes, for solving complex problems when the parameters are known, for aggregating data, and for simulation or control of systems. Because all computational tasks involve information, computers are often called information processors. It is in this context that the human brain is often thought of as a computer (Haugeland, 1988). There are several fundamental reasons as to why this analogy is thought to be apt. Firstly, it is assumed that the most characteristic and therefore defining function of neuronal systems is representation. That is, brain states represent states of some system –outside world or the body itself, using information-, where the transitions between the states can be explained as computational operations on representations. The

second is based on the assumption that it is possible to define the computability of representations based on a highly abstract mathematical domain. This latter concept led to the familiar and the catholic abstraction of the Church-Turing Universal Machine (Church, 1936; Turing, 1936)

Church-Turing machine, which is more commonly known only as the Turing machine, is a conceptual abstraction that says that any function that is adequately well defined can be executed step-by-step, with simple 'if in state X and when input Y is received, then do Z' type of rules. In essence, then, a Turing machine is a device that obeys a set of rules in a finite number of steps in order to accomplish something on an input, giving rise to an output. Given that the brain receives information, and processes it (albeit in a manner that we still do not understand), the nervous system can therefore be reasonably approximated to a (highly complex) input-output device. Because of this, what happens in the brain may be characterized in terms of some mathematical function, thus achieving the status of a Church-Turing machine. The conceptual similarity of the brain and a Turing machine offers many advantages in studying how the brain works. For instance, in a very simplified scheme, neurons can be thought of as signaling to each other by simply indicating states of "on" and "off". This is equivalent to "1" and "0" of a binary computer. Using this analogy, it is now possible to simulate fairly complex artificial neural networks, which may someday allow us to understand the basic underpinnings of how memories are made and so on. However, there are several critical issues that must be kept in mind when the brain is approximated to a Turing machine. First and foremost, the computer analogy of the brain is not ontologically committed. This means that, as it stands today, the description of the brain as a computer does not describe the existence of the brain in any biological sense (Roland, 1994). It has been said that the 'computer is not a model of the brain, and explanations that assume it is are actively dangerous and pernicious for the progress of neuroscience (Kirsh, 1993). Secondly, thinking of the brain as a Turing machine does not reveal anything about the internal workings of the machine (or the brain) itself. This is because, as has been shown clearly, there is no way to obtain an absolute answer to the internal states of the universal machine, other than by directly examining the machine's internal states (Church, 1936; Turing, 1936). Thirdly, all Turing machines run on recursive sets of instructions (Church, 1936; Turing, 1936). Otherwise, they will never get to the issue of operating on information that is input. What this means is that however complex, Turing machines are finite entities, that simply obey algorithmic laws. Whether the brain's internal states can ever be completely resolved, whether neuronal populations work according to algorithms and whether the brain, despite its immense computational complexity is still a finite entity, are perhaps the most fundamental questions that remain to be answered by modern day neuroscience. Recent methodological progress in neuroscience may someday allow us to answer the first question. The work presented in this thesis may help answer the latter.

INTERFERENCE

Life of a human being is complicated. Often, one must perform several concurrent tasks, each of which may be detrimental to several aspects of life itself or how a person's life is organized. An example is driving a car while trying to talk on a wireless phone, or, manually piloting an airplane that has several dozen independent subsystems that need to be simultaneously read-off and operated. Each

component of these tasks has its own set of stimuli, stimulus-response associations and a whole set of behavioral repertoire associated with it. The ability to efficiently deal with these maneuvers depends on how information is processed and coordinated across tasks. Success or failure of this co-ordination may have significant consequences in many real world circumstances. Therefore, it comes as no surprise that over the past many decades, a great deal of intellectual curiosity and fascination has been devoted to the study of human behaviors involving concurrent multiple task performance.

A by-product of this fascination was the observation that sometimes the brain cannot perform two simultaneous tasks as efficiently as it performs one task at a time. Although the earliest references to the problem of multiple task performance go back to the classical Greek period (see Neumann, 1987), it was T.W. Telford who in 1931 reported the first psychophysical investigation on human dual reaction time task performance using simple auditory reaction time tasks (Telford, 1931). He showed that when people perform rapid successive reaction time tasks for two auditory stimuli presented in rapid and close succession, the reaction time to the second auditory stimulus is significantly prolonged as compared to each of the RT tasks that are performed individually. Telford called this phenomenon the psychological refractory period (PRP). Summarizing the seminal work of Telford, as well as her own, Margaret Vince wrote in 1949 that “the human being can therefore not be expected to deal adequately with a series of stimuli requiring discrete responses unless the stimuli are spaced at intervals of at least 0.5 seconds” (Vince, 1949).

Since then, numerous variations of dual reaction time (RT) task experiments have been reported in the scientific literature (Welford, 1952; Pashler, 1994; Meyer and Kieras, 1997; Parasuraman, 1998; Pashler, 1999). What is notable is that the search for exceptions for the psychological refractory period has in general been unsuccessful. The only report that suggested that there might be exceptions to the PRP induced reaction time delays (Brebner, 1977) has not been replicated, and its methodology has been criticized (Pashler, 1999). On the other hand, there are several psychophysical reports that suggest that extensive practice can reduce some of the PRP induced reaction time delays (Parasuraman, 1998; Van Selst et al., 1999; Ruthruff et al., 2001). However, results unequivocally showing that it is possible to completely eliminate the delays do not exist in the literature. So wide has been the gamut of empirical dual task experiments that have been performed that it is now generally accepted that the PRP effect is a universal phenomenon that generalizes across nearly all combinations of task pairs and response requirements.

In present day neurophysiological literature, the performance decrement that can be quantified in dual task experiments in terms of increased RT, and / or increased error rates to the second stimulus is known as dual task interference (DTI) (Herath et al., 2001). However, there is some degree of confusion and clutter in the nomenclature dealing with interference. Firstly, this is because many different types of interference have been described. The most common type of interference referred to in the literature is the classical PRP effect. Within a few years of the introduction of the PRP phenomenon, Stroop (1935) wrote his seminal paper describing what is commonly known as “Stroop interference” (Stroop, 1935). In the recent years, there have been references to proactive (Randolph et al., 1992; O’Carroll et al., 1993; Uhl et al., 1994) and retroactive (Tendolkar et al., 1997) interference. By definition, proactive interference results from information given prior to the task that is to be performed. Retroactive interference on the

other hand is claimed to occur due to information that follows the task that must be performed. Similarly, a concept of 'central interference' involving as yet undefined 'executive functions', as opposed to early, stimulus level interference and reference to interference of cognitive type has appeared in the recent literature (Grachev et al., 2001). Although there are behavioral similarities among all these interference phenomena, in that they all produce reaction time delays, or increased error rates as compared to respective baseline tasks, it has become increasingly difficult to conjoin these in a cohesive discussion because of this confusing nomenclature.

Despite the confusion in nomenclature and classification of the phenomenon itself, the fact that behaviorally observable interference occurs between tasks when two tasks are to be performed near simultaneously is not in doubt any more. With this, the debate has shifted over the years to finding the locus or loci of the interference. Yet another focus that kept numerous researchers busy was to produce what has been called cognitive models that will fit the empirical observations of interference. The idea was to explain how interference occurs when two sets of information are being processed concurrently. Not surprisingly, there has been great enthusiasm in producing different types of "cognitive models" to explain the psychological refractory period (PRP) effect and interference. Telford gets the credit for proposing what can be claimed the first ever "explanation" for interference (Telford, 1931). He proposed that interference is due to a mechanism akin to the electrical refractoriness that has long been observed in stimulated nerve-muscle preparations. Welford proposed that the PRP effect is due to the temporal overlap of what he calls 'organizing times' for tasks when such overlap may cause "the information arriving from a stimulus be 'held in store' until the central mechanisms are free" while information from a preceding stimulus is being dealt with (Welford, 1952). He thus laid the foundation to all the successive psychological models that attempted to explain the mechanism of interference. These models include the single channel hypothesis (Telford, 1931; Welford, 1952), perceptual bottle neck models, including early and late filter theories (Broadbent, 1965), response selection bottle neck models (Pashler, 1994), movement production bottle neck models (Karlin and Kastenbaum, 1968; Keele and Neill, 1978), unitary resources theory (Kahneman, 1973; Wickens, 1991), multiple resources theory (Navon and Gopher, 1979; McLeod and Posner, 1984), theory of functional cerebral distance (Kinsbourne and Hicks, 1978) and more recently what has been described as a cognitive architectural model (Meyer et al., 1995; Meyer and Kieras, 1997). Detailed descriptions of these models and theories will not be provided here. Briefly, however, it must be mentioned that although these models are becoming increasingly complex, none has so far been able to explain interference on a reasonable neurophysiological basis.

Regardless of the immense progress that has been made in the scientific study of the brain and the nervous system over the past decades, our inability to explain interference and many other functions of the brain at present has been attributed to a number of conceptual and scientific obstacles (Roland, 1994). Some of these impediments are due to a number of philosophical positions, including the failure to distinguish between models and non-models, lack of ontological (ontology: a branch of metaphysics concerned with the nature and relations of being) commitment in the models that have been proposed, and constraints of the scientific vocabulary (Pylyshyn, 1986). Of these, the issue of metaphors is particularly important to the present discussion. For instance, the concept of a bottleneck, although

intuitively accessible to almost anyone with a little imagination, is very unlikely to be ontologically committed to the physiology of the neurons. Similarly, whereas a neurophysiological model must contain a simplified description of the part of the nervous system under study, and must accurately portray the cardinal properties of architecture, function, physiology and biochemistry and so on, the previously mentioned psychological models do not conform to these requirements of a model (Kirsh, 1993). These models thereby lose their usefulness in our understanding of how the brain works or how interference occurs. On the other hand, lack of investigative methods to adequately describe neuronal network activity and their properties, and our inability at present to impose information processing constraints and informational requirements on models of brain processes, has also hindered progress in our understanding of how the brain works.

Despite these limitations, there has been a re-emergence of interest in the neurophysiology of dual task performance and interference that coincided with the fascinating advances that had been made in the field of human functional brain imaging. As it is now possible to observe the physiological changes involved during clearly and empirically defined human behaviors with the use of modern functional imaging methods, this emerging interest is particularly opportune. Using methodologies such as PET and fMRI, several dual task brain-imaging studies have been reported (see below for a detailed review of these experiments).

ON FUNCTIONAL ORGANIZATION OF THE HUMAN BRAIN AND THE CORTICAL FIELD HYPOTHESIS

Since the 19th century, there had been many attempts to understand how the human cerebral cortex is functionally organized. The earliest discussions on this issue were spurred by Gall and Spurzhein (see Ackerknecht, 1956) when they declared that the human brain is organized to perform approximately 35 specific functions. From these early beginnings of anatomical phrenology, the conceptual journey moved hither and thither between notions where the whole brain was supposed to work in concert to produce behaviors, to the work of Hughlings Jackson who first introduced the concept of topographic organization, and later, for Broca's and Wernicke's description of focal lesions causing specific deficits. These concepts paved the way to the cytoarchitectonic maps of Brodmann that described 55 cortical areas (Brodmann, 1909), Vogt that described approximately 200 cortical areas (Vogt and Vogt, 1926), Von Economo (1925) and many others that are still widely used today. More recently, the organization of the cortex was shown to be columnar, in that neurons with similar response properties tended to be grouped in vertical columns that have a diameter of 0.5-1.0 mm (Mountcastle, 1957; Hubel and Wiesel, 1977; Mountcastle, 1997). Later, with the finding of cytochrome oxidase staining of the cortex that show punctate regions with strikingly regular spacing (Horton, 1984), it is now widely thought that the cortex is organized in a modular fashion. Recently however, this concept has been criticized because of several reasons. First, there is no way to unambiguously define the boundaries of the modules (which by definition are discrete entities) and also because it has not yet been possible to show that the connectivity within a module is different from the surrounding modules, a property expected of discrete entities. For these reasons, it has been argued that, at least in

the case of the visual system, a given cortical area is organized as a number of superimposed maps, each representing different stimulus attributes (Swindale, 1998). Along these lines, it has been claimed that the visual “cortex is composed of mosaics of functional domains for the different properties” (Hubener et al., 1997). Another conceptual framework for the functional cortical organization that has been discussed recently is the cortical field hypothesis (Roland, 1993; Roland and Zilles, 1998). Many recent empirical studies have shown that there are large depolarization fields that spread horizontally in cortical layers II and III during all types of sensory and motor functions (Sawaguchi, 1994; Kleinfeld and Delaney, 1996; Horikawa et al., 1998; de Curtis et al., 1999; Roland, 2002a). These depolarization fields that cover a few square millimeters, emerge and rapidly spread across sub-columnar levels of spatial resolutions (100-200 μm) and decay within a few hundreds of milliseconds while being surrounded by the back ground activity (Roland, 2002a). The depolarization fields do not obey the columnar organization of the cerebral cortex. Moreover, the individual columns can only be engaged in computations that are strictly limited to one particular aspect of a stimulus. In other words, patches and columns are not active in isolation. On the other hand, it is necessary to compute many aspects of a stimulus in order to obtain a cohesive representation of a stimulus. The only way to accomplish this would be to use large populations of neurons that far exceed the combinatorial possibilities of a column. As such, depolarization fields that characterize cortical fields (i.e., the domain of the neurons that locally depolarize in supra-granular layers) have been proposed as the computational unit of the brain (Roland, 2002b). The cortical field model therefore is an alternative to the columnar organization of the cerebral cortex.

The cortical field hypothesis (CFH) proposes that if two different brain tasks make use of the same cortical fields, the tasks cannot be performed simultaneously. This is a testable neurophysiological/neuroanatomical hypothesis that obviates the need for metaphors and analogies to explain the mechanism of DTI. From a neurophysiological point of view, there is now ample evidence to show that the human brain engages in computations and information processing by producing dynamically organized neuronal populations behaving in a cooperative fashion (Sanes and Donoghue, 2000). A cooperatively organized dynamic neuronal field computing a particular task lasts a few hundred milliseconds. It has been postulated that such dynamic fields decay and reorganize giving rise to newer fields depending on the computational requirements of the tasks being performed (Roland, 2002a). The logical outcome of cooperative computations occurring across dynamically organized neural populations would be that two different brain tasks, A, and B, requiring the participation of one or more major overlapping fields, cannot be performed simultaneously. The consequence of trying to perform tasks A and B simultaneously under such circumstances would result in increased reaction times and/or error rates. This is the interference principle of the CFH. Investigating interference phenomena along a specific neural hypothesis enables one to discern the exact nature and underpinnings of the mechanisms of dual task interference and even the reasons for limitations of attention. More importantly, hypotheses such as the CFH would provide useful organizing principles to study and understand how the brain works.

NEUROIMAGING OF INTERFERENCE

STROOP INTERFERENCE

In 1935 Stroop described a study in which “pairs of conflicting stimuli, both being inherent aspects of the same symbols” were presented simultaneously (Stroop, 1935). He found that “the difference in time for reading the words printed in colors and the same words printed in black is the measure of the interference of color stimuli upon reading words”. In other words, when the name of the color is incongruent with the color of the ink that is used to print the word (red in black ink), time required to read such words aloud are longer than when red is printed in red color. Over the years, the Stroop task and many of its variations remained among the most commonly investigated behavioral tasks in relation to the study of interference. The intensity of these investigations is only paralleled by the number of hypotheses that have been advanced to explain the word-color incongruity dependent interference (RT increase). It has been proposed that the Stroop interference results from *conflicts in perceptual encoding* (Hock and Egeth, 1970). These authors claimed that red color stimulus, for example, may “somehow conflicts with the written word ‘black’ stimulus” in the early stages of information processing. Another hypothesis claims that interference occurs as a result of *response competition* (Morton and Chambers., 1973; Posner and Snyder, 1975). According to this claim, processing of information for color naming and simultaneous word reading results in a “horse race of the two stimuli, each along one of two separate parallel pathways to a single, limited-capacity (verbal) response channel”. According to the authors, “the faster horse, [sic] or the stimulus belonging to a faster information-processing pathway, will win the race to the “response bottleneck”, although, they did not clarify why the information processing may be faster in one stream than in the other. Other authors claimed that interference effects may result from the greater “*automaticity*” of reading compared with color naming (Posner and Snyder, 1975; McLeod and Posner, 1984), although, once again, no explicit claims about how one task may be “more automatic” than the other has been made. More recently, it has been suggested that the Stroop interference may represent an *inherent property of parallel distributed processing systems* (Cohen et al., 1990). The difficulty with this theory is that it is difficult to understand why an inherently parallel process must have inherent limitations.

Therefore, despite the intensive study of word-color interference, the neural mechanisms behind it remain patently obscure. Anatomically, a number of lesion studies have suggested that left frontal lobe lesions slow down the task performance (Perret, 1974), and that lesions in the right lateral prefrontal cortex contribute to a greater number of response errors (Vendrell et al., 1995). Furthermore, several accounts of functional neuroimaging studies have shown increased activation of numerous brain regions that included the anterior cingulate cortex during performance of the Stroop task. These studies discussed the said activations in the context of how these particular brain areas may be involved in conflict monitoring, error detection and ‘online monitoring of performance’ (Pardo et al., 1990; Bench et al., 1993; George et al., 1994; Larrue et al., 1994; Taylor et al., 1994; Carter et al., 1995).

However, as will be discussed in detail later, none of these reports addressed the possible mechanisms that lead to the interference (increased RT) when word-color incongruity is to be responded to.

A more recent claim is that the process of perceiving the color of a stimulus, reading out the name, and naming it, share a number of cortical fields in several brain areas. These include a number of visual areas, the human middle temporal cortex, Broca's area 44 and several of the cortical motor areas. Therefore, it is possible to view the Stroop interference as a concurrent reading and naming process that attempts to share cortical fields. Based on this argument, it has been argued that Stroop interference maybe explained on the basis of the cortical field hypothesis (P.E. Roland 2002, Personal Communication).

DUAL TASKS THAT INTERFERE

Interference, as a phenomenon that generically demonstrates limitations of information processing in the brain, has sparsely been reported in neuroimaging literature. On the other hand, several factors have diminished the value of the few imaging experiments that have been published and prevented their findings from being conclusive or particularly illuminating from a physiological point of view. Firstly, some of the early reports on the brain activity elicited by interference were reported as by-products, or almost as afterthoughts of experiments designed to study other behavioral tasks. This prevented dual task interference (DTI) from receiving the depth and critical analysis it deserved. Secondly, many of the recent imaging experiments contextualized their findings based on remnants of psychological metaphors such as "resource allocation models" (Bunge et al., 2000). Others introduced concepts such as "interference over the premotor cortex" (Passingham, 1996) which are difficult to be precisely understood in physiological terms, or "interference manipulations" (Bunge et al., 2001), even as interference itself has never been physiologically characterized. As was discussed earlier, these descriptions are not ontologically committed to the phenomenon of interference, nor are they amenable to experimentations based on current knowledge and methodologies. Consequently, although, a majority of the hitherto reported findings enabled labeling of cortical regions purportedly associated with DTI, the experiments lacked clearly defined neurophysiological and neuroanatomical hypotheses that explain the mechanism of DTI, despite the importance of labeling cortical areas involved in dual task performance. Furthermore, because complex behavioral paradigms were used in these experiments, it is difficult to draw simple physiological principles from their findings. Equally importantly, the investigators who performed these experiments have not reported adequately on direct intersections of brain activations between single tasks that then comprised the dual tasks that were investigated. Despite the aforementioned limitations however, these studies have now paved the way to a more systematic investigation of interference.

The first such imaging study of interference in fact investigated the neural basis of what the authors claimed to be the "central executive" of working memory system (D'Esposito et al., 1995). In this experiment, subjects were engaged in two concurrent working memory tasks performed while being imaged with fMRI. The authors hypothesized that the dorso-lateral prefrontal cortex is involved

in dual task performance. Using a semantic judgment task and a spatial rotation task concurrently during imaging, they found that the dorsal-lateral prefrontal cortex and several other frontal areas located in the BA9, BA 46 and anterior cingulate cortex are significantly more active only when the two tasks were performed simultaneously. The authors concluded that their findings suggest that some of these neural substrates may underlie working memory and its “central executive system”. Although they had no way of physiologically defining, explaining or examining the central executive system using their study design or the findings, an important concept emerged from the findings of this study. This was, that the different simultaneous “operations” that produce spatially overlapping activations in the brain can lead to interference (increased errors). Around this time, Passingham (1996) reported an attempt to distinguish between those actions that people attend to and those that the subjects were not required to attend to. He used a series of PET studies that independently examined brain activations associated with learning of motor skills, or brain activation associated with verb generation for this purpose (Passingham, 1996). It was shown that new motor skill learning is associated with increased regional cerebral blood flow in the prefrontal cortex and the anterior cingulate cortex. However, once the tasks are well learned (i.e., “ become [sic] automatic”), these activations do not appear under the scanning conditions. Subjects engaged in a verb generation task also activated the same parts of the prefrontal cortex, in addition to the Broca’s area. The author psychophysically investigated interference, by studying concurrent performance of a sequential finger-tapping task while subjects were also engaged in a verbal task. Concurrent performance of these two tasks showed increased RT and increased errors. Combining these findings, Passingham (1996) suggested that interference can occur if both tasks engage the same perceptual or motor systems. Sequential finger tapping engages the lateral premotor cortex and the primary motor cortex hand area while word production engages the frontal operculum and the face area of the motor cortex. This led to the claim that interference occurs centrally, in the frontal cortex, which includes the cingulate cortex. It was claimed that this is because sequential finger tapping task learning, as well as verb generation, makes demands on the frontal lobe simultaneously. The overall conclusion therefore was that interference can occur if two tasks engage a common area, although at that point, this hypothesis was not explicitly tested.

A similar approach was also undertaken by other authors (Klingberg and Roland, 1997; Klingberg, 1998). They used a number of working memory tasks independently scanned with PET, and several psychophysical experiments, to show that performance of visual, somatosensory or auditory working memory tasks individually activate a similar set of cortical areas that include the left inferior frontal gyrus, the right superior frontal gyrus, the left frontal operculum, the right supra-marginal gyrus, and the right anterior cingulate cortex. Based on these findings the authors predicted that performing two working memory tasks near simultaneously would cause interference. This prediction could be confirmed psychophysically. In the dual working memory (WM) task, a visual and an auditory WM task that were separated by more than 1000 ms were concurrently performed by the subjects. (This design prevented motor responses to the WM tasks being performed within 400 ms, a feature that would become an important consideration in the design of the paradigms that formed the present thesis.) The authors found that performance of the two WM tasks simultaneously did not activate additional cortical areas other than the sum total of the areas that were activated by the single

WM tasks. Thus, the authors could not find any areas “ which could be associated with dual task specific cognitive-operations such as task co-ordination or divided attention”. Once again, the overall conclusion from these studies was that two tasks that would near simultaneously address the same cortical areas do interfere. On the other hand, authors had failed to consider the likelihood that each WM task occupy, among others, large volumes in the right inferior frontal cortex, which turned out to be specifically associated with interference in dual RT tasks. As both WM tasks activated nearly the same cortical areas, the Klingberg et al (1997, 1998) did not find brain regions that are associated with interference.

In a study reported in 1998, subjects were involved in a Wisconsin Card Sorting Test (WCST) and a complex reasoning task involving working memory (Goldberg et al., 1998). The authors found that when subjects were performing the two tasks simultaneously, there was increased regional cerebral blood flow in several prefrontal areas including the right middle frontal gyrus and several other cortical areas. This finding confirmed and extended previously reported findings (D’Esposito et al., 1995). The single tasks themselves activated most of these areas. However, there was a significant attenuation of the activity in the prefrontal cortex as compared to the situation where the tasks were performed separately. The authors concluded that “increases in cognitive workload does not necessarily recruit and then sustain cortical neurophysiological resources, but rather may actually be accompanied by a diminution of cortical activity”. They discussed this conclusion on the basis of a limited central executive that is located in the prefrontal cortex, claiming that a reduction of activation in the prefrontal cortical activity, and hence a limited central executive is associated with declines in task performance (interference).

D’Esposito et al (1999) reported a study on “neural substrate and temporal dynamics of interference effects”. Using letter probes as stimuli in what they called recent negative probe task, and non-recent negative probe task, the authors showed that, as compared to non-recent negative trials, RT in the recent negative trials were slower (interference). Related to this, there was an increased BOLD signal in an area that was located in the ventro-lateral inferior frontal gyrus. This was attributed to a mechanism involved in what the authors called “interference resolution, because it’s fMRI and behavioral profiles are consistent with a mechanism that would detect and resolve the conflicting signals...” However, despite this claim, the interference (i.e., increased RT) caused by the recent negative probes remained behaviorally, and could not be accounted for by the interference resolution mechanism proposed by the authors.

Around this time, study designs for dual task imaging studies gradually became quite complicated, as is exemplified by the tasks used in the fMRI experiment that investigated neural correlates of what was called a “branching task” (Koechlin et al., 1999). Subjects were engaged in a number of tasks that were called (a) delay, (b) dual task, (c) branching and (d) a control task. The stimuli were letter strings that were presented with inter-stimulus interval of 3000 ms. Although the main purpose of this study was to examine the importance of the fronto-polar prefrontal cortex in the context of how the brain engages in a task with instructions that branches from one to the other , the dual task main effect revealed increased activity in the posterior dorsolateral prefrontal cortex (Brodmann Area 9) and the lateral parietal cortex near the intra-parietal cortex bilaterally. In effect,

the authors did not find additional cortical areas that are specific to interference. Their conclusion with regard to these findings ran along the possibility that these brain areas are involved in the “allocation of ‘attentional resources’ between successively alternating stimuli” and as such offered no insights on how the performance of two tasks brings about interference from a neurophysiological point of view.

The study by Dove et al (2000) too did not explicitly investigated interference, but addressed the question of the neural correlates of what they called “executive control involved in switch costs” when subjects alternate back and forth between two tasks. They found that when subjects are involved in switching between symbolic stimuli there was bilateral activity in the posterior prefrontal areas, the thalami and several other areas including the left intra-parietal area. Although the authors claimed that their switch condition had “high interference because the same stimulus dimensions were relevant for both tasks” this contention was not explicitly tested. Their overall conclusion was limited to the possibility that the lateral prefrontal cortex is somehow “involved in executive control, although not exclusively so”.

Functional anatomy of “attentional resources”, the “supervisory attentional system” and the “central executive” was the theme of a study reported by Adcock et al (2000). Tasks in the experiments reported in this study included faces that had to be identified, and verbal categorization. The dual-single contrast included significantly increased activity in the intra-parietal sulcus (IPS), the middle frontal gyrus and the inferior frontal gyrus. However, as in the studies mentioned above, these areas were also activated by the single tasks themselves. The authors claimed that the increased activity seen in the dual-single contrast can be “parsimoniously accounted for by the additive effects of component task activations”. Interference specific activity could not be explicitly tested because the study design did not allow the authors to do so.

Further investigations in to the central executive was reported by Bunge et al (2000). They claimed that the working memory (WM) task that they used in the study was specifically designed to measure “executive WM”. Combined with a sentence-reading task, they utilized a very complicated experimental paradigm. The response times were slower in the dual task situation (interference), although the accuracy levels were similar to what was observed in the single tasks. Sentence reading, the WM task, and the combined dual task all activated the left inferior frontal gyrus, right middle frontal gyrus, left superior frontal gyrus, and precuneus. The authors claimed however that “the dual tasks activated the frontal cortex to a greater extent than the performance of either task in isolation”, and that dual task performance is not associated with increased activity in additional brain areas over and above what was already activated by the individual tasks. The authors then claimed that this finding is supportive of what they call a resource model [sic] “whereby demands of dual task performance are met by increased activation in brain regions that subserve performance of component tasks”.

In a recent paper that claimed that “limitations on the concurrent performance of two unrelated tasks challenge the tacitly assumed the independence of two brain systems that seemingly have little overlap”, interference was examined by using two cognitive tasks that involve largely non overlapping brain regions in the respective sensory and association cortices (Just et al., 2001). The authors tested the hypothesis that the dual tasks would activate brain regions that would approximate the conjunction of the areas that are activated by the single tasks. However, they found that the BOLD signal during

their dual task reflected substantially less brain activity in the temporal and parietal association areas, as well as the sensory areas than the mathematical conjunction of the activity between the two single tasks. These findings were discussed in the light of putative biological constraints such as metabolic processes, neurotransmitter and neuro-modulator functions. Unfortunately, the authors did not explicitly demonstrate in their analysis how the activations of the single tasks would intersect. Such an analysis would have enabled them to predict the brain activations of the dual tasks that they investigated were in fact spatially non-overlapping. On the other hand, the authors claimed that the dual task related decreased BOLD signal may reflect some aspect of limited attention. They also embarked on a discussion on the possibility that the BOLD signal of a dual task that uses the same cortical areas may be less than the conjunction of the single task related BOLD signals from the same areas simply because of the non linear nature of the BOLD signal (Friston et al., 2000). However, although theoretically interesting, they did not extend the discussions to the biological mechanism behind this non-linear BOLD signal that is less than the sum of its constituents.

In summary, there are only a few dual task paradigms that have been investigated with functional brain imaging methods. The tasks used in these experiments were often rather complex, and included WCST, reasoning, hierarchical WM paradigms, task switching of symbolic information, semantic tasks, and long term memory tasks. While the stimuli and the behavioral paradigms were very complex and different from each other, the studies themselves either addressed the issue of interference from various psychological points of view or addressed it physiologically only peripherally. Yet, remarkably, the caudal prefrontal cortices, IPA, ventral premotor cortex including area 44 (Broca's area), and several other areas such as the cingulate cortex were significantly active during concurrent task performance in all these reports. All the reported tasks psychophysically demonstrated interference in terms of increased RT or increased errors when performed near simultaneously. Except for D'esposito who showed additional cortical areas that are associated with dual task conditions that interfere, many studies showed that the cortical activity associated with dual task performance is the sum total of the activity associated with the individual single task conditions that were investigated. On the other hand, at least two studies (Goldberg et al., 1998; Just et al., 2001) showed an absolute attenuation of prefrontal activity associated with dual task performance. Thus, the studies so far reported have generated some incongruent results, as well as a number of unanswered questions concerning the neural correlates of interference and its mechanisms.

ATTENTION... DIVIDED?

Humans engage in what is called attending to the tasks, when faced with the need to perform a particular mental operation -be it perceiving a stimulus, responding to a stimulus, or engaging in an abstract logical operation- under conscious control. Intuitively, it is clear that we may not be able to perform many of the tasks that we routinely perform if we did not have the ability to pay attention to the things that we do. On most occasions, our attention is focused. On other occasions, by the very nature of the task that needs to be performed, attention has to be divided between two tasks (Braun,

1998). This is a *sine qua non* in the case of dual tasks. Therefore, a brief review of attention in general and divided attention in particular is considered here.

Although it has been famously said that “everyone knows what attention is” (James, 1890), there are no exacting psychological or physiological descriptions of what it actually is. Several controversial theories claim that attention is a causal force that influences perception and other brain activities, or that it is a by-product of processes such as stimulus priming, or that it is a result of competing neural interactions. So far, none of these assertions has actually been tested physiologically. It has been claimed that one of the important outcomes of the dichotomy between whether attention is a cause or an effect is closely related to the question of whether there exist separate attentional systems. Several researchers have made the strong claim that there are separate attentional systems, while others have

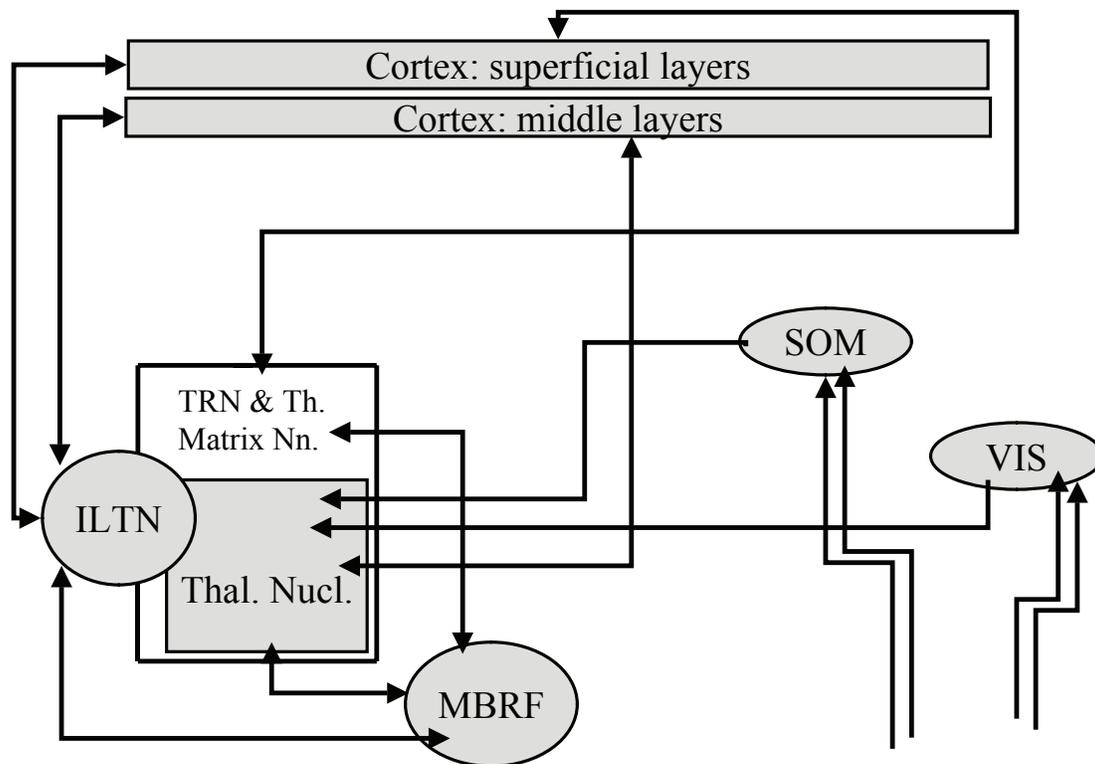


Figure 1: Schematic representation of some of the neural structures that are known to be important in modulation attention. Arrows indicate anatomical connectivity, which is often excitatory, but in certain instances, such as in the case of some thalamic reticular nuclei neurons that are GABA-ergic, can be inhibitory. ILTN: Intra-laminar thalamic nuclei; MBRF; Mid brain reticular formation; TRN: Thalamic reticular nuclei; Thal.Nucl: thalamic relay nuclei; Th.matrix Nn: Thalamic matrix neurons; Som: Somatosensory input; Vis: Visual input. The interplay between these structures are thought to modulate attentional modulation of sensory input. Note that the thalamic matrix neurons diffusely relay on the superficial layers of the cortical areas that are widespread across the cortex, whereas connections from the major thalamic nuclei relay on the middle layers of the cortex.

claims that attention is an emergent property of other processing activities (see Parasuraman, 1998 for a detailed review).

Although the exact nature or characteristics of attention is unclear, at a functional level, we know that attention is a state where there is heightened physiological arousal, associated with surface EEG recordings that show a generalized decrement of signal amplitude along with desynchronization. It is known that the midbrain reticular formation (MBRF) is important for the EEG desynchronization and the associated increased alertness of the brain (Moruzzi and Magoun, 1949). A portion of the midbrain reticular formation projects to the intra-laminar thalamic nuclei, which then project to the caudate nucleus and to the prefrontal cortex, especially to the layer I, while other projections extend diffusely over many areas of the cortex. It is also known that when subjects go from a strictly defined and behaviorally controlled rest state to a state of increased alertness, there is a general increase of cerebral blood flow (Roland and Larsen, 1976). A large proportion of this cerebral blood flow increase appears to be due to diffuse activation of the cerebral cortex, irrespective of the particular task that the subjects performed when they moved from the rest state to the test state (Roland, 1993). It has been claimed that this diffuse increase in cortical activity is the result of projections from the intra-laminar thalamic nuclei (ILTAN) to various parts of the cerebral cortex. Further, it has been clearly demonstrated that the intra-laminar thalamic nuclei themselves show increased activity (i.e., increased regional cerebral blood flow as measured with PET) (Kinomura et al., 1996), the MBRF-ILTAN-CORTEX system may be seen as participating in modulating the level of alertness or attention (Jones, 1998a, b; Jones, 2001).

Anatomically, several brain regions are implicated in maintaining different states of arousal or attention (namely, general alertness, sustained attention, divided attention, vigilance etc...). These include the sub-cortical projection systems of the cholinergic basal forebrain, the noradrenergic locus coeruleus, midbrain dopaminergic nuclei and the serotonergic dorsal raphe nucleus (Coull, 1998; Parasuraman, 1998). In addition, several brain imaging studies have shown that the intra-laminar thalamic nuclei (Kinomura et al., 1996), pulvinar (LaBerge and Buchsbaum, 1990), and the midbrain reticular formation (Kinomura et al., 1996) perform important attentional functions. On the other hand, evidence from many visual imaging studies have consistently implicated the superior parietal lobule in attentional orienting (Corbetta et al., 1991; Corbetta et al., 1995; Nobre et al., 1997; Vandenberghe et al., 1997; Culham et al., 1998; Kastner et al., 1998). Moreover, the superior frontal cortex (Corbetta et al., 1995) and the cingulate cortex (Pardo et al., 1990; Bench et al., 1993; Carter et al., 1995), are active in selective attentional tasks along with several parietal areas (see Kastner and Ungerleider, 2000 for a detailed review). These findings indicate the likelihood that the brain regions mentioned above are particularly important in the behaviors that require different forms of attention. A recent review, (Kastner and Ungerleider, 2000) has suggested that the activity in the fronto-parietal areas does not reflect the attentional modulation of tasks. The authors suggested that the said activity is rather due to attentional operations themselves. However, at present, it is not possible to explicitly dissect out the task related activations from the attentional activations observed in these regions.

As is clear from the foregoing discussion, there are several descriptive varieties of attention. One is the selective or focused attention, where, for instance, a subject focuses on a particular stimulus, or a stimulus feature. Focused attention is described in association with the different sensory modalities

(visual/auditory etc), or as their functional varieties (e.g., focused visuo-spatial attention). Another dichotomy that is often discussed is the distinction between serial attention and parallel attention. There is an extensive literature dealing with focused attention. Therefore, an extensive treatment of the subject will not be attempted here.

Divided attention refers to situations where the brain consciously and simultaneously processes two stimuli, or attempts to engage in two mental processes. This type of attention is essentially different from focused attention in that the brain attempts to process two (or more) streams of information in a fashion that can intuitively be described as parallel.

Only a very few neuroimaging studies have explicitly studied the question of neural correlates of divided attention. The first attempt to study neural correlates of divided attention was reported by Corbetta and others. (1991). They used visual stimuli where the subjects had to attend to the velocity of a moving visual stimulus, its color and/or the shape simultaneously. Division of attention between these different attributes of the stimuli increased the regional cerebral blood flow in several cortical areas including the dorsal lateral prefrontal cortex, the middle frontal gyrus, inferior parietal cortex and the anterior cingulate cortex. In their study, the authors found that the magnitude of the cerebral blood flow response decreased in certain regions when the subjects divided attention between two features of the stimuli, and overall, there were fewer regions activated than the selective attention conditions. These latter findings remain unreplicated to date.

Several other studies that attempted to address other, but perhaps related issues reported similar brain activations under divided attention conditions (D'Esposito et al., 1995; Madden et al., 1996; Corbetta, 1998; Koechlin et al., 1999; Dove et al., 2000; Iidaka et al., 2000). The findings from these studies appear to confirm that a set of areas that include the bilateral caudal prefrontal areas near or including the frontal eye fields, and the cortex lining the intra-parietal sulcus bilaterally are involved in conditions where attention is divided. It is worth noting however, that each of these studies mentioned here used some form of a visual stimulus in their paradigms. On the other hand, at least one PET study recently reported that division of attention reduces brain activity in the left prefrontal area and the medial temporal areas (Anderson et al., 2000). However, similar to the other studies cited above, the authors in this study (Anderson et al., 2000) reported that division of attention also increases activity in the fronto-parietal network bilaterally, the cingulate cortex and several other areas. What is interesting about these overall finding is that the same set of fronto-parietal areas have been reported to be active in a large number of visual directed attention tasks (see review by Kastner and Ungerleider, 2000), indicating that these areas are likely to be consistently involved in all forms of attention.

Although these imaging findings have consistently shown that the fronto-parietal network and the cingulate cortex that was described is associated with general or divided attention, until recently there have been no corroborating evidence for this. Recently however, it has been reported that the neurons in the lateral agranular frontal cortex in rats have divided attention correlates when single unit recordings were used to obtain post-stimulus time histograms from a group of rats engaged in simultaneous temporal processing task (Pang et al., 2001). Although the rodent frontal agranular cortex is clearly different from the human frontal cortex, these findings are encouraging, given that evolution

has often tended to retain the basic patterns and templates of biological systems that are reasonably functional.

In all the above-mentioned studies, the behavioral results show a decrement of performance (increased reaction time, decreased accuracy) when two tasks are simultaneously performed. However, no studies have investigated the possible interplay between simply performing two tasks simultaneously, division of attention, which is required by the very nature of a dual tasks in order to perform the two component tasks of the dual task, (Braun, 1998), and the reaction time increments and increased errors that occur when two tasks are performed under these circumstances.

Methodological issues

PSYCHOPHYSICS

One of the most important goals of modern neuroscience is to establish the interplay and correlates between perceptual and neuronal events. To objectively accomplish this, a cardinal requirement is the ability to describe behavioral phenomena. Psychophysics was introduced by G. T. Fechner in 1860 as a transdisciplinary research methodology to provide many of the essential tools for this purpose (Fechner, 1860).

At present, psychophysical methods are frequently used in conjunction with the objective, albeit indirect, neurophysiological methods such as PET and fMRI. Although the combined psychophysical-imaging studies rarely provide clear-cut answers at present, this strategy allows a conceptual way to complement and confirm the findings from one method with the other.

ON REACTION TIMES

A large proportion of the work described in this thesis is based on reaction time measurements. Therefore, some important issues that concern reaction time (RT) measurements merit attention.

Historically, the first attempts to measure RTs is attributed to Helmholtz (1850), (Southall, 1925) and later Donders (1869), who actually succeeded in describing a workable methodology to measure and calculate reaction times. Since then, reaction times remain perhaps one of the most extensively measured variable in experimental psychology.

Reaction time is the time that elapses between the onset of a stimulus and the onset of a response to that stimulus. What is measured as a reaction time therefore include all events that take place at the stages of perceptual encoding at the receptor level, nerve conduction, spinal-cortical-sub-cortical-spinal processing, nerve conduction and finally the time a muscle need to contract.

Several different types of reaction times have been described. Simple reaction times are measured when the same response is to be made to a single, randomly repeated stimulus. In this type of reaction time tasks, the stimulus and the response are deterministic, and lack any ambiguity. In dual RT tasks that were used in the work presented in this thesis, there were two stimuli from two sensory modalities, but within each task block the responses for each stimulus was were kept completely unambiguous. This distinction is important because in another type of reaction time tasks, called disjunctive, or choice reaction time tasks, there are several stimuli, and the responses are to be selected according to different attributes of the stimuli.

Several cognitive and behavioral attributes such as the choice, and decisions affect RT task performance. Fitts and Seeger (1953) first described that keeping the stimuli and their response unambiguous or deterministic will lead to the fastest reaction times possible, when stimuli are supra-threshold (Fitts and Seeger, 1953). This is what is known as the stimulus-response compatibility principle, and is an important consideration in designing reaction time experiments. In addition to the S-R associations, several other factors affect the RT measurements. These include: (a) the type of

stimulus (visual RT being slower than the somatosensory or auditory RT); (b) signal strength of the stimulus (where the RTs decrease exponentially until an asymptote is reached, as the stimulus strength increases); (c) preparatory set (d) stimulus similarity; (e) motivation of the participant; (f) practice; (g) age. (See <http://biae.clemson.edu/bpc/bp/Lab/110/reaction.htm>, for a review of additional factors that affect reaction time performance.) Even when all these factors are considered in evaluating RT data, the issue of performance accuracy must still be dealt with. Formal definitions of what constitutes an error in a reaction time experiment are few in the standard textbooks and references. In their seminal work, Green and Swets (1966), described definitions of what are misses and false alarms by using a matrix to sort the RTs to correct hits {(yes) | stimulus}, misses {(no) | stimulus} and false alarms {(yes) | no stimulus} or (yes) | stimulus. This enables one to define what constitute an error in the RT data. In the work that has described here, we defined misses and false alarms as errors (Green and Swets, 1966; Gescheider, 1997), and the recorded RT data that conformed to the errors were excluded from the analysis.

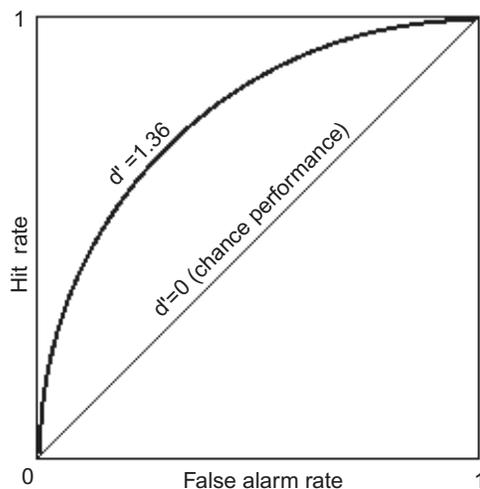


Figure 2: Schematic representation of a receiver-operating characteristic (ROC) curve. These curves are obtained by plotting hit rates against false alarm rates. The degree to which the ROC curve approaches the upper-left hand corner of the plot depends on the sensitivity of the observer. Therefore, different curves can be obtained by manipulating discriminability of the stimulus, and the sensitivity of an observer. For supra-threshold stimuli, high d' , which is an index of sensitivity of the observer lies towards the left-upperhand corner of the plot and indicates high hit rates and low false alarm rates.

The RT tasks that we used are signal detection tasks. All signals were supra-threshold. However, even with supra threshold stimuli, it is assumed that a participant sets a criterion to respond based on what s/he specifies as the amount of information that is sufficient for a response when engaged in signal detection situations (Green and Swets, 1966). As this criterion is set depending on the instructions given as well as the participants' decision of what may be an acceptable number of errors, the relationship between the RTs and error rates tend to be non linear. This leads to the issue of speed-accuracy trade off. It is usual that the instructions given to the subjects to specify that the RT speed as well as highest

possible accuracy are equally important. Even then, it is difficult to assess what is the speed-accuracy trade off adopted by the subject. Several methods have been developed to deal with this problem. One such method is called the d' which is a measure of observer sensitivity and is defined as $d' = z(\text{hit rate}) - z(\text{false alarm rate})$, where z is the normalized t-scores for the hit rate and the false alarm rates. A d' of zero describes chance level discrimination between noise and the signal which is a complete overlap of signal plus noise. A d' of 1 describes moderate performance, and a d' of 4.65 (when the hit rate is 0.99 and false alarm rate is 0.01) is considered the ceiling level performance where signals are completely discriminated from the noise. A variation of the d' measure is to study the area under the receiver-operating characteristic curve (ROC curve), which is obtained by plotting hit rate against false alarm rates. Using the ROC curves, it is possible to show that the same sensitivity can result from different hit rates and false alarm rates; for a given d' , a more conservative criterion will produce both lower hit rates and false alarm rates, whereas for a more liberal criterion, the hit rate and the false alarm rate will be much higher.

Despite the progress the modern neuroscience has made over the years, the interpretation of RT data and performance accuracy remains enormously difficult. On occasion, researchers are able to correlate their psychophysical findings to the objectively measured neural responses, or PET/fMRI signals. Even so, the exact meaning of such correlations remains difficult to interpret or comprehend with the current state of the knowledge. Despite this however, psychophysics remains perhaps the most important measure of behavior because only psychophysical measures can truly be construed as the direct behavioral manifestations of the neuronal activity in the brain. Therefore, the often-encountered difficulty of psychophysical data not leading to strong conclusions must not be interpreted as a weakness of psychophysics itself, but rather as a weakness emanating from the lack of knowledge behind the consequences of neural activity leading to the behavior being measured.

IMAGING THE HUMAN BRAIN AT WORK

Both PET and fMRI are well established neuroimaging methods. Therefore detailed methodological descriptions will not be given here (see Roland, 1993; Moonen and Bandettini, 1999 for detailed descriptions of these methods). These two imaging methods are both indirect measures of neural activity that take place in the brain: PET usually measures the regional cerebral oxygen utilization or regional oxygen flow, while fMRI measures the blood oxygen level dependant (BOLD) signal. These measures of neurovascular responses are considered to be tightly coupled to active populations of neurons. In general, there is evidence to suggest that the physiological variables (rCBF or BOLD) that these imaging methods measure, accurately portray neural events such as excitatory synaptic activity averaged across an area in the brain limited by the spatial and temporal resolution of the particular method being used. However, there are unresolved issues. For details of what is known about the coupling of neural activity and the signals measured with functional imaging see the reviews listed here (Magistretti and Pellerin, 1997, 1999; Moonen and Bandettini, 1999; Magistretti and Pellerin, 2000; Logothetis et al., 2001).

There are several other issues that are relevant to functional brain imaging that merit being mentioned here because of their conceptual importance.

All forms of imaging have an often undisclosed noble intention: to faithfully render the reality that is being imaged. To achieve this, two important steps must be fulfilled in any given type of imaging method. Firstly, a signal must be recorded or registered. Secondly, the recorded signal must be developed or reconstructed so that a representation or a model of the [imaged] object is created. Since neither recording the signal nor its reconstruction is ever perfect, imaging eventually and always yields a partial and incomplete rendering of reality. A further complication arises here because of the virtually infinite number of representations that can be created from any object that is being imaged. Therefore, although a flower can be represented as a black and white or a color photograph, a cinematograph or even a cartoon, what is the reality represented in a given image of the flower remains an unanswered, or perhaps an unanswerable question.

This then leads to the issue of fidelity (accuracy in details) of the images. In the case of brain imaging, to what level of fidelity does an image represent the imaged activity of the brain? The answer to this question has two aspects because fidelity is a measure of both reliability and validity. Reliability of a finding can be ascertained by its replicability. Unfortunately, replication of functional imaging findings remains a contentious issue at present, probably owing to the desire on the part of the scientists to first charter the unmapped waters, and not due to any particular technical limitations intrinsic to the methods themselves. As has been already done for some of the functional characteristics of the primary sensory motor areas and some of the brain areas involved in cognition, replication of findings will be a matter of time for most of the novel imaging findings that remain contentious at present. A good example of this is the increased activation of the supplementary motor area in sequential finger tapping tasks, a finding that has been consistently replicated in over 50 imaging studies so far.

Validity on the other hand is a particularly intricate and vexing issue because sometimes images may contain representations of unintended, or unknown realities. At a more technical level, the remaining issues of resolution (both spatial and temporal), which are also aspects of validity, compound this question because they indicate the degree of completeness of the rendering of reality. Accurate descriptions of how imaging findings relate to behavior on the one hand and to neural activity on the other, must also be resolved forthwith.

In any case, unlike the structural imaging of the brain where there already exists a fairly sophisticated, *a priori* knowledge of the object being imaged, which thus allows a fairly accurate rendering of the reality by imaging, functional neuroimaging often lacks the sophistication and perhaps the predictability afforded by *a priori* knowledge. This however can be seen as a mixed blessing because the absence of *a priori* knowledge can occasionally lead to unexpected basic discoveries (Papanicolaou, 1998).

Certain limitations inherent to currently available functional imaging methods may have affected the outcome of the experiments that are reported in this thesis. One such important issue is the limited temporal resolution of the functional MRI. Although the current state of the art temporal resolution for fMRI is approx. 1000 ms (Dale and Halgren, 2001), this is far greater than the time scale of inter-stimulus interval at which interference in dual motor RT tasks occur. As such, currently it is

not possible to study two neural events that occur under approximately 1000 ms as in the case of dual RT tasks with inter-stimulus interval shorter than 400 ms. that are described in this thesis. A similar issue concerns the spatial resolution of the fMRI signal. However the potential spatial resolution of the fMRI signal has improved to a few hundred microns, (Zarahn, 2001) and when this technology is more widely available, more detailed, and reliable descriptions of functional anatomy of the brain would be forthcoming.

ON MAPS...

Making maps, or cartography, is serious business. Once a map is made, someone is likely to use it as a guide, to find information about what is known, or to map the structure in greater detail. Because of this, map makers must be careful about what they do. Mapping of the functions of the human brain is no different. The basic tenant is to understand the functional organization of the human brain. However, to reach this goal, one must be able to understand not only what a map represents, but also, why does one want to map the brain? This question rests on others such as what is a map? And what can be mapped? Moreover, when a map is made and a cortical area is described, one must ask, what exactly is a cortical area? Unfortunately, most of these questions often go unasked.

A map is an ordered representation of locations. In the case of functional brain maps, they represent the underlying neural activity that produces a behavior, in the broader sense of the word. The purpose of making maps can quite simply be to understand the functional specialization of the human brain, with the hope that this understanding will allow us to integrate the knowledge from other neurobiological disciplines and come to a fuller understanding of how the brain works. As was described in the previous paragraphs, what can be measured with the currently available imaging methods are limited to a few indirect physiological variables. Fortunately however, these variables have turned out to be tightly coupled to the physiological properties and activity of neurons (Logothetis et al., 2001). Because of this, it is now possible to produce functional activation maps of the brain with a fair degree of validity. And yet, most functional activation maps that are being produced today lack one of the most important properties of a standard topographical map; borders.

A topographical map has borders that define territories. Without borders, maps can be meaningless, especially if the original intention of making the map was to study what is sometimes called the functional architecture or functional specialization. At present, most brain maps that describe some functional correlate depend on the classical Brodmann or Von Economo maps that were produced early in the last century to do so (Brodmann, 1909; Von Economo and Koskinas, 1925). One of the features of these maps was that, with a few exceptions, these cartographers subjectively decided upon the borders between the areas that they described in their maps, although a number of distinctive criteria to define borders between cytoarchitectonical areas were also described. However, it is worth remembering that many of these quasi-objective criteria had to be applied subjectively, without the possibility of any form of formal measures or quantifications to describe the borders thus defined.

Although referring to brain areas using a 3D stereotaxic co-ordinate system (Talairach and Tournoux, 1988) is a common practice, this is often limited to localizing the maxima of brain activity measured with imaging experiments. Therefore, a need exists to obtain observer independent borders between cortical areas that are functionally and anatomically different. One such methodology is to use cytoarchitectonic maps. These methods represent anatomical descriptions of cortical areas with statistically defined borders. This way, when two adjacent areas on the cortical surface are described, the border between the two areas can be defined without any ambiguity (Schormann and Zilles, 1998; Amunts et al., 1999; Schleicher et al., 1999).

In summary, maps, and mapping, are concepts that deserve serious thought and preparation. Once the functional topography of the brain is mapped, additional techniques are necessary to understand how the computations within a mapped cortical area are carried out. In one extreme we only process crude, indirect measures of neuronal activity that we used to image the functions of the brain. In the other extreme, although there exists a very sophisticated knowledge about the electrical and molecular activity of single neurons, we have no idea as to how they cooperatively perform all the computations that we map with imaging. Bridging this gap is probably one of the most important goals of modern neuroscience.

A map comprising blobs of BOLD signals may seem like an unlikely candidate to fulfill such a goal. However, it must be remembered that the BOLD signal is a physical manifestation of a biological phenomenon. Albeit indirectly, it is tightly coupled to the electrical activity in neurons under study (Logothetis et al., 2001). Electrical activity in neurons is, in turn tightly coupled to the molecular events that occur in the neuronal membrane. As it is currently assumed that the neurons engage in computations and thereby information processing by way of electrical and molecular signaling between them, the BOLD signal therefore is a reflection of how information is processed in the brain. On the other hand, molecular methods that study minute components of neurons, or electrophysiological studies with single or multi unit recordings cannot look at the [sic] larger picture of how large populations of neurons interact. Therefore, it is likely that, with further advances in the analytical methods and MRI technology, functional brain mapping with fMRI is likely to play a key role as a bridge between our understanding between molecular and electrical events in populations of neurons that process information on the one hand and overt, measurable behaviors on the other.

Main aims of the thesis

This thesis contains data and findings from the first systematic investigation of psychophysical performance during visual and somatosensory dual RT tasks. In order to provide neurophysiological explanations for the psychophysical findings, the cortical field hypothesis, and several other neurophysiological hypotheses were used to formulate a general investigative framework. That way, the imaging work reported in this thesis examines the validity of these hypotheses as neurophysiological mechanisms of dual task interference.

Findings from the experiments described in Part B were then speculatively integrated with neuroanatomical and neurophysiological findings from other sub-disciplines of neuroscience to accommodate the main aim of the thesis: to explain dual task interference with plausible neurophysiological mechanisms.

- The main aim of the work described here was to investigate potential neurophysiological mechanisms that would explain how and why RTs are prolonged and/or error rates are increased when two RT tasks are performed near simultaneously
- We explored the effect of ISI on RT speed and performance accuracy using a number of psychophysical experiments. Imaging experiments were used to locate the neural correlates of dual task interference.
- An attempt was made to psychophysically differentiate the RT delays due to division of attention, from the RT delays due to a possible occupancy of motor structures by the response to the first stimulus when there are two responses to be made within 400 milliseconds. The psychophysical differences were then investigated by imaging experiments to elucidate whether divided attention and interference due to motor field occupancy would produce dissociable activation patterns.
- Another factor investigated was whether having to assign a motor effector after the stimuli were received, as opposed to *a priori* assignment of an effector, would lead to increased RTs. This was discussed as a causal mechanism of RT delays observed in dual RT tasks resulting from essentially serial processing of information in some parts of the brain.
- Further, we psychophysically investigated a putative physiological mechanism of reaction time increments that may be due to neural computations that are necessary to establish stimulus-response associations.
- One way to invalidate the CFH is to find behavioral tasks that are computed by completely dissociable brain areas, and to show that when these tasks are performed simultaneously, interference still occurs. The first step of such an approach would be to find such tasks. With PET and different types of visual object recognition tasks, we investigated a possible set of candidate tasks for this purpose.

Experiments and Results

PAPER I - PSYCHOPHYSICS OF DUAL REACTION TIME TASKS

As mentioned earlier, one of the main purposes of studying behavior is to understand how behaviors are controlled by the brain. However, before taking this fateful step towards the understanding of the neural control of human behavior, behaviors themselves must be quantified, and understood. Only then can one seriously study the neural correlates of a given behavior.

When work on this thesis began, there existed a wide and an important void in dual reaction time (RT) task literature. Although many combinations of task types had been investigated under dual task situations, dual RT data of somatosensory RT tasks performed with RT tasks of other modalities (e.g. auditory or visual) has remained scarce. We wanted to obtain data to confirm that somatosensory-visual dual RT task performance conform to the general pattern observed with other dual RT tasks, in that ISI shorter than 400 ms will produce interference. Secondly, we wanted to systematically investigate the RT performance patterns of simple dual RT tasks, with hypotheses based on neurophysiological concepts. Thirdly, we wanted to study the feasibility of modifying the classical dual RT task paradigms to conform to the practical requirements and limitations of functional brain imaging studies. For instance, although a usual psychophysical experimental session lasts anywhere between 30-40 minutes at a time, it is not possible to have such prolonged experimental sessions during fMRI scanning. We have noted that the optimum length of a dual RT task length while a subject is being scanned in the MR scanner is around 4 minutes per session, which is considerably shorter than a psychophysical experimental session. When experimental sessions are made shorter, questions about statistical power are invariably raised, because the amount of data that can be collected becomes limited. In addition, a behavioral paradigm for a block design fMRI experiment requires that all different task types and controls be included in the paradigm that comprises the scanning session. This requirement further limits the number of data points that can be collected.

Given all these practical constraints and concerns, it is still important to be able to obtain reliable psychophysical data from scanning experiments, because ideally, one wishes to be reassured that the subjects performed the task that they were supposed to, according to the instructions, and without major differences from the behavioral outcomes that could be obtained outside the scanner. Therefore the behavioral tasks in this experiment were designed such that they could be directly ported to a functional neuroimaging experiment without any modifications.

Several psychophysical hypotheses were tested here using a number of behavioral paradigms.

Experiment A: Responding to two rapidly presented stimuli from two sensory modalities (visual and somatosensory) encompass several task components. These include, perceiving two sensory stimuli from two different modalities, dividing attention between them, and performing two discrete, independent responses to the stimuli. Our psychophysical hypothesis was that the dual task interference occurs only when the inter-stimulus interval between the two stimuli is less than 400 ms. We examined this hypothesis by using simple RT tasks for visual and somatosensory modalities.

Experiment B: When RT increases in a dual visual-somatosensory RT task can this be simply due to the fact that two sensory modalities were involved, and hence there was a fundamental need to divide attention? Experiment B was designed to examine the psychophysical hypothesis that

interference (increased RT and/or increased error rates) occurs even in situations where division of attention between two sensory modalities is not necessary. All stimuli were of the visual modality. Thus, the task components included perceiving the visual stimuli and performing two discrete, independent responses to the stimuli.

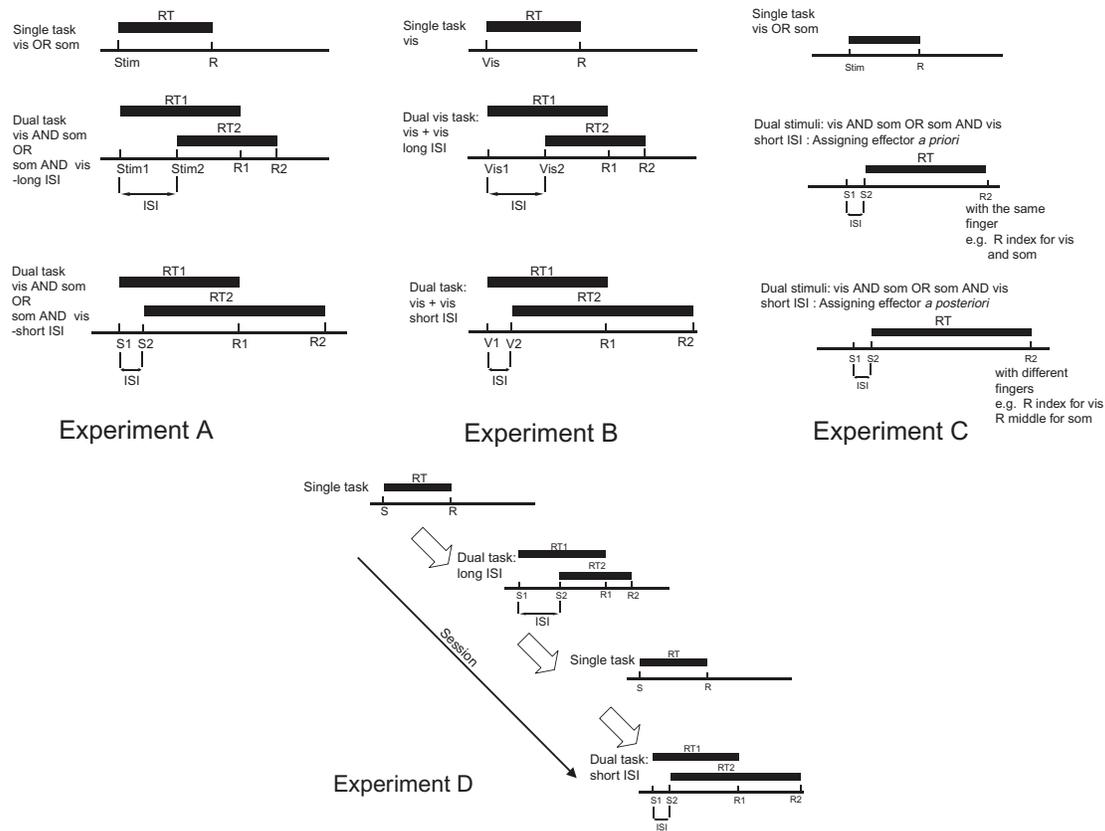


Figure 3: Schematic representations of the psychophysical experiments described in Paper I. Experiments A, B, and C were of block design type, where each of the depicted trial types were individually presented as experimental blocks. In experiment D, there were 4 trial types, and these were presented with random inter-trial intervals, within a single experimental session. legend: RT: reaction time; S1 and S2: stimulus 1 and stimulus 2; R1 and R2: response 1 and response 2 for the respective stimuli; ISI: inter-stimulus interval; som: somatosensory stimulus; vis: visual stimulus.

Experiment C: Many neurophysiological studies have shown that the neurons in primary motor cortex and the premotor cortex, and the spinal interneurons maintain instructions related, anticipatory and preparatory activity that precedes the actual movement. Such neural activity is called the “anticipatory set”. It is also known that the set related neural activity could be modified by incoming sensory stimuli, or by instructions that the animal/subject has received before the task. This modifiability or biasing of preparedness allows one to execute motor behavior depending on the stimulus perceived, instructions received or decisions made. We hypothesized that were the subjects to use either the index finger or long finger, they cannot antecedently organize the sub-cortical motor loops, and especially the spinal network, to accommodate both effectors. As it takes 90-110 ms to assign the spinal excitatory bias (Fetz et al., 2000), the RTs in the case of index finger/middle finger must be

prolonged by approximately 100 ms as compared to the condition in which only one finger is used to respond to stimuli from both modalities. We also investigated the likelihood that division of attention between two stimuli itself can cause prolongation of RT, and whether this would be an independent causal mechanism of RT prolongation under dual stimuli conditions. This experiment differed from experiment A in the following important aspect: subjects had to encode two sensory stimuli from two different modalities, dividing attention between them, but performing a single discrete deterministic response to a predetermined stimulus. Therefore, we expected that it would be possible to differentiate the effects of performing two RT tasks from those of divided attention.

Experiment D: It is assumed that the brain computes and maintains stimulus response (S-R) associations whenever a stimulus is presented and a response is required (Fitts and Seeger, 1953). In conventional block design experiments, a given trial type is presented for a block of time, so that the S-R association remains stable over time during the block. Thus, the subject, responding to the stimuli, can maintain a somewhat stable, finite plan towards the responses that are to be made. On the other hand, if trials are presented randomly, maintenance of a steady state S-R association, and a response plan becomes impossible. In this experiment, we studied the psychophysical outcome of dual RT task performance when trial types are randomly presented. The psychophysical hypothesis that we tested was that inability to have steady state response plans, or delays incurred while establishing stimulus-response associations owing to temporal uncertainty of the trial occurrences will prolong all RTs, and would thus indicate an additional mechanism of interference.

PAPER I - SUMMARY OF PSYCHOPHYSICAL RESULTS

Overall, findings from the series of RT experiments that we have described in paper I demonstrated a number of possible mechanisms for interference in dual tasks. Firstly, RT to the second stimulus of a pair of stimuli significantly increases only when the ISI is less than 400 ms. This RT increase has a linear relationship to the ISI, in that shorter the ISI, the longer the RT delay. When the ISI is more than 400 ms, the RT to the second stimulus is statistically similar to the RTs of single task conditions in each modality, indicating that under such conditions, interference does not occur. The prolongation of RT2 is not dependant on the presence of signals of two sensory modalities comprising the pair of stimuli. Rather, RT2 is prolonged even when two stimuli from one modality are responded within 400 ms. In contrast, RT1 prolongation is due to divided attention between two stimulus modalities. The RT prolongation that appears to be due to divided attention occurs within an ISI range much wider than 400 ms, i.e., up to about 1200 ms, which was the upper limit of the ISI that we investigated. Thirdly, when the motor effector was to be assigned *a posteriori* as compared to the *a priori* assignment of effectors, this causes prolongation of RT in single RT tasks with dual stimuli. Fourthly, when a subject has to transiently shift between S-R associations and can not maintain a steady state response plan over a period of time, this too appears to prolong RT1. Errors in the form of misses are significantly

increased only when two conditions are fulfilled. The stimuli pair must belong to two different sensory modalities, and the subject must attempt to respond to the two stimuli within 400 ms.

Although it has often been speculated that females are faster and more accurate than males in performing simultaneous tasks, this conjecture could not be validated in this extensive series of psychophysical experiments. In all task combinations that we examined here, interference occurred irrespective of the sex of the subject, and there were no statistically significant differences between the sexes in the degree of interference in terms of RT delays or error rates.

Paper II - Neural Correlates of dual task interference and divided attention

This functional neuroimaging study was derived from the psychophysical experiments that was described in paper I, experiment A.

Dual tasks, by definition, require division of attention between the two tasks (Braun, 1998). As was described in paper I, the behavioral outcome of divided attention is likely to be reflected by the increased error rates or prolonged RT to the first stimulus (RT1) of a pair of stimuli presented in close temporal proximity. Interference, which is classically the increased error rates, or prolonged RT to the second of a pair of stimuli (RT2) presented in close succession, may, or may not be due to an additional, specific, physiological phenomenon. At the time that these experiments were performed, no studies had been able to distinguish neural correlates of division of attention between two simultaneously performed tasks, from those of interference that may occur between them. If there were a distinction between the cortical structures engaged in division of attention in dual tasks and those being active in dual task conditions that interfere, this would substantiate that these are two different physiological phenomena. Furthermore, if differences in activation of cortical areas were associated with different psychophysical results, for example, a differential effect on RT1 and RT2 it would further corroborate that the division of attention and interference are indeed two different neurophysiological phenomena.

Using the same behavioral paradigm of single and dual reaction time tasks that we used in the psychophysical study described in experiment A, paper I, we investigated a number of neurophysiological hypotheses. Firstly, we tested whether two RT tasks, when performed simultaneously would occupy the same motor cortical regions thus leading to interference, as proposed by the cortical field hypothesis. The second hypothesis was whether dual task performance would require engagement of additional cortical regions in excess of the regions that would be active in each of the component tasks, had these two tasks been performed as single tasks. Thirdly, we investigated the hypothesis that neural correlates of performing two simultaneous tasks could be dissociated from those of interference and that there is cortical activity specific to the interference. We expected that confirmation of this hypothesis would suggest that the neural correlates of dual task performance and those of interference are distinguishable from one another.

Subjects underwent fMRI while performing single RT tasks to visual and somatosensory signals or to a combination of these in two dual task situations with short and long inter-stimulus

intervals (Figure 4). They responded to the visual stimuli by pressing a button with the middle finger and to the somatosensory stimuli with the index finger of the right hand. Our behavioral paradigm did not require the task related activity such as working memory, choice or decisions, and the such to be retained over time, so that the cortical activity specific to dual tasks was not contaminated by short-term memory related cortical activations. This has been a major confound in all previously reported dual task imaging paradigms (D'Esposito et al., 1995; Klingberg and Roland, 1997; Corbetta, 1998; Klingberg, 1998; Koechlin et al., 1999; Adcock et al., 2000; Bunge et al., 2000; Dove et al., 2000). We expected that the elimination of this confound therefore would allow us to clearly delineate and compare brain activations specifically associated with single tasks and dual RT tasks with and without interference respectively.

PAPER II - BEHAVIORAL FINDINGS FROM THE SCANNING EXPERIMENT

For the both long and short ISI dual tasks, the RT1 in each modality was significantly longer than the single RTs whereas the RT2 was significantly different from the single RTs only in the short ISI dual task. Thus, during the dual task condition with the short ISI, the reaction time to the second of the two stimuli (RT2) was significantly prolonged as compared to that of the dual task with the long ISI, irrespective of whether the second stimulus was somatosensory or visual. RT2 increased linearly when the ISI decreased below 400 ms. As mentioned, RTs to the first stimulus, (RT1) in both dual RT task conditions were also significantly longer than the single RTs. Thus, it could be shown that while RT1 in all dual tasks increased significantly irrespective of ISI, RT2 only increased as a function of ISIs less than 400 ms. Further, there was a significant probability of subjects missing responses to the stimuli in dual task condition with a short ISI. Therefore, in the dual task condition with the short ISI, there was a strong interference effect behaviorally, while both dual tasks also showed strong effects on RT1 that could parsimoniously be attributed to divided attention. Overall, these findings were a remarkable replication of the findings from experiment A in Paper I.

PAPER II - BRAIN ACTIVITY

The main findings of this experiment showed that :

- The single visual and single somatosensory RT tasks engaged almost identical cortical gray matter tissue in the cortical motor regions of 4a, 4p, SMA, CMA, the basal ganglia and the ventral anterior and the ventral lateral nuclei of the thalamus that receive the output from the activated parts of the basal ganglia.
- Under dual task conditions, contralateral areas 4a, 4p, SMA, CMA, bilateral basal ganglia, ventral anterior and the ventral lateral nuclei of the thalami including the intra-laminar thalamic nuclei were predicted to be activated by the component visual and somatosensory RT tasks of the dual task. This prediction could be directly validated by showing that visual and somatosensory

dual RT tasks in fact activate nearly an identical spatial extent in these structures as activated by the single RT tasks.

- Dual task interference (where RT to the second stimulus -RT2- is prolonged and errors are increased when ISI is less than 400 ms) is specifically associated, and strongly correlated with increased activity in a cortical field located within the right inferior frontal gyrus. This is the first instance where interference specific cortical activity has been demonstrated.
- The RT1 prolongation occurs irrespective of the ISI, when subjects receive stimuli from two sensory modalities. It is likely that this is due to the division of attention between the two modalities.
- Dual RT conditions, as compared to single RT conditions activated brain areas located bilaterally in the superior frontal cortex including the frontal eye fields, the intra-parietal sulcus (IPS) and the supramarginal gyri.

These findings illustrated that the increment of RT1 and RT2 (i. e. interference) seen in dual RT tasks are two different psychophysical phenomena emanating from dual task situations and that these mechanisms are very likely to be due to different neurophysiological correlates.

PAPER III - EFFECTOR ASSIGNMENT STRATEGIES AND DIVIDED ATTENTION IN PROTRACTED REACTION TIMES

The increased RTs in the dual tasks that we observed in experiment A of paper I, and paper II above (Herath et al., 2001), could have been either due to division of attention between the two modalities or having to assign the response to the appropriate finger rapidly. Perhaps, the RTs would not have been prolonged if there were only one stimulus-response (S-R) association (i.e. consistent, same finger flexions for both modalities), and therefore only one way to assign an effector for both stimuli. Alternatively, RT prolongation would have been absent if there was no need to divide attention. Because of this, one of the questions examined in the present experiment was whether having two possible effectors in readiness for a motor act would produce increased RTs as compared to a condition that has only one effector in readiness (irrespective of the stimulus modalities) to be triggered by the appearance of a stimulus. At present, the neural correlates of such an RT increase remains largely unexplored. Another question that we studied here was what had hitherto remained a largely unexplored issue of the neural correlates of divided attention *per se* producing RT delays in simple RT tasks. Specifically, we wanted to investigate whether the RT prolongations that occur due to divided attention could be anatomically dissociable from motor activity related interference.

In this experiment, we investigated four hypotheses, two psychophysical,, and two neurophysiological. The first psychophysical hypothesis examined was that the RTs were predicted to be prolonged when subjects attend to two modalities instead of one: that is, division of attention between

sensory modalities can produce an interference like effect. The second psychophysical hypothesis was that there would be increments of RTs when the effector was specified by the stimulus as opposed to when the effector was specified *a priori*. In one condition subjects responded to visual stimuli with one finger (e.g., right middle) and to the somatosensory stimuli with another (e.g., right index). Our hypothesis was that the brain would have to assign the effector *a posteriori* to the stimuli. In the other condition, both visual and somatosensory stimuli were to be responded with the same finger (e.g., right index) within a session. Here, the effector could be assigned and kept ready *a priori* to the appearance of stimuli. It was predicted that there would be an RT prolongation in the former condition as compared to the latter. The third and the fourth hypotheses are neurophysiological in nature. As these RT tasks are effectively single RT tasks, and because the motor areas that control the two fingers overlap to a very large extent (Alexander and Crutcher, 1990; Kawashima et al., 1994; Karni et al., 1995; Sanes et al., 1995; Roland and Zilles, 1996), we expected that the brain activity between the two effector condition and the single effector condition to be similar, reflecting the increased neural activity in the same motor neural populations. The final hypothesis that we tested was that the divided attention would increase neural activity in areas outside the motor cortical regions, and that this increased neural activity, reflected by the increased BOLD signal, would be anatomically dissociable from the cortical activations associated with the control of finger movements that are represented in the motor areas.

PAPER III - BEHAVIORAL FINDINGS FROM THE SCANNING EXPERIMENT

There were two components that were psychophysically separable in the RT increases that we observed in this experiment. The pattern of RTs was Single RT < V-S ONE EFF RT < V-S TWO EFF RT. There was a significant increase between RTs of dual stimuli as compared to the RTs with single stimuli. This RT prolongation could be similar to the prolongation of RT that occurred in divided attention that we demonstrated in our former study (Herath et al., 2001). The RTs increased further when the effector could be only specified by the incoming stimuli (V-S TWO EFF) as opposed to the condition where effector being specified *a priori* (V-S ONE EFF). It must be noted that V-S ONE EFF RT and V-S TWO EFF RT only differed in that the V-S TWO EFF RT required rapidly assigning the effector for the second stimulus only when the brain had received that stimulus. We showed that the single RTs are comparable to the RTs that have been reported elsewhere in literature. There is an additional delay (increased RT), in response to when two stimuli from two modalities were presented within an ISI of <400 ms, although only one response was required using the same finger for both modalities. This was attributed to the delay caused by division of attention. Further delays in RTs appear to be due to the essentially serial nature of how an effector can be assigned subsequent to the perception of a stimulus. RT tasks had an average d' of 4.38 with $p(\text{hits}) = 0.98$ and $p(\text{false alarms}) = 0.01$, indicating that subjects perceived stimuli and responded according to the instructions. Between different tasks, there were no statistically significant differences at $p < 0.05$ of the $p(\text{hits})$, $p(\text{false alarms})$, $p(\text{misses})$, and $p(\text{anticipatory responses})$.

PAPER III - BRAIN ACTIVITY

- Division of attention between two stimulus modalities showed increased BOLD signals in a bilateral network of cortical areas that included the depths of precentral sulci adjacent to the frontal eye fields, and the cortex of the intra-parietal sulci. Additionally there were increased activations in the L putamen, the L anterior cingulate gyrus (ACC) and the L middle frontal gyrus. As the subjects responded to only to one stimulus, although they divided attention between the two that comprised the pair, this finding conclusively shows that the bilateral fronto-parietal network of cortical areas that were active here is engaged in divided attention, and not doing two tasks at the same time.
- Each of the reaction time tasks activated a nearly identical set of cortical loci that included the following areas: contralateral primary motor cortex, supplementary motor area (SMA), and the cingulate motor area (CMA), bilaterally the basal ganglia, particularly the putamina, the globus pallidus, the ventral anterior and ventral lateral thalamic nuclei, despite the psychophysical data showing an incremental pattern of the RTs where Single RT < V-S ONE EFF RT < V-S TWO EFF RT.
- Cortical areas that were active due to division of attention between stimuli are anatomically distinct from the cortical areas that are active in motor control of the RT tasks.

PAPER IV - TWO DISTINCTIVE MECHANISMS OF VISUAL RECOGNITION; A TENTATIVE MODEL TO TEST CFH.

As was mentioned in the introduction, the cortical field hypothesis claims that “If two different brain tasks make use of one or several identical fields, they cannot be performed simultaneously. From knowledge of field activations one can predict which types of tasks will interfere” (Roland, 1993; Roland and Zilles, 1996; Roland, 2002a). It has been claimed that the interference principle is fundamental for the field activation hypothesis (Roland, 1993; Roland and Zilles, 1996; Roland, 2002a). If two tasks can be executed simultaneously without any increase in reaction time or number or errors, despite that the two tasks rely on one or more identical or mainly identical fields, the cortical field hypothesis fails. Finding such tasks that can be studied using currently available neuroimaging methods has been difficult, however. The flip side of the above argument where two tasks that engage anatomically and physiologically dissociable mechanisms can be studied under dual task constraints in order to further understand how the brain process simultaneous information streams. For instance, if task A and task B have anatomical correlates that are fully dissociable, and therefore logically appear to have distinct physiological mechanisms, what will be the outcome of performing two such tasks simultaneously?

Before this question can be addressed, it is essential that tasks that are fully dissociable both anatomically and physiologically be found. Although at the first glance this may appear to be easy,

given the extensive connectivity of neurons in the brain, and also given the brain's ability to dynamically reorganize its neuronal populations so that the same neuronal population can perform a multitude of tasks at different times, finding two tasks that obey the full double dissociation is somewhat difficult.

The visual system in the human brain is perhaps the most extensively studied neural system. At present, it is widely accepted that visual information is processed in two hierarchically organized, parallel streams. The ventral streams process information with regard to "what" whereas the dorsal stream processes information on "where" with regard to objects perceived. On the other hand, despite a large body of extensive empirical data, how the brain recognizes objects remains largely unexplained (Boucart et al., 2000; Gerlach et al., 2000; Ishai et al., 2000a; Ishai et al., 2000b; Logothetis, 2000; Mazer and Gallant, 2000; Rentschler et al., 2000; Riesenhuber and Poggio, 2000; Tanaka, 2000; Riesenhuber and Poggio, 2002). We investigated two possible computational strategies and their neuro-anatomical substrates. Visual recognition can be based on category specific cues extractable from the patterns. For instance, humans can recognize the color "blue" as being blue. In this case, the semantic label "blue" is used to specify the visual category. It is also possible to recognize patterns simply because they have been seen before. In this instance, the recognition is based on representations of that particular pattern stored in memory. In the visual category based recognition we expected to see increased cortical activity in areas that act as the interface between visual image representations and their semantic representations or more simply, the areas that may be involved in processing meanings of viewed objects and patterns. In memory based pattern recognition, we expected increased brain activity in cortical areas that are active in retention and recognition of visual short-term memories. As the search for "blue" or "quadrangle" may be viewed as finding targets among distracters (i.e., other colors and geometric figures in the patterns viewed), we attempted to partition the brain activity of memory driven recognition by using visual recognition tasks with and without different types of distracters embedded within the patterns (i.e. color and long term memory distracters).

Using computer-generated geometric patterns that were drawn from a pool of 400 such items, we used the following tasks to investigate this question, i.e., whether it is possible to devise behavioral tasks with completely dissociable anatomical substrates. (i). Object recognition by visual category specific cues (CatRec), (ii). Recognition based on short-term memory (STM), (iii). Short-term memory with color distracters (STMCOLDISTR), (iv). Short term memory with long term memory distracters (STMLTMDISTR).

With the psychophysical findings from the study, we demonstrated that visual patterns can be recognized by (a) using visual category specific information extractable from the pattern, and (b) matching a perceptual description of the pattern to a representation of that pattern previously stored in memory. Using PET, we then showed that the visual category based recognition activated the R angular gyrus, L superior parieto-occipital cortex and the L inferior temporal gyrus, while the short term memory based recognition strategy activated the precuneii bilaterally

i. e.,
Category based recognition > STM based recognition ∈ Right angular gyrus, Left superior parieto-occipital cortex and Left inferior temporal gyrus

and,

STM based recognition > Category based recognition \in Left and Right precunei

The formal definition of a dual dissociation is $A \rightarrow A'$ but not B' whereas, $B \rightarrow B'$ but not A' . Brain activation findings from this study show that the visual object recognition based on semantic categories, and object recognition based on memory templates, conform to physiological and anatomical double dissociation.

Discussion

OCCUPANCY OF THE SAME NEURAL POPULATIONS MAY CAUSE DUAL TASK INTERFERENCE

When two simple stimuli from the same sensory modality or from different modalities are presented near simultaneously, and when subjects are asked to respond to both stimuli using unambiguous S-R associations, there is a robust delay in the RT to the second stimulus in each modality. However, this occurs only when the ISI is less than 400 ms. Psychophysically, the RT prolongation that occurs under these circumstances is linearly related to the ISI.

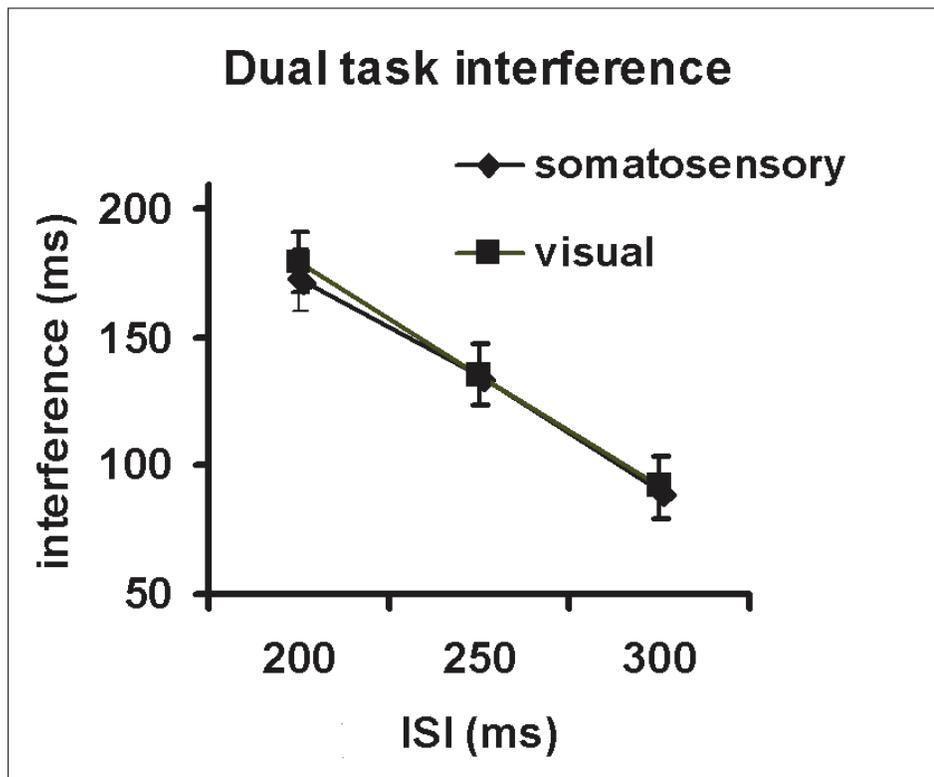


Figure 4: This graph shows the relationship of reaction time increments to the inter-stimulus interval. Interference, which, in this instance, is the increased RT to the second stimulus of a pair of visual-somatosensory or somatosensory-visual stimuli when they are presented with an inter-stimulus interval (ISI) of less than 400 ms is linearly related to the ISI, and is indicative of some form of an occupancy of neural activity coding for the reaction to the first stimulus, thereby delaying the RT to the second stimulus which is depicted here as interference.

When single RT conditions are contrasted to a motor control task that enables one to dissect out the neural activity of the motor components of the RT tasks, the corresponding statistical contrasts of both the visual and the somatosensory single RT conditions show engagement of almost identical gray matter tissue in the cortical motor areas that included areas 4a and 4p, the supplementary motor area (SMA) and the cingulate motor areas (CMA). The caudate nuclei, the putamina, the globus pallidus as well as the anterior and the ventral lateral nuclei of the thalami bilaterally were also engaged by both RT tasks. By showing that the volume of the cortex engaged by *both* single RT tasks (intersection:

motor structures common to both RT tasks) was 82% of the volume that was engaged by *either* (union: motor structures activated by one or the other RT tasks) the visual or the somatosensory RT tasks, it was possible to predict that the approximate sum of the neuronal populations corresponding to the individual single RT tasks would also be engaged when the visual and the somatosensory RT tasks were performed concurrently. This indeed was the case. The dual RT task conditions with somatosensory and visual stimuli activated the very same cortical motor areas and sub-cortical motor structures as was predicted by the *union* of the cortical activation patterns of the single RT tasks of visual and somatosensory modalities.

The *single* visual and *single* somatosensory RT tasks engaged almost identical cortical gray matter tissue in the cortical motor regions of 4a, 4p, SMA, CMA, the basal ganglia and the ventral anterior and ventral lateral nuclei of the thalamus receiving the output from the activated parts of the basal ganglia. Previously, near identical motor representations for the fingers have been reported in the literature (Alexander and Crutcher, 1990; Kawashima et al., 1994; Karni et al., 1995; Sanes et al., 1995; Roland and Zilles, 1996). Although it is known that there exist highly demarcated motor maps for digit representations in the primary motor cortices in several primate species (Wu et al., 2000), no topographical demarcations for digit control have ever been described in any of the other structures that comprise the motor circuitry. This indicates the possibility that the overall motor control is more likely to be undertaken by large neuronal populations that can be shared between digits. Therefore, the common field activations that we have shown are in close agreement with the hypothesis that interference between concurrently performed tasks is due to engagement of the same motor systems (Roland, 1993; Passingham, 1996; Roland and Zilles, 1998). The brain activations associated with the RT tasks of different modalities are known to converge on the motor regions such as areas 4a, 4p, CMA, SMA (Naito et al., 2000), basal ganglia, the ventral lateral and the ventral anterior nuclei of thalami. These structures were predicted to be active and subsequently found to be active in the coding and the execution of index finger flexion in response to the somatosensory stimuli and middle finger flexion in response to visual stimuli in the dual reaction time (RT) tasks. However, only in the dual task condition in which the ISI were shorter than 400 ms, (i. e., the dual RT condition that produced interference), the RT₂ increased linearly, as the inter-stimulus interval was progressively shortened below 400 ms. The most parsimonious physiological interpretation for this would be that it would take some time for the motor structures to change from the coding and control of the index finger flexion to that of the middle finger flexion and vice versa. If the large common engagement of the motor areas 4a, 4p, SMA, CMA and the sub-cortical motor structures imply that about 80% of the neural populations engaged in the visual RT and the somatosensory RT of the dual task are identical, a possibility that is supported in the literature (Lamarre et al., 1983; Salinas and Romo, 1998; Naito et al., 2000), this could be one of the causal mechanisms of the interference. The linear increase of the RT₂ as the ISI decreased could signify that the neuronal population(s) at one or more of these motor structures needed an approximately fixed time interval to change the coding of a response to a visual stimulus to coding the response to a somatosensory stimulus (Fu et al., 1995). This type of interference would be in accordance with the predictions of the cortical field hypothesis (Roland, 1993; Roland et al., 1998; Roland, 2002a). The consequence of the interference mechanism, of whatever nature, is that, at least for RT tasks with short

cross modal inter-stimulus intervals, the brain either misses the response to the second stimulus, or makes a delayed response, as shown by the behavioral results.

MOTOR OCCUPANCY ACTIVATES ADDITIONAL CORTICAL AREAS THAT CORRELATE WITH INTERFERENCE

Occupancy of a neural population by a task could lead the recruitment of additional neuronal populations in situations where interference tends to occur. This may be reflected in additional cortical activations associated with reaction time delays. In fact, there is a cortical region located in the right inferior frontal gyrus that was specifically associated with interference. The activity within this cortical field is strongly correlated with the increased RT for the second stimulus. This is as if the brain needs to recruit the cortical field located in the right inferior frontal gyrus (RIFG) when dual tasks interfere, when interference (i.e. increased RT2) occurs due to the occupancy of the same neuronal populations by the computation of the RT1. The additional activation located in the right inferior frontal gyrus appears only when the ISI is less than 400 ms. One may recall that the temporal certainty of the stimulus occurrence (i. e., that one stimulus is immediately followed by another of a different modality, albeit with a short, but random ISI), is much more deterministic in the short ISI condition than that in the long ISI condition (Georgopoulos et al., 1981; Lecas et al., 1986). Therefore the planning of motor actions for each of the RT tasks can be carried out with the certainty that one stimulus would follow another shortly. Moreover, the responses required by the dual tasks are conditional in that the subjects were to execute a specific, arbitrary response for the visual and somatosensory stimuli. The conditional associations were similar in both dual tasks, and had very high stimulus-response compatibility, a property that is known to reduce dual task interference (Georgopoulos et al., 1981). Thus, the conditional associations of responses in the dual tasks cannot account for the increased activity in the cortical field located in the right inferior frontal gyrus. On the other hand, it has been reported that neurons in the motor cortex particularly in the primary motor area, are capable of encoding information for short term storage of sequential stimuli for forthcoming movements (Johnson et al., 2001). In the case of dual RT tasks with inter-stimulus interval less than 400 ms, this storage mechanism may be occupied by the first stimulus, and therefore the information about the second stimulus may be relayed to a site that is connected to the primary motor cortex, such as the ventral premotor cortex, (PmV) that forms part of the activity located in the right inferior frontal gyrus. As the fMRI BOLD signal is a reflection of postsynaptic activity, the neuronal activity related to this information relay may then be reflected as increased BOLD signal at the post-synaptic location, when measured with fMRI (Magistretti and Pellerin, 1997, 1999; Logothetis et al., 2001). In this way, we have shown that when two RT tasks interfere, neuronal populations in the right inferior frontal gyrus (RIFG) show increased activity that is specifically associated with increased RT to the second stimulus (Herath et al., 2001). We showed that such increased RIFG activity occurs when two RT tasks are to be performed within 400 ms of each other. As the motor neuronal populations are then occupied by the first response, the second response is postponed until the occupancy is terminated. This perhaps leads to the increased activity located in the right inferior frontal gyrus

(Herath et al., 2001). The report by Herath et al (2001) is the first physiological demonstration of a neuronal correlate of dual task interference (where “correlate” is logically defined as ‘when A occurs, B occurs’). When there is no response to the first stimulus, this behavioral specification that makes the RT tasks essentially single tasks. This was the case when subjects receive two stimuli but respond only to the second stimulus. In this case, there is no occupancy caused by the motor response to the first stimulus and therefore no increased activity that is localizable elsewhere in the brain other than the motor structures.

Although the above mentioned brain activation findings have been validated only for dual RT tasks involving stimuli from two sensory modalities, we have psychophysically shown that the RT

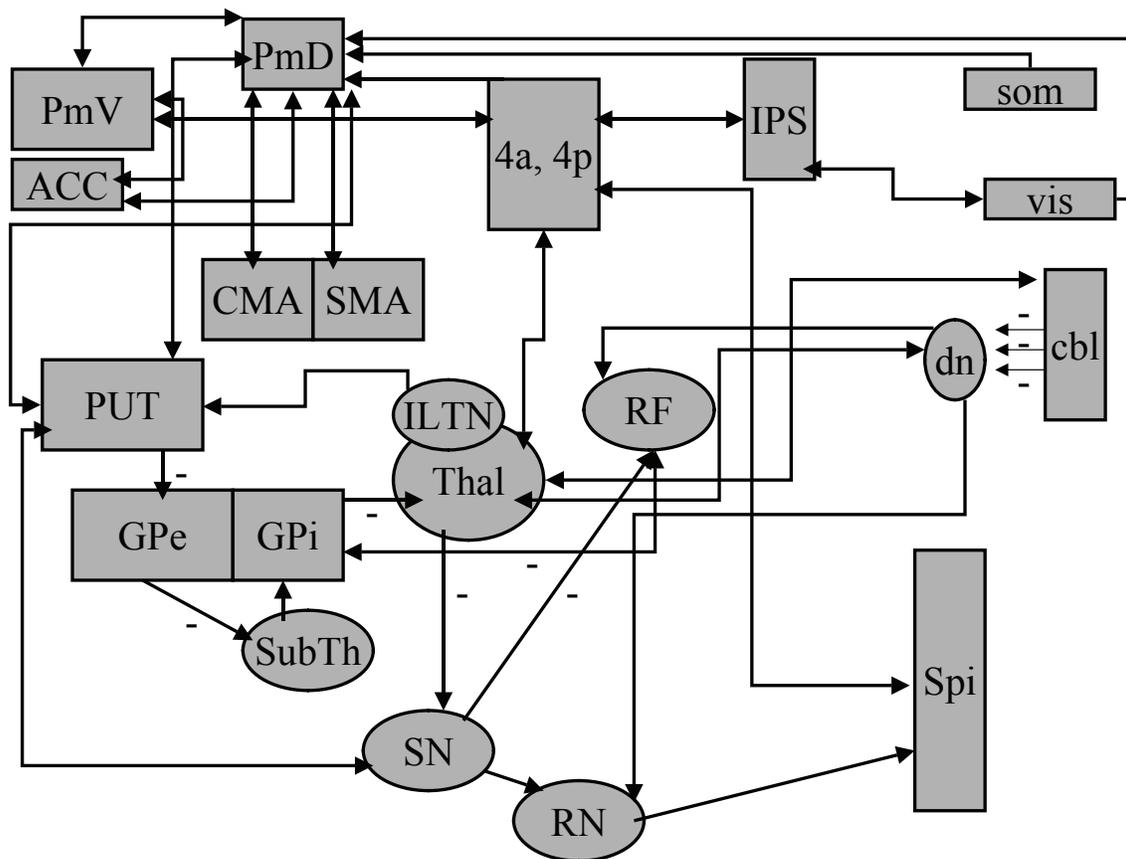


Figure 5 : A schematic representation of main structures involved in motor circuitry. Arrows indicate known anatomical connectivity between various cortical and subcortical areas. When known to be inhibitory, such connections are indicated by a dash (-). Most other connections are assumed to be excitatory. **legend:** 4a and 4p: Primary motor cortex; PmD: Dorsal premotor cortex; PmV: Ventral premotor cortex (including parts of the right inferior frontal gyrus); CMA: Cingulate motor area; SMA: Supplementary motor area; ACC: Anterior cingulate cortex; PUT; Putamen; GPe: Globus pallidus externa; GPi: Globus pallidus interna; SubTh: Subthalamic nucleus; RN: Red nucleus; Thal: Thalamus; ILTN: Intra-laminar thalamic nuclei; RF: Reticular formation; IPS; Intra-parietal sulcus; som: Somatosensory areas; vis: Visual areas; cbl: Cerebellum; dn: Dentate nucleus; Spi: Spinal cord.

delays to the second stimulus are comparable even when subjects respond to two stimuli from the same modality (visual). These psychophysical findings are in close conformity with what has been reported in literature over many decades (Telford, 1931; Vince, 1949; Welford, 1952). As the reaction time delays that occur in dual modality conditions are very likely to be due to occupancy of motor neuronal populations, we speculatively suggest that, even under the single modality dual RT conditions (such as the visual-visual dual RT task described in the experiment B in paper I) with inter-stimulus interval less than 400 ms, the RT delay for the proximate stimulus that we psychophysically observed, may be due to a mechanism that is likely to be similar to the occupancy of motor neuronal populations for a fixed, limited amount of time.

The RT tasks that we have investigated here are not simultaneous. Instead, they are near simultaneous, with the shortest ISI being 250 ms. The main reason for this is that at present, there is no unambiguous way to differentiate the possible masking effects that the simultaneous stimuli may impose on each other of cross modal masking, specifically between somatosensory and visual modalities (Pashler, 1994). There have been several reports in the literature that support the possibility that cross modal masking is a ubiquitous phenomenon than was previously thought. (Meredith and Stein, 1985; Meredith et al., 1987; Spence et al., 2000; Debowy et al., 2001; Messinger et al., 2001; Taylor-Clarke et al., 2002). Although it is known that masking effects occur at much shorter ISIs than 250 ms, i.e. specifically in the range of 20-50 ms, the above mentioned reports have indicate the possibility of cross modal masking effects at greater time intervals. Given that there have been reports that provide support for a recurrent feedback hypothesis of cross-modal integration, brain areas that are traditionally thought of as unimodal, like primary somatosensory cortex (SI) and secondary somatosensory cortex (SII), may only be so in terms of their afferent projections (Shimojo and Shams, 2001). Responses to a primary modality may be modulated by stimulation in a second modality via recurrent projections from multimodal areas. For example, neural responses to a visual target within unimodal visual cortex can be modulated by tactile events (Macaluso et al., 2000). Therefore, until it is possible to design experiments that would minimize cross modal effects, the study of interference may be limited to near simultaneous RT task conditions with ISIs that are longer than the time spans where masking may occur.

A pertinent example of simultaneous task performance concerns the simultaneous performance of motor tasks as in the case of a pianist playing with both hands. In this case, the motor tasks of the two hands are expected to interfere because of the attempted activation of the same neural populations in the SMA, CMA and basal ganglia, which are important in motor programming. When both hands play the same melody, it may be possible to use one motor program (which may be generated in the dorsal premotor cortex, the supplementary and pre supplementary motor areas, and fed forwards to the M1 in both hemispheres) and therefore to achieve some degree of perfection that lacks any discernible interference. However, if the two hands were to play two different melodies simultaneously (which may have to be generated in the dorsal premotor cortex, supplementary and pre-supplementary motor areas simultaneously and fed forwards separately to the primary motor cortex in the two hemispheres), this would produce interference, and the subsequent difficulty in achieving “perfection” even after many years of practice.

PHYSIOLOGICAL MECHANISMS OF DIVIDED ATTENTION IN RT INCREMENTS

Psychophysical results from the experiments described in paper I conclusively show that when subjects attend to two stimuli, reaction times are prolonged as compared to conditions when they attend to only one stimulus at a time. This appears to be due to a different mechanism than the one responsible for delays in the RT to the second stimulus when ISI is less than 400 ms. This is because, under dual RT conditions, even if all stimuli belong to the same modality (e. g. visual – see experiment B in Paper I), the RT to the second stimulus is still prolonged while the RT to the first stimulus is not. However, when this possibility was investigated with dual RT tasks, there was a major confound that affected the precise interpretation of the findings. When subjects respond to two stimuli, they have to attend to both stimuli, and, in fact perform two RT tasks as well. Therefore, it could be argued that the RT prolongation that was observed may be due to either one of these possibilities. A psychophysical experiment where subjects received two stimuli, but were required to respond only to the second stimulus avoided this confound as was described in experiment C paper I. There, although they divided attention between two stimuli, the RT tasks were essentially single tasks. As the Figure 6 shows, one component of prolongation of RTs was due to the division of attention between two stimuli as compared to selectively attending to a single stimulus from a single modality at a time.

Associated with these RT delays that are due to divided attention were the brain activations that occurred bilaterally in the cortical areas of caudal prefrontal and intra-parietal regions that have been reported in several studies previously (D'Esposito et al., 1995; Corbetta, 1998; Koechlin et al., 1999; Dove et al., 2000; Herath et al., 2001). Although an attempt was made, it was not possible to completely differentiate the behavioral and neural correlates of doing two tasks near simultaneously from divided attention in the experiment described in paper II (Herath et al., 2001). This is because, as mentioned earlier, in the behavioral tasks that we used in that study, subjects performed two motor RT tasks near simultaneously while dividing attention between them, thus obviating the possibility of differentiation between the two computations. In the imaging study reported in paper III, we resolved this issue by asking subjects to divide attention between two modalities while performing only a single motor RT task at a time. With this, we showed that the brain areas that are associated with the division of attention are very similar to what has been previously described in conditions associated with divided attention. This study therefore is the first to conclusively show that these fronto-parietal cortical areas are not only associated with sustained attention, but also with divided attention as well.

What could be the neurophysiological mechanism of RT increments caused by division of attention? Over the years, this particular question has never been directly addressed.

It is now well established that a canonical set of cortical areas are activated in circumstances when attention is divided, particularly when the visual modality is involved (Corbetta et al., 1991; Corbetta, 1998; Kastner and Ungerleider, 2000). Several pieces of evidence suggest that these cortical areas, by their connectivity to the thalamus, may have the capability to produce the delays in the reaction times to the first stimulus (RT1) that were observed as the behavioral correlate of divided attention. Firstly, there is evidence that the thalamic reticular neurons form a nexus on the cortico-thalamic pathways where different parts of the cortico-thalamic projections establish connectivity (Sherman and Guillery,

1996; Adams et al., 1997; Guillery et al., 1998; Sherman and Guillery, 1998; Guillery and Sherman, 2002). Secondly, it is currently accepted that the midbrain reticular formation (MBRF) is highly active and fires in a desynchronized manner when a subject becomes aroused and alert. Thirdly, EEG desynchronization and behavioral changes can be produced by electrical stimulation of the central mesencephalon, and more specifically the central tegmentum and the nucleus cuneiformis that form parts of the MBRF (Moruzzi and Magoun, 1949). It is also known that the MBRF has an inhibitory effect on the thalamic relay nuclei that are adjacent to the MBRF areas that are active (Skinner and Yingling, 1976; Yingling and Skinner, 1976). Therefore, a possible outcome of these connections in the reticular nuclei would be to provide inhibitory pathways that go from the reticular nucleus to the respective thalamic relay nuclei. Fourthly, the thalamic matrix neurons (Jones, 1998a, b) which are implicated in the maintenance of high frequency oscillations across widely distributed cortical areas by the virtue of their diffuse thalamo-cortical, and reciprocal cortico-thalamic connectivity (Jones, 1998a, b; Jones, 2001) are closely related functionally and anatomically, to the thalamic reticular neurons. Therefore, it is possible that, when a subject decides to divide attention, the activated neurons in the attentional network of the caudal prefrontal areas and the cortex of the intra-parietal areas may relay on the thalamic reticular neurons via the excitatory cortico-thalamic matrix neurons. This may then inhibit the thalamic sensory relay nuclei via projections from the reticular neurons that are inhibitory. The projections from the sensory relay nuclei to the respective primary and other sensory cortical areas is an essential prerequisite in order to produce behaviors such as motor responses. On the other hand, the intra-laminar thalamic nuclei, which are intimately associated with the reticular neurons, project to the caudate nucleus and the putamen that are important components of the motor circuitry. The interactions between these neurons may be potential candidates for causal mechanism of delayed RTs that are observed in conditions where attention is divided.

Over the years, attention has often been considered a limited resource commodity. As has been described before, one of the classical behavioral outcome measures of this attentional limitation has been the delays in reaction times, as the ones that we have reported in this thesis. In addition to the mechanism proposed above, there has been at least one effect to explain the physiological basis of attentional limitations. In a recent paper, electrophysiological evidence was presented to suggest that the attentional tuning of populations of neurons in human middle temporal (MT) cortex is far broader than the tuning of the same neuronal populations by their respective sensory inputs (Scannell and Young, 1999). The authors suggested that the consequence of this would be that the attentional tuning can influence the baseline firing of many cells, while only influencing the sensory response modulation of a very few cells. This broader attentional tuning of neurons with narrow sensory tuning has been claimed to make attention a limited resource commodity (Scannell and Young, 1999). As previously described, thalamo-cortical interplay has been claimed as an important modulator of attention. If attention can influence the baseline firing of neurons, and if attention itself is modulated by thalamo-cortical and cortico-thalamic neurons, these findings enable a clearer understanding of physical and biological limitations of attention at a neuronal level.

RT DELAYS CAUSED BY EFFECTOR ASSIGNMENT STRATEGIES

When subjects respond to stimuli in RT tasks, the brain must deal with several issues related to the motor control of the task. These include aspects associated with the stimulus to be responded to, planning the motor act itself, and any required or associated cognitive aspects of the motor task. Moreover, several reports discuss the possibility that neurons in the motor cortices signal not only the movement itself, but rather, several other aspects of a given movement (Cheney, 1985; Wise and Mauritz, 1985; Riehle and Requin, 1989; Riehle et al., 1997; Toni et al., 1999; Georgopoulos, 2000; Sanes and Donoghue, 2000; Li et al., 2001). One such aspect of activity reflected by neurons in the motor cortex is called the 'motor set' or the preparedness related activity. Although conceptually an abstract one, motor set or motor preparedness can be objectively demonstrated by increased, instructions related, anticipatory and preparatory activity in the primary motor and pre motor cortical neurons, that precede the actual movement (McCormack et al., 1967; Evarts and Tanji, 1974; Lecas et al., 1986). It is also known that motor set related neural activity could be modified by incoming sensory stimuli, or by instructions that the animal received before the task. Such modifiability of sets, or the invariant nature of motor neuronal activity that precede the actual execution of the motor task, allows selection of motor behavior depending on the instructions and decisions made by the animal (Evarts, 1974; Evarts and Tanji, 1974). Although previous evidence indicated that the set related activity of neurons is only limited to supra-spinal neurons, recently, it has been shown that the lower brain stem neural loops and the spinal neurons themselves can participate in such motor preparatory activities (Maier et al., 1998; Perlmutter et al., 1998; Fetz et al., 2000). This indicates that the spinal neurons can be biased, or 'made to be prepared' towards a particular population of anterior horn cell depending on the stimulus or the instructions that had been received. Biasing of anterior horn cells, and therefore an effector, by the sub-cortical neuronal loops and spinal neurons can be achieved by at least two ways. Firstly, if the effector is predetermined regardless of the stimulus/stimuli, then, the spinal assignment of an effector could be done prior to the arrival of the stimuli. This way, the assigned effector would be in a 'state of readiness' to respond as fast as possible as the stimulus is perceived, and the appropriate code from the cortical motor areas are relayed to the spinal cord. The other way to respond to a stimulus is to simply await the actual arrival of the stimulus, and then to assign the effector appropriately, according to the behavioral instructions. This will be the case if there is more than one effector available. In this situation, even if the stimulus –response mapping is wholly deterministic for each stimulus-response pair, the effector can not still be determined until a stimulus is perceived and the S-R map is determined by the brain. The consequence of this strategy will be that when subjects have to respond by assigning effectors *a posteriori* as compared to *a priori* assignment of effectors, there will be an increased RT in the former, compared to the latter.

From a behavioral point of view, it is important to note that in the paradigm used in Paper III, there were no alternatives: subjects were expected to respond to the second stimulus, and they did so. Accordingly, there was no stimulus selection. Did subjects 'select' a response when a stimulus to which they must respond follows a warning? Visual stimulus was deterministically linked to the response with one finger. The somatosensory stimulus deterministically linked to the response with another

finger. There were no alternatives. In the other condition with a visual and somatosensory stimulus, the same finger was used to respond to whatever the stimulus was. Again the subjects had no alternatives and understood the instructions as shown by psychophysical data.

Effect divided attention, specifying effectors a priori vs. a posteriori.

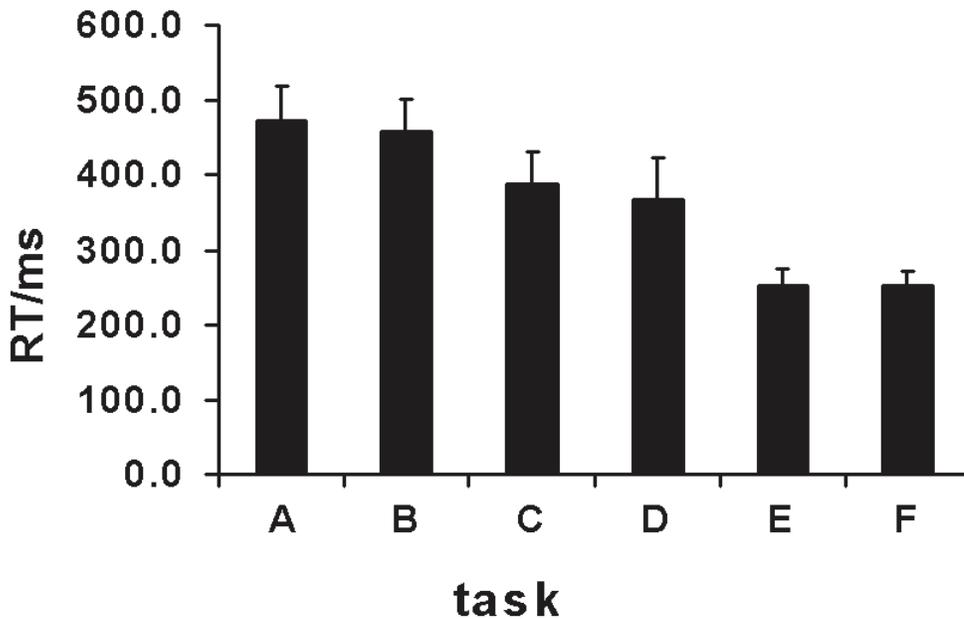


Figure 6: A = V-S TWO EFF som RT; B – V-S TWO EFF vis RT; C = V-S ONE EFF som RT; D = V-S ONE EFF vis RT; E = single vis RT; F = single som RT. Graph showing the mean reaction time performance in the different behavioral tasks that were used in the scanning experiment. Note that the RTs show the pattern that single RT << RT in dual signals with single effector << RT in the dual signals with two effectors. Error bars indicate SD.

As can be seen from the graph (Figure 6), when subjects received two stimuli and responded only to the second stimulus, there is a significant difference between the RTs simply depending upon whether they were able to specify the effectors *a priori* or not. Under these task constraints, the prolongation of RTs could be due to the different strategies that the subjects may have used. One intuitive strategy is to be engaged in a ‘gambling game’ where subjects decide *a priori* that the second stimulus would be, say, visual, and therefore the effector would be the index finger. However, if the second stimulus then turns out to be somatosensory, they have to reconfigure the response preparedness and then execute the correct finger flexion appropriately. As the neurons in the M1 and premotor areas require a approximately finite time period to complete one computation before they can be reconfigured for a new computation, (Fu et al., 1995), the occupancy of the motor preparedness caused by the “gambling strategy” may postpone the preparation and execution of the correct response finger. Such a scenario would also be consistent with the cortical field hypothesis (Roland, 1993; Roland

and Zilles, 1998; Roland, 2002a), that says that if two brain tasks make use of the same cortical fields, the tasks cannot be performed simultaneously. However, the psychophysical findings make it unlikely that the subjects resorted to a guessing game in responding to the stimuli. Firstly, the variance of the RTs was not significantly different. Secondly, as the average d' of 4.38 shows, there were very few false alarms. Therefore, the only likely possibility that explains the RT prolongation in the V-S TWO EFF task would be that the effector was specified only after the signal was perceived. In this case, if subjects have to use either the index or middle finger, they cannot in advance organize the sub-cortical motor loops, particularly the spinal network to accommodate both effectors. As it takes 90-110 ms to initiate and stabilize the spinal excitatory bias (Fetz et al., 2000), the RTs in the case of index finger/middle finger must be prolonged by approximately 100 ms compared to the condition in which only the index finger is used. Our psychophysical data corresponds closely to this explanation.

When we neuroimaged these tasks, we investigated the possibility that the V-S ONE EFF will produce higher BOLD signals in the motor structures as compared to the V-S TWO EFF condition. This would be reflected as increased BOLD signals in the motor areas 4a, 4p, the basal ganglia, and cerebellum. However, we did not observe such differences between the V-S ONE EFF and V-S TWO EFF conditions. This may be due to the possibility that there was no *a priori* preparatory activity in the supra-spinal areas during the V-S ONE EFF condition, because the ISI of less than 400 ms that followed the first stimulus of the pair was adequate for the preparatory activity to be generated anew in the sub-cortical and spinal neurons (Maier et al., 1998; Perlmutter et al., 1998; Fetz et al., 2000). Thus, there were no identifiable differences in brain activations of motor areas between the RT tasks. All RT tasks -single, dual as well and dual stimuli with single responses- activated a nearly identical set of motor structures to a similar spatial extent. There was adequate statistical power in the random effects analysis to conclude that this is not a false negative result. Therefore, one of the more parsimonious explanation for the RT delay that occurs when effector is to be specified *a posteriori* to the stimuli is that the delay is due to some processing that takes places in the spinal cord, which was outside the field of view of the scanner during the experiment. Therefore, one interesting possibility that is suggested by this finding is that in the brain, the index and middle fingers use common neuronal populations in the motor structures. This possibility is in line with several other similar findings that provided extensive evidence that finger representation in the human motor cortex is extensively overlapping (Alexander and Crutcher, 1990; Kawashima et al., 1994; Karni et al., 1995; Sanes et al., 1995; Roland and Zilles, 1996).

What is the meaning of the interpretation that RTs are prolonged when effectors have to be specified solely dependant on the stimuli as compared to the ability to specify effectors *a priori*? The most parsimonious answer would be that some brain processes are always organized serially. Therefore, if the effector is not pre-specified (by instructions or the intentions of the subject), then the final specification of the effector has to follow the arrival of the stimulus. In this case, the time necessary to assign the spinal neurons will be added to the reaction time, thus prolonging the RTs. This likelihood is possibly a generic one, and is therefore likely to be applicable in dual RT tasks as well. However, with the psychophysical experiments that we have performed so far, we cannot test this possibility.

There have been extensive discussions indicating that computing motor activity in the brain occurs in a parallel distributed manner (see, Kurata, 1994). The finding that the spinal interneurons themselves have instructional and set related activity has been claimed to be a further confirmation of this possibility. However, the finding that there are RT delays incurred during motor tasks (see the next paragraph), even in the presence of parallel distributed computational mechanisms that extend to the level of the spinal cord, there remain questions about the validity of claims of parallel distributed computing of motor tasks (Fu et al., 1993; Kurata, 1993; Crammond and Kalaska, 1994; Kalaska et al., 1997; Shen and Alexander, 1997a, b; Bastian et al., 1998; Crammond and Kalaska, 2000). More likely, the RT delays are suggestive of some form of serial processing of motor computations in certain instances.

ON S-R ASSOCIATIONS AND RT INCREMENTS

The physiological mechanisms that we have proposed to be the basis of RT increments under the specific task constraints are unlikely to be the only possibilities that lead to RT increases and error rates. This was evidenced by the findings from experiment D in paper I. There, subjects responded to two stimuli from two modalities, using deterministic S-R associations for each stimulus. S-R compatibility is a concept that variously describes the relationship between the characteristics of the stimulus and the response in terms of their congruency or how a stimulus and a response are mapped together. For instance, it is said that there is a high S-R congruence or compatibility between deterministic finger responses to simple sensory stimuli, where as the compatibility is supposed to be less for symbolic stimuli and their finger responses. In general, an S-R mapping is considered to be a part of a sensory motor transformation before a motor response to a sensory stimulus can be executed. In this context, RTs are reported to be shortest when stimuli and their responses are directly mapped to each other without any ambiguity. RT increases are known to occur when S-R pairs have lower degrees of compatibility or congruence as in the case of symbolic cues that evoke motor responses (Fitts and Radford, 1966), or when mapping between S-R pair is other than direct, as in the case of a response to a stimulus that is conditional upon another cue that yields additional information about the stimulus. As mentioned, the S-R compatibilities for each of the trial types used in the present series of experiments were very high and deterministic. The stimuli were not symbolic and were presumably directly mapped to the responses. Moreover, a very high stimulus-response compatibility and associations are known to reduce dual task interference (Georgopoulos et al., 1981). However, unlike a block design experiment where the temporal uncertainty for a given trial type is deterministic, experiment D of paper I showed that when different trial types are presented randomly, there were RT increases as compared to the presentation of same trials over a period of time. Why would this be? At present very little is known about how temporal uncertainty, or how uncertainty about which trial would come next affect RT task performance. Recently, it has been reported that synchronous spiking activity in the monkey motor cortical areas during preparation for action is not maintained at a significant level for more than 100-200 ms. Periods of synchrony instead appear to occur several times within the same behavioral trial (Riehle et al., 2000). What this means is that during an ongoing trial the motor cortical neurons do not

achieve an inherently stable firing level, but rather, they dynamically modulate their activity even within the same trial. Moreover, it is known that there are cells sensitive to arbitrary S-R mapping rules in the primary motor cortex of the monkey. These neurons code for temporal evolution of coding the stimulus, and capable of applying any remapping rules and deriving motor responses that could be identified in the temporal evolution of the neuronal activity during a trial (Georgopoulos, 2000). What this suggests is that each of these processes take a finite, measurable time to accomplish. The significance of these findings comes to light when one considers that changing from one dynamically active neuronal population to another requires an approximate period of time, because many movement parameters are serially processed. (Fu et al., 1995; Johnson and Ebner, 2000; Johnson et al., 2001). It must be remembered that it is unlikely that only the cortical neurons are engaged in computations associated with temporal uncertainty. Recently, an fMRI study had demonstrated that the activity in the caudate nucleus specifically increased when the predictability of trials decreased (Bischoff-Grethe et al., 2001). Another fMRI study showed that the prefrontal cortex, the parietal, and the temporal cortices are all involved in decision making when the level of uncertainty of trials increased (Paulus et al., 2001; Paulus et al., 2002). However, at present, it is difficult to explain how the RTs are prolonged when there is temporal uncertainty associated with deterministic S-R associations.

ERRORS DURING RT TASK PERFORMANCE

In the present series of experiments, error rates only increased when two conditions were fulfilled. First, it seems that subjects will had to be dividing attention between two sensory modalities as in experiment A, C, and D, described in paper I. Secondly, subjects were required to make rapid responses to two stimuli within 400 ms, as in Experiment A and D. The error rates, in the form of misses were increased only in experiments A and D, described in paper I. Clearly, divided attention itself, rapidly switching motor sets, or rapidly responding to stimuli within the same modality, does not increase the error rate. The neurobiological correlate of this phenomenon thus appears to be far more complex than the RT prolongation caused by each of these brain functions. The neural correlates of error detection and performance monitoring that may be important in dual task performance are currently localized mostly to the cingulate cortex (Badgaiyan and Posner, 1998; Carter et al., 1998; Carter et al., 1999; Bush et al., 2000; Kiehl et al., 2000). Carter et al have postulated that the increased cingulate activity in conflict monitoring situations is an indication that the brain is attempting to recruit additional association cortical areas such as the prefrontal cortex to resolve the conflict. The way to test this postulate would be to devise an imaging paradigm that would show sequential activation of the cingulate cortex, followed by the prefrontal activations during conflicting task situations, and the subsequent correction of conflict that can be validated behaviorally. Until this is achieved, the exact role of these error detection modules will remain unclarified, especially since there seem to be no psychophysical findings to indicate that the errors can indeed be corrected or that such attempts have in fact been made by the brain during the tasks.

ON LOCUS OF INTERFERENCE

Over the past several decades, experimental psychologists have hotly debated the causation of interference in dual tasks (Mewhort et al., 1991; Pashler, 1994; Pashler et al., 2001). They have put forward many theories and metaphors. Among these were the arguments that interference may occur at relatively early stages on the perceptual processing streams of the respective sensory signals, a theory popularly known as early selection theory of dual task interference (Broadbent, 1965). The main theme of the opposing theory was that interference occurs at later stages of stimulus processing, or even at the stages of response selection or execution (Karlin and Kastenbaum, 1968; Kahneman, 1973; Wickens, 1991). These two theories have been generally viewed as mutually exclusive. However, at present, these latter models are favored by the experimental psychologists. In the present series of experiments, we have almost exclusively focused on the possibility that interference occurs at a relatively later stage (such as in programming, selecting or executing a response) of the neurophysiological and computational hierarchy of responding to stimuli. Our findings do not discount the possibility that other kind/s of interference may occur at the early stages of stimulus processing, particularly owing to modulation by divided attention. In any case, our findings dispute the most prominently prevailing psychological theory of a unitary central bottleneck as the causative mechanism of interference phenomena. More importantly, we have demonstrated the possibility of looking at interference and other forms of RT delays without resorting to esoteric metaphorical schema. Instead, we have discussed the possibility to look at these phenomena from a neurophysiological point of view.

A number of neuroimaging studies reported before this thesis was written demonstrated the need to approach the investigation of dual task interference phenomena in a more systematic manner. Most of these studies utilized complex cognitive tasks under dual task settings (Klingberg and Roland, 1997; Klingberg, 1998; Adcock et al., 2000; Bunge et al., 2000; Dove et al., 2000; Bunge et al., 2001). When performed under dual task conditions, these complex cognitive tasks appeared to activate neuronal populations that are similar to those activated by each of the tasks singly. These activations were mostly located in the frontal cortex. A careful look at the findings from these studies would have indicated that the frontal cortex brain activations of dual tasks that subjects underwent, in fact, would have been the algebraic union of brain activations of single tasks. This is equivalent to having two overlapping cortical fields being active in the frontal cortex. As such, dual task interference that these authors had reported would correspond to the predictions of cortical field hypothesis. On the other hand, these former studies have not tested any explicit neurophysiological principles that would generalize across all dual task conditions. Rather, the emphasis has been to show increased brain activity that may or may not be associated with interference. These concepts has had a substantial impact on the thinking of brain activity related to interference effect. The actual neural mechanisms of interference cannot be explored by such an approach. To do so, a neurophysiological hypothesis that takes into account the layered and lateral microanatomy and circuitry of the cerebral cortex, and is independent of the spatial localizations of the increased brain activity is necessary. From a neurophysiological point of view, there is now ample evidence to show that the human brain engages in computations and information processing by producing dynamically organized neuronal populations behaving in a cooperative

fashion (Roland, 2002a). A cooperatively organized dynamic neuronal field computing a particular task lasts a few hundred milliseconds. It has been postulated that such dynamic fields decay and reorganize giving rise to newer fields depending on the computational requirements of the tasks being performed. The logical outcome of cooperative computations occurring across dynamically organized neural populations would be that two different brain tasks, A and B, requiring the participation of one or more major overlapping fields can not be performed simultaneously (Roland, 1993; Roland and Zilles, 1998). The consequence of trying to perform tasks, A, and B simultaneously under such circumstances would result in increased reaction times and/or error rates. This is the interference principle of the cortical field hypothesis. Investigating interference phenomena along specific neural hypotheses such as this, is an essential step towards understanding the general organizing principles of how the brain works.

The psychophysical finding of performance costs associated with division of attention and dual task interference has long been considered to be a serious limitation of the parallel processing capability of the brain. The findings that division of attention, changing conditional S-R associations, rapid switches between motor programs and performance of motor tasks under very short inter-stimulus intervals all leading to reaction time delays, raise fundamental questions about parallel processing as a general purpose mechanism in the human brain on a more physiological framework. This is because, if the brain were truly a parallel processor, concurrent simple RT tasks should not lead to interference. As a logical consequence, we see that findings of these experiments that were described in this thesis have raised the need to reconcile the notion of computational parallel processing with the interference phenomena that occur under concurrent multi-tasking situations. Investigating these phenomena with specific neurophysiological hypothesis would allow us to really elucidate why the human brain is limited in certain aspects of its information processing capabilities.

Conclusions

- Motor activity of RT tasks to simple stimuli, whether performed under dual RT conditions, or as single RT conditions, activate a nearly identical set of cortical and sub-cortical areas that include areas 4a, 4p, SMA, CMA, basal ganglia, and the ventral and the anterior thalamic nuclei.
- When humans rapidly respond to two stimuli that are presented within 400 ms of each other, the RT to the second stimulus is prolonged and the error rates are increased as compared to the situation where only one stimulus is presented at a time.
- The RT prolongation described above occurs irrespective of whether the stimuli belong to the same modality.
- The causal mechanism of the reaction time delay under dual reaction time conditions with ISI less than 400 ms appears to occur when cortical and sub-cortical regions such as areas 4a, 4p, SMA, CMA, basal ganglia, the ventral and the anterior thalamic nuclei are occupied by planning and execution of the first reaction time task for a finite length of time. This occupancy prevents the reaction time task to the second stimulus from accessing a nearly identical neuronal populations from these same brain regions. This finding is in concordance with the predictions of the cortical field hypothesis.
- When motor areas are occupied by the reaction time task related activity to the first stimulus, a cortical area located in the right inferior frontal gyrus shows increased activity. This increased activity is specifically correlated with the increased reaction time to the second stimulus.
- When compared to single RT tasks, dual RT tasks additionally activate a set of brain areas in the superior caudal parts of the prefrontal cortex and the cortex of the intra-parietal sulcus bilaterally.
- Under the dual RT task conditions, the prefrontal-parietal activity is the result of division of attention between two stimuli and not due to near simultaneous performance of RT tasks.
- The motor cortical activations and the brain activations related to divided attention are logically and anatomically dissociable. Such dissociability of functions appear to be a general property of the functional organization of the brain.
- Putative motor cortical occupancy and divided attention prolong RTs by different physiological mechanisms.
- When humans assign motor effectors solely dependant on the reception of a stimulus as compared to *a priori* assignment of stimuli, this too can cause a prolongation of RTs, but not error rates. This is very likely to be due to the essentially serial nature of sensory-motor transformation, and therefore is an additional physiological mechanism of RT prolongation when subjects receive multiple stimuli near simultaneously.
- RT increments observed during dual RT tasks may also occur when subjects are faced with temporal uncertainty of stimuli, particularly when this requires them to rapidly change the S-R mappings in order to produce rapid RTs to stimuli.
- Neurophysiological mechanisms and correlates of errors during RT task performance remain unclear at present.
- The above conclusions show that dual task interference (RT delays, and increased error rates) can be investigated using neurophysiological hypotheses, without recourse to metaphorical models and descriptions.

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