Progress in Neurobiology xxx (2013) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Progress in Neurobiology

journal homepage: www.elsevier.com/locate/pneurobio

Inhibition and impulsivity
Behavioral and neural basis of response control

Andrea Bari *, Trevor W. Robbins

Behavioral and Clinical Neuroscience Institute, Department of Experimental Psychology, University of Cambridge, Cambridge CB2 3EB, UK

ARTICLE INFO

Article history:
Received 20 April 2012
Received in revised form 24 May 2013
Accepted 26 June 2013
Available online xxx

Keywords:
Inhibition
Impulsivity
Go/no-go
Stop-signal task
Delay discounting
Reversal learning
Executive functions
Prefrontal cortex

ABSTRACT

In many circumstances alternative courses of action and thoughts have to be inhibited to allow the emergence of goal-directed behavior. However, this has not been the accepted view in the past and only recently has inhibition earned its own place in the neurosciences as a fundamental cognitive function. In this review we first introduce the concept of inhibition from early psychological speculations based on philosophical theories of the human mind. The broad construct of inhibition is then reduced to its most readily observable component which necessarily is its behavioral manifestation. The study of 'response inhibition' has the advantage of dealing with a relatively simple and straightforward process, the overriding of a planned or already initiated action. Deficient inhibitory processes profoundly affect everyday life, causing impulsive conduct which is generally detrimental for the individual. Impulsivity has been consistently linked to several types of addiction, attention deficit/hyperactivity disorder, mania and other psychiatric conditions. Our discussion of the behavioral assessment of impulsivity will focus on objective laboratory tasks of response inhibition that have been implemented in parallel for humans and other species with relatively few qualitative differences. The translational potential of these measures has greatly improved our knowledge of the neurobiological basis of behavioral inhibition and impulsivity. We will then review the current models of behavioral inhibition along with their expression via underlying brain regions, including those involved in the activation of the brain's emergency 'brake' operation, those engaged in more controlled and sustained inhibitory processes and other ancillary executive functions.

Contents

Abbreviations: 5-CSRTT, 5-choice serial reaction time task; 5-HT, serotonin; ACC, anterior cingulate cortex; ADHD, attention deficit/hyperactivity disorder; BA, Brodmann area; DA, dopamine; DNAB, dorsal noradrenergic bundle; DRD2, dopamine receptor 2 gene; ERP, event-related potentials; FEF, frontal eye field; IFC, inferior frontal cortex; IFG, inferior frontal gyrus; IFJ, inferior frontal junction; LC, locus coeruleus; M1, motor area 1; MDMA, 3,4-methylenedioxy-N-methylamphetamine; MRI, magnetic resonance imaging; NE, norepinephrine; OCD, obsessive-compulsive disorder; OFC, orbitofrontal cortex; Pre-SMA, pre-supplementary motor area; PFC, prefrontal cortex; RT, reaction time; SMA, supplementary motor area; SSD, stop-signal delay; SSRI, selective serotonin reuptake inhibitor; SSRT, stop-signal reaction time; SST, stop-signal task; STN, subthalamic nucleus.

* Corresponding author. Present address: Department of Neurosciences, Medical University of South Carolina, 173 Ashley Ave, BSB 409 Charleston, SC 29425, United States. Tel.: +1 8438134839.
E-mail address: andbari@gmail.com (A. Bari).

0301-0082/$ – see front matter © 2013 Published by Elsevier Ltd.
http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

1. Historical introduction

In the words of the father of American psychology William James (1842–1910) inhibition [Lat. *inhibere*, to restrain] is "*. . . not an occasional accident; it is an essential and unremitting element of our cerebral life*" (James, 1890; p. 583). Scientists and philosophers have long been interested in the nature of inhibitory processes at the psychological, neurophysiological and cognitive level. Plato's allegory of the human soul viewed as a charioteer driving a chariot pulled by two horses having opposite characters, well represents the inhibitory function of will. In order of being able to drive the chariot in the intended direction, the inclination of the two horses has to be tightly controlled. Similarly, in 1650 Descartes wrote that: "*if anger makes us rise our hand to strike, our will can usually hold it back; if fear incites us to run away, our will can stop us, and so on with the other passions*" (as cited in Diamond et al., 1963; p. 15). Inherent to this philosophical view of inhibition is the existence of a choice between conflicting courses of action, which has been extensively discussed in their influential book 'Inhibition and choice' by Diamond et al. (1963). The concept of inhibition was introduced in the scientific literature at the beginning of the 19th century to explain a large number of phenomena, from simple spinal reflexes to more abstract psychological processes, although it became commonly used in neuroscience only in the second half of the century (Smith, 1992). Before then inhibition was thought to derive from some form of excitation or by its cessation (Macmillan, 1992), and even when directly observed during controlled experiments, it was ignored, rejected as an error in the experimental procedure or as deriving from fatigue ('exhaustion') of the nerves (Meltzer, 1899).

1.1. Development of the concept of inhibition

> "When physiologists have solved the problem of inhibition, they will be in a position to consider that of volition". (Morgan, 1891; p. 461)

According to Smith (1992) the word 'inhibition' initially made its appearance in the scientific literature as the mechanism by which intellect controls passions and the will wins over impulses, in an intellectual context influenced by Plato and Aristotle's moral psychology. In the first half of the 19th century, making the first steps towards an empirical psychology with his controversial work, Franz Joseph Gall thought that "*The laws of nature, for instance, ordain that the faculties of an inferior order should obey those of a superior order. . .*" (Gall, 1835; Vol. I, pp. 230–231). Although Gall did not explicitly consider inhibitory interactions between the different 'faculties', his hierarchical view of mental processes resembles most modern conceptualization of inhibitory control. On the contrary, the German philosopher-psychologist Herbart (1776–1841) extensively used the term inhibition ('hemmung') in a non-hierarchical fashion to describe the force that prevents cognitive contents to aggregate indiscriminately by keeping dissimilar ideas momentarily out of consciousness (Dunkel, 1970; Macmillan, 1996). However, while he used the concept of 'associative inhibition' as an umbrella term for what we now call proactive and retroactive inhibition in the context of learning and memory, various theorists after him tried to explain the loss of consciousness during hypnosis as some sort of cerebral inhibition (Bramwell, 1903). In psychiatry, the concept of inhibition was soon adopted to describe the behavior that characterizes certain mental disorders. As reported by Macmillan, in 1843 the German psychiatrist Griesinger "*adopted a straightforward physiological explanation*" suggesting that "*Ideas passed into normal action whenever they were not hindered by this* [volitional] *control but in the two main classes of insanity – the depressive and the excited – there was either too much or not enough inhibition, respectively. In this conception, will and inhibition were virtually equated and symptoms were interpreted physiologically*" (Macmillan, 1996; p. 9). The common idea in the early theorizing about inhibition seems very much linked to the concepts of will and consciousness, such that only with high levels of self-awareness is possible to exert (or contrast) inhibitory control over one's behavior. Things were different in neurophysiological theories.

One of the first observations of the inhibitory action of nerve impulses was made by John and Charles Bell in the muscles of the eye. They did not use the term inhibition and wrote as a footnote: "*The nerves have been considered so generally as instruments for stimulating the muscles, without thought of their acting in the opposite capacity. . .*" (Bell and Bell, 1827; Vol. 2, p. 223). Similarly, drawing from his experiments on the frog's sciatic nerve stimulation, in 1838 Volkmann wrote: "*It becomes clear* [. . .] *that the brain contains the cause for the hindrance in the activation of the nervous principle. . .*" (as in Smith, 1992; p. 77). However, it is generally acknowledged that it was the early observations on the effects of vagal nerve stimulation on heart rate that posed the foundations for the first theories on the inhibitory action of nerve impulses (Gaskell, 1886; Weber and Weber, 1966). This phenomenon was first observed by Volkmann, who subsequently dismissed it as resulting from an invalid procedure (Volkmann, 1838a,b, 1842). Weber and Weber (1845) made the same observation, but were the first to define it 'inhibition', whereas the concept of 'inhibitory system' in physiology was first discussed by Lister in a communication to the Royal Society of London (Lister, 1858). Thus, while Smith (1992) emphasizes the description of peripheral inhibition by the Weber brothers in 1845, according to MacLeod et al. (2003), the observation made by Sechenov (1863) that stimulation of certain areas of the frog's brain inhibits spinal reflexes can be considered the point of origin of the concept of (central) inhibition in physiology. Finally, in 1874, the concept of inhibition was included by the father of experimental psychology Wilhelm Wundt (1904) in his seminal textbook: "*The two mutually supplementary forms of energy that we designated, from their mechanical effects, excitation and inhibition* [. . .] *appear throughout as the simple substrate of nervous function.*" (Vol. 1, p. 324); "*The whole course of the* [nerve] *stimulation is then dependent upon the constantly varying play of excitation and inhibition.*" (Vol. 1, p. 70).

Still widely cited, the classical definition of inhibition formulated by Brunton in 1883 is reported in the Oxford English

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Dictionary (c.f., Pilkington and McKellar, 1960) and, although it refers to inhibition as a physiological concept, it can be applied to a variety of phenomena: *"By inhibition we mean the arrest of the functions of a structure or organ, by the actions upon it of another, while its power to execute those functions is still retained, and can be manifested as soon as the restraining power is removed. It is thus distinguished from paralysis, in which the function is abolished, and not merely restrained."* (Brunton, 1883; p. 419).

However, by the end of the 19th century, the concept of inhibition was still not universally accepted. Meltzer wrote in 1899 that "*. . . the phenomenon of inhibition is distrusted in physiology, had to fight on general grounds at every step for the establishment of any new fact, and has still to fight for recognition as an independent vital force.*" (Meltzer, 1899; p. 661). Nevertheless, it is possible to recognize in the work of many authors the principle that higher-order brain structures control lower-order ones, consistently with the nowadays accepted role of phylogenetically recent brain regions (prefrontal lobes) in restraining and controlling primitive instincts and passions originating in older brain structures. The idea that attention and inhibition are closely related was also already present in the early psychophysiological theories (e.g., Ferrier, 1876; Volkmann, 1838a). It was only at the turn of the 20th century that the concept of inhibition was widely accepted in neurophysiology and linked to the name and works of Sherrington (1906). He was awarded the Nobel Prize in 1932 for Physiology or Medicine for his work on neural inhibition as a fundamental principle in the organization of the central nervous system. The beginning of the 20th century was also the turning point for the concept of inhibition in the behavioral sciences and the period in which the first attempts to systematically classify different types of inhibition were made. Meltzer (1899) published a practical classification of forms of inhibition for physiologists and, three decades later, Skaggs (1929) presented a systematic description of the major categories of inhibition in psychology making the first distinction between voluntary (or active) and involuntary (or passive) forms of inhibition. In their psychological dictionary, English and English (1958) listed at least 22 types of inhibition, some of which are summarized in Table 1.

In his work on conditioned reflexes, Pavlov (1927; p. 377) described excitation and inhibition "*. . .as two fundamental properties, the most important manifestations of activity, of the living nervous elements.*" The concept of inhibition was thoroughly developed by Pavlov with the distinction between different subtypes including external (or indirect) and internal (or direct) inhibition (Reid, 1960). His 'external inhibition' is more akin to passive avoidance (Ursin, 2005) and primarily originates outside the brain regions where the reflex response is initiated. Stimuli eliciting orienting or defensive responses would be particularly powerful generators of external inhibition. On the other hand, 'internal inhibition' corresponds to what is usually called 'extinction' (misleadingly, according to Pilkington and McKellar, 1960) of a conditioned response. Pavlov thought that as a result of extinction training a previously excitatory conditioned stimulus becomes inhibitory under definite conditions, rather than merely returning to its neutral pre-conditioning state. On the contrary Konorski, who first described operant conditioning, proposed that the phenomenon of extinction – and thus pavlovian internal inhibition – is based on the formation of excitatory associations between antagonistic centers (Konorski, 1967). He distinguished between three types of inhibitory training: 'retroactive inhibition' akin to reversal learning, 'drive inhibition' similar to extinction and 'motor act-inhibition' which occurs when a response has to be withheld in order to avoid punishment or obtain a reward (Ursin, 1976). Both Pavlov and Konorski have used various methods to quantify conditioned inhibition such as the 'summation' and the 'retardation-of-acquisition' procedures (see Rescorla, 1969). Another behaviorist influenced by Pavlov's thinking was Hull who, although concerned with instrumental learning rather than classical conditioning, distinguished three types of inhibition: reactive, conditioned and the aggregate inhibitory potential, which is the sum of the first two (Hull, 1943). It transpires from these examples that the dominant tendency in the early behaviorism and learning theories was moving toward a more frequent use of the concept of inhibition to explain overt behavior. Harlow and Hicks (1957) went further pointing out that errors are responses made to irrelevant aspects of a situation and that become inhibited during the learning process (Pilkington and McKellar, 1960). Thus, Harlow's learning theory does not need to postulate the formation of new associations by excitatory mechanisms, but only the inhibition of inappropriate responses (Fig. 1).

In the psychoanalytic works of Freud, the concept of inhibition has always been problematic (Macmillan, 1992). He defined inhibition as *"the expression of a restriction of an ego-function. A restriction of this kind can itself have very different causes"* (p. 6) and linked it to the concept of anxiety: *"Some inhibitions obviously represent a relinquishment of a function because its exercise would produce anxiety"* (Freud, 1959; p. 4). However, the earlier Freudian conception of inhibition is more akin to a lack of excitation – "the libido may simply be turned away" – whereas later he describes a model of 'lateral' cathexis (Freud, 1966 as cited in Macmillan, 1992) through which the ego exercises its inhibitory functions (Fig. 2). Somewhat related to Freud's view, Skinner thought of inhibition as the result of excessive punishment (Skinner, 1953). It is probably with Eysenck that the concept of inhibition became central to psychological theories (Pilkington and McKellar, 1960) particularly due to his work on the differences between introverts and extraverts, which has had a great influence on modern personality research (Eysenck, 1947; Gray, 1972). Perhaps of greater significance for the present discussion is the concept of inhibition elaborated by Hughlings Jackson (1931a) who considered response inhibition as being the prerequisite for the successful occurrence of an antagonistic or incompatible response. In Jacksonian terms 'release of function' is the result of the removal of inhibitory control from the higher centers over the lower centers of the nervous system (Pilkington and McKellar, 1960), an idea originally introduced by Anstie (1864) and empirically demonstrated by Head and Holmes (1911) who observed excessive response output after the destruction of fibers running from the cortex to the thalamus.

1.2. The search for the neural 'locus' of inhibition

> "This inhibitory influence of higher over lower nerve centres we shall see reason to extend into the region of the encephalic centres themselves." (Ferrier, 1876; p. 18)

Since the first empirical studies, the focus of scientific enquiries has been on the search for a locus of inhibition in the nervous system. Sechenov (1863) first claimed the discovery of a central inhibitory locus in the brain stem, while others came to the conclusion that there are no specific inhibitory centers, but the activity of higher centers represses that of lower ones (e.g., Goltz, 1869). Wundt commented on Sechenov's hypothesis of inhibitory centers of the brain by stating: *"But if any given sensory excitation may be inhibited by the stimulation of any other sensory element, the sphere of inhibition – as Goltz justly observed – becomes coextensive with the sphere of sensory excitation, and the assumption of specific inhibitory centres falls to the ground."* (Wundt, 1904; p. 91). In his early work, Wundt proposed an 'intracellular' theory of inhibition where stimuli that reach the central part of a nerve cell have inhibitory effects, whereas those reaching the periphery are predominantly excitatory and thus he thought that there is no need to postulate the existence of special inhibitory centers. Later,

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Table 1
Descriptions of the different uses of the term 'inhibition' and its subtypes directly quoted or adapted from the cited source. Where possible, the original terminology has been preserved.

Entry	Source	Description
Inhibition	English and English (1958, p. 262)	Restraining or stopping a process from continuing or preventing a process from starting although the usual stimulus is present; or the hypothetical nervous state or process that brings about the restraint A mental condition in which the range and amount of behavior is curtailed, beginning or continuing a course of action is difficult, and there is a peculiar hesitancy as if restrained by external agency The process whereby an instinctual process is prevented from coming into consciousness by the activity of the superego
	Meltzer (1899, p. 661)	A temporary diminution or abolition of a vital activity brought about by an internal or external stimulus
	Skaggs (1929, p. 311)	Some sort of interference exerted by one mental process upon another Voluntary: an active, self-conscious effort which results in inhibition Involuntary: any form of inhibition which is not the direct issue of an effortful conscious process. It acts on a passive level and may be a negative aspect of a positive voluntary process
	Konorski (1967, p. 312)	A definite response of the organism (either peripheral or intercentral) elicited by a given stimulus and mediated by a given process in the nervous system is decreased or abolished by another central process produced by another stimulus, or even by the same stimulus if its physiological role has been changed
Associative inhibition	English and English (1958, p. 47)	The weakening or blocking of an associative bond when its cue item becomes associated to anew response The difficulty of forming associative bonds because of prior associations
Central inhibition	English and English (1958, p. 262)	Inhibition of nerve impulses by a process or processes within the central nervous system
Conditioned (or differential) inhibition	Pavlov (1927, p. 68)	A new stimulus is occasionally added to the conditioned stimulus and this combination is never followed by the unconditioned stimulus [i.e., reinforcement]. The new stimulus gradually makes ineffective the presentation of the conditioned stimulus, although this latter retains its full power when singly applied
Conditioned inhibition	Hull (1943, p. 300)	Stimuli closely associated with the cessation of a response become conditioned to the inhibition associated with the evocation of that response, thereby generating conditioned inhibition
Connective inhibition	English and English (1958, p. 263)	The increased difficulty in recalling separate parts that is experienced after the parts have been grouped into a connected whole
Cortical act-inhibition	Stanley and Jaynes (1949, p. 26)	The rising of the synaptic threshold of those neural units necessary for the execution of an observable response-pattern
External inhibition	Pavlov (1927, p. 44)	A weakening or complete disappearance of the reflex [conditioned] response due to the appearance of a disturbing factor or a strong, unusual stimulus at the time of application of the conditioned stimulus. The investigatory reflex is excited and the conditioned reflex is in consequence inhibited
Inhibition of return	Posner and Cohen (1984, p. 541)	A peripheral visual stimulus both summons attention and serves to inhibit the processing of further information at that position in space
Inhibitory potential	Hull (1943, p. 319)	Associated with every reaction potential there exists an inhibitory potentiality which oscillates in amount from instant to instant according to the normal "law" of chance
Internal inhibition (Extinction)	Pavlov (1927, p. 68)	In extinction the positive conditioned stimulus is temporarily transformed into a negative or inhibitory one by the simple method of repeating it several times in succession without reinforcement. [Internal inhibition includes also inhibition of delay, differential inhibition and conditioned inhibition]
Latent inhibition	Lubow and Moore (1959, p. 416)	Nonreinforced pre-exposure to a stimulus results in a rate of conditioning which is slower than to a novel stimulus
Lateral inhibition	Levine and Brown (2007, p. 282)	Mutual inhibition, directly or indirectly, between neurons or node at the same level of processing
Proactive inhibition	Whitely and Blankfort (1933, p. 852)	The detrimental influence of a condition introduced prior to learning upon a subsequent recall
Reactive inhibition	Hull (1943, p. 300)	Whenever a reaction is evoked in an organism there is created as a result a primary negative drive; this has an innate capacity to inhibit the reaction potentiality to that response; the amount of net inhibition generated by a sequence of reaction evocations is a simple linear increasing function of the number of evocations; and it is a positively accelerated increasing function of the work involved in the execution of the response; reactive inhibition spontaneously dissipates as a simple negative growth function of time
Retroactive inhibition	Muller and Pilzecker (1900, p. 179)	The processes that serve the formation of associations in a list of syllables continue for some time after reading of the list, but they can be weakened by another mentally effortful task during this time resulting in an inhibition
Social inhibition	English and English (1958, p. 263)	A restraint upon behavior by group standards or by overt group action
Inhibitory reflex (or reciprocal inhibition)	English and English (1958, p. 263)	The decrement in the activity (tonus) of a muscle that follows the excitation of its antagonist

Q39 Hull, C. Ed (1943) *Principles of Behavior*. Appleton-Century-Crofts: New York.
Levine, D. S. and Brown, V. R. (2007) Uses (and abuses?) of inhibition in network models. In: *Inhibition in cognition*. Eds. D. S. Gorfein, C. M. MacLeod. American Psychological Association: Washington, DC.
Lubow, R. E. and Moore, A. U. (1959) Latent inhibition: the effect of nonreinforced pre-exposure to the conditional stimulus. *J Comp Physiol Psychol* **52,** 415-419.
Muller, G. E. and Pilzecker, A. (1900) Experimentelle Beiträge zur Lehre vom Gedächtniss. *Zeitschrift für Psychologie und Physiologie der Sinnesorgane. Ergänzungsband* **1,** 1-300.
Posner, M. I. and Cohen, Y. P. C. (1984) Components of visual orienting. In: *Attention and performance X*. pp. 531-556. Eds. H. Bouma, D. Bouwhuis. Lawrence Erlbaum: London.
Whitely, P. L. and Blankfort, G. (1933) The Influence of Certain Prior Conditions Upon Learning. *Journal of Experimental Psychology* **16,** 843-853.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

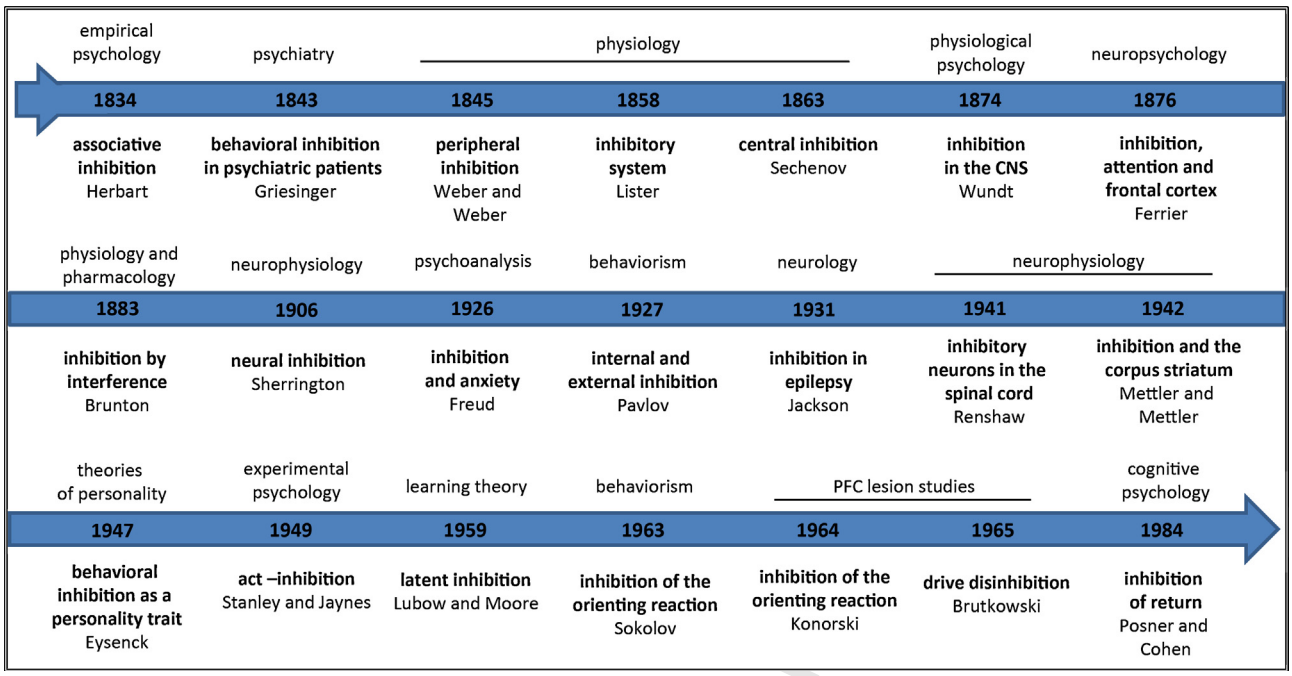

Fig. 1. Representative timeline showing some of the most important publications that had a strong impact on the development of the concept of inhibition in the 19th and 20th centuries.

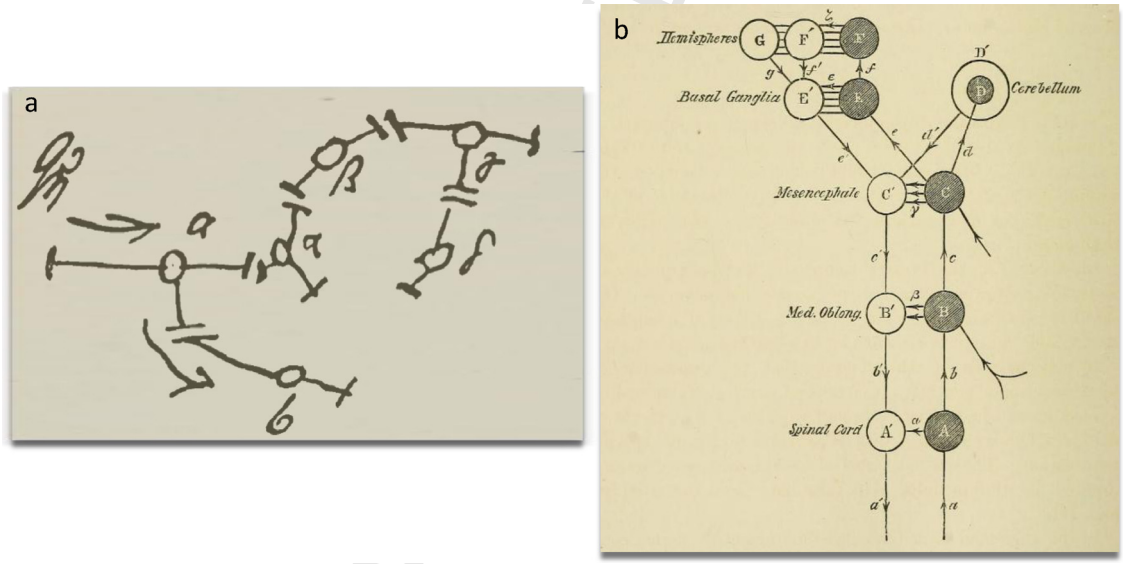

Fig. 2. a) The diagram represents Freud's concept of the inhibitory mechanism. Q_n is the neural energy (excitation) that is supposed to flow from neuron *a* (which contains an unpleasant memory) to neuron *b* (the "key neurone" that produces negative feelings if excited). Q_n is thus diverted elsewhere to other neurons (α, β, γ, δ), which include the ego (Freud, 1895). b) Ferrier's "Schematic Diagram of the Cerebro-spinal Nerve-centers" where he identifies the frontal regions (G) as "inhibitory-motor centers", whereas (F) and (F′) represent the sensory and motor regions of the cerebral hemispheres (Ferrier, 1876; Fig. 58, pp. 290, 294).

inhibition was at the very heart of Wundt's theory of apperception and the central function of the 'apperceptive organ' was to inhibit sensory information that was not the focus of attention (Diamond et al., 1963).

The first to attribute explicitly the faculty of inhibition to the frontal lobes of the brain was David Ferrier (1876, 1878; Fig. 2). He wrote: *"In proportion to the development of the faculty of attention are the intellectual and reflective powers manifested. This is in accordance with the anatomical development of the frontal lobes of the brain, and we have various experimental and pathological data for localizing in these the centres of inhibition, the physiological substrata of this psychological faculty."* (Ferrier, 1876, p. 287) and *"But besides the power to act in response to feelings or desires there is also the power to inhibit or restrain action, notwithstanding the tendency of feelings and desires to manifest themselves in active motor outbursts"* (Ferrier, 1876, p. 282). Ironically Ferrier withdrew his theory in later works (Diamond et al., 1963; Macmillan, 1992): *"It is not, however, necessary to assume, as Setschenow and others have done, that there is anything specific in this restraining or inhibitory action of the encephalic centres, or that there are special inhibitory centres in the brain."* (Ferrier, 1886; p. 70). Although Ferrier's hypothesis was prematurely abandoned, subsequent experimental data supported his argument about the inhibitory role of frontal areas. For example, lesion of the prefrontal cortex (PFC) was demonstrated to

interfere with the ability of laboratory animals to perform delayed response tasks (Jacobsen, 1936; Pribram et al., 1952; Weiskrantz et al., 1960), and to cause extreme hypermotility (French, 1959a,b) and perseveration (Mishkin, 1964). However, the pattern of deficits observed in different species after frontal ablation was not precisely defined and scientists ambiguously described it with expressions such as 'inertia of the excitatory process' (Konorski, 1957, as in Brutkowski, 1965) or 'lack of act-inhibition' (Stanley and Jaynes, 1949).

Summarizing the data available at his time, Brutkowski wrote that "... it has been hypothesized that a decreased ability to suppress the existing preferences and aversions, or the loss of inhibition of competing response tendencies is the basic impairment produced by frontal lobe damge [sic damage] ..." (Brutkowski, 1965; p. 732). Brutkowski also noted that this disinhibition not only caused increased general responsiveness or hyperactivity, but also emotional hyperexcitability which he thought may be the consequence of the loss of inhibitory control of cortical areas on hypothalamic centers. This led him to distinguish between 'response perseveration' (the inability to shift from one response to another), linked to damage of the prefrontal-caudate-subthalamic-hippocampal system, and 'drive disinhibition' (more related to motivational and emotional process) associated with a prefrontal-hypothalamic-amygdaloid complex (Brutkowski, 1965). This latter conceptual subdivision is somewhat similar to the one we will make below based on contemporary models of behavioral inhibition. Finally, bilateral ablation of the striatum was also found to have similar effects to those of PFC lesions, which led Mettler and Mettler (1942) to conclude that "... the striatum is an inhibitory mechanism, subject to cortical control and forming a significant link in the inhibitory path from the cortex to the motor neurone." (p. 250).

Since the first observations of the inhibitory role of cortical and hypothalamic areas on spontaneous and evoked motor activity in anesthetized animals at the end of the 19th century, scientists have sought to associate different forms of inhibition to specific brain regions, whereas many believed that inhibition was a general and fundamental function of the cortex (e.g., Stanley and Jaynes, 1949; Tower, 1936). Several other brain areas including basal ganglia (Jung and Hassler, 1960), hippocampus (Kimble, 1968) septal nuclei (Ellen and Powell, 1962) and cerebellum (Moruzzi, 1950) were described as having inhibitory functions since their destruction would cause hyperkinetic syndrome, over-responding or disinhibition. The search for inhibitory loci in the brain, however, was pursued not only by lesion experiments but also through electrical stimulation techniques (Delgado, 1964). Magoun and Rhines (1946) considered the brainstem reticular formation to be the converging area for inhibitory commands from the cortex (McCulloch et al., 1946) and cerebellum (Hare et al., 1936) before they are conveyed to the spinal cord, whereas Kaada hypothesized that inhibitory commands were funneled downward through the hypothalamus (Ursin, 1976). Kaada (1951) obtained strong somato-motor inhibition by stimulating several brain areas including the orbital cortex, the anterior cingulate gyrus and subcortical structures (Pribram, 1961). The effect of brain stimulation on motor activity was so general that Hunter and Jasper (1949) defined it as 'arrest reaction'.

More recently, scientists have begun exploring more defined forms of inhibition by using *ad hoc* tasks that explicitly measure the ability to suppress pre-potent responses rather than automatic reflexes. In support of a prefrontal locus for inhibition, single-unit recordings obtained from non-human primates revealed the role of the principal sulcus – a PFC region corresponding to Brodmann area (BA) 46 – in modulating inhibitory performance during go/no-go tasks. In addition, stimulation of this same area led to reduced activity in the primary motor cortex and response suppression (Sasaki et al., 1989). Further evidences of the inhibitory function of frontal areas have been obtained in human subjects by using a variety of techniques such as magnetoencephalography (Sasaki et al., 1993), electroencephalography (Gemba and Sasaki, 1989; Jodo and Kayama, 1992), event-related potentials (van Boxtel et al., 2001) and positron emission tomography (Kawashima et al., 1996). On the other hand, the importance of the basal ganglia in response suppression was first demonstrated by electrical stimulation of the dog caudate nucleus by Danilewsky in 1875 (Delgado, 1964). The inhibitory role of these subcortical nuclei is also supported by the strong motor inhibition caused by stimulating neurons just outside of the globus pallidus – the output structure of the basal ganglia – in monkeys (Horak and Anderson, 1984).

1.3. Defining cognitive and behavioral inhibition

> "... while we may admit that control of movement is merely a control of ideas, the involving of motor mechanisms gives these forms of inhibition a certain descriptive significance and distinctiveness." (Skaggs, 1929; p. 312)

It is clear from the historical introduction that the concept of inhibition has been invoked to describe a wealth of phenomena. Due to the wide range of meanings attributed to the term inhibition, Pilkington and McKellar (1960) recommended to accompany it with some qualifying adjective in order to clarify the intended meaning and the level of analysis. It is following this recommendation that we will try to better define the main focus of the discussion that follows in the next sections. Before that, however, we will briefly review the most common uses of the concept of inhibition in the broad literature. Although these various concepts overlap to some extent, a sharp distinction can be drawn between neural (both in the physiological and connectionist sense) and other kinds of inhibition (MacLeod, 2007). This is not to say that we have to abandon one for the study of the others, but that they belong to different levels of analysis (MacLeod et al., 2003). For instance, it is not easy to relate synaptic inhibition to inhibitory interactions between different brain areas or to the concept of inhibition at the behavioral level (Ursin, 1976). However, research on neural and cognitive functioning has been symbiotic especially in this field of study: principles of neural inhibition have been used to describe the properties of hypothetic executive inhibitory mechanisms and these same cognitive constructs have informed neural modeling (Klein and Taylor, 1994). Notably, Fuster (2008; p. 353) wrote that: "*...we may plausibly view the inhibitory prefrontal role as a form of lateral inhibition on neural representations that detract from current behavior – resembling a similar phenomenon in sensory physiology*".

Research on *automatic* forms of inhibition has progressed from the early investigations on the inhibitory activity of nerve stimulation on simple reflexes (e.g., Sherrington, 1906) to more sophisticated phenomena. Two of them should be mentioned here for the important influence they have had on the development of modern learning theory and cognitive psychology. The first is 'latent inhibition' (Lubow and Moore, 1959), the phenomenon that causes a difficulty in acquiring a conditioned response to a stimulus if the subject has been pre-exposed to it in the absence of any reinforcement. The second is 'inhibition of return', initially described by Posner and Cohen (1984) as a mechanism for the coordination of attention and eye movements, which facilitates scanning of novel locations in the environment in order to avoid waste of attentional resources. The initial facilitation caused by a peripheral cue is followed by a decreased detection of items at the same location. This inhibition is mediated reflexively by primitive retinotectal pathways and is thought to have an important role in the control of visual attention and reflexive orienting (Rafal and Henik, 1994).

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

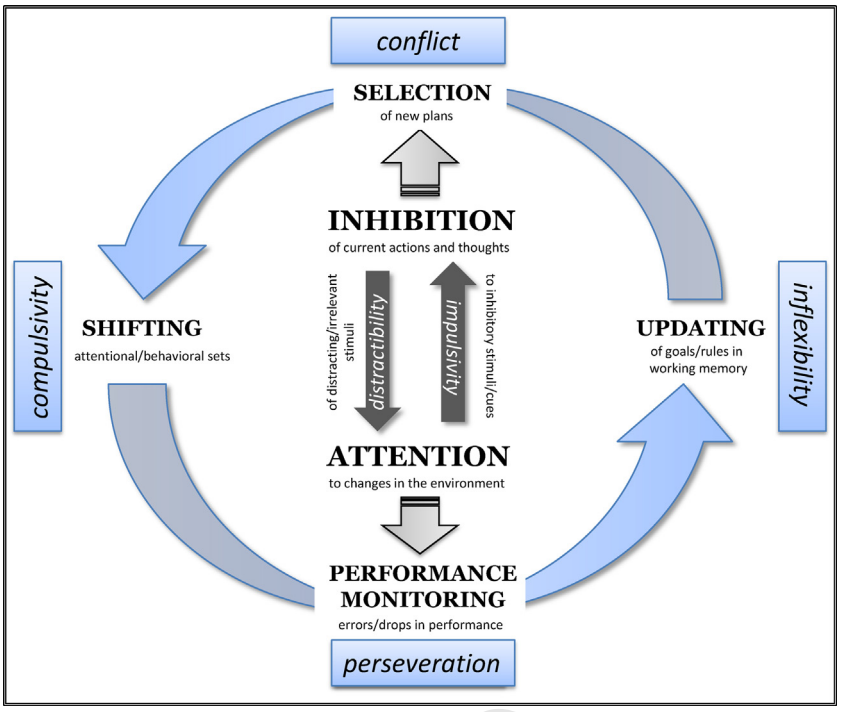

Fig. 3. Schematic representation of the hypothesized relationship (simplified) between different executive functions. Attention and inhibition are central in this model and are assisted by ancillary processes. *Attention* to changes in the subject's environment (internal or external) is essential in order to detect stimuli that signal the need to *inhibit* the current course of actions or thoughts. During a hypothetical task, *performance-monitoring* brain areas inform the system of a drop in performance and request an alternative plan of action. The goals are then *updated* and a new plan is *selected*. Finally, the organism *shifts* attentional and behavioral resources to the newly implemented plan and closes the circle until the next perturbation of the environment. In the diagram the hypothesized behavioral consequences of deficits in any of the executive functions are represented in italics.

On the other hand, *voluntary* inhibition is generally considered as a sub-component of cognitive control which is a higher-order supervisory process – 'executive system' – which optimizes and regulates lower-order functions (Miller and Cohen, 2001). It is evident that 'cognitive control' is an umbrella term, which also includes several interrelated executive processes such as inhibition of pre-potent tendencies, but also the updating of working memory content and shifting between tasks or attentional sets (Miyake et al., 2000). The controversy on whether, and to what degree, inhibition has to be included among executive functions is still unresolved. Some authors sustain that inhibition is one of the fundamental and unifying component of executive control (e.g., Barkley, 1997; Zacks and Hasher, 1994; Dempster and Corkill, 1999), whereas other propose that inhibition depends almost exclusively on other executive functions and do not support the existence of an inhibition-specific factor (e.g., Alderson et al., 2010; Friedman et al., 2008). In between these two extreme views, some models hypothesize that inhibition is separable from other executive functions, but there exist a common unifying factor, at least for some of them (e.g., Duncan et al., 1997; Miyake et al., 2000). However, borrowing Luria's idea of 'interactive functioning systems' (Luria, 1973), it is easy to see how different executive functions need one another for the successful execution of any cognitive process in which they are involved. For example, we need to pay attention to cues that signal a sudden change in the environment in order to inhibit the current flow of thoughts and actions when they are no more appropriate, and then select and shift to a new behavioral set. Thus, only with the concerted action of attention, inhibition and cognitive flexibility we can successfully monitor our performance in relation to external or internal feedback and update our plans/goals to better cope with an ever changing environment (Fig. 3).

Considering the way inhibitory processes exert their functions some authors adopted a 'threshold' model (e.g., Norman and Shallice, 1986), where cognitive representations that are not relevant for the task at hand are in a state of elevated threshold for activation. Thus, they emphasize competitive activation of processing pathways and consider inhibition mostly as an indirect ('passive') consequence of higher activation (or facilitation) of alternative, to-be-selected courses of action or thoughts (Herd et al., 2006; Kimberg and Farah, 1993; Miller and Cohen, 2001; Munakata et al., 2011; Strack and Deutsch, 2004). For instance, Egner and Hirsch (2005) concluded from their results obtained by using functional magnetic resonance imaging (fMRI) that selective attention acts by increasing activation in task-related brain areas and not by suppressing activity for non-relevant content. This conclusion has been criticized by Aron (2007) on the basis of the inability of fMRI to detect inhibition at the neural level (Nakamura et al., 1997). On the other hand, several studies have shown that sensory components of event-related potentials (ERPs) are enhanced for stimuli presented at the attended location and suppressed for to-be-ignored stimuli, although here the controversy is on which process (inhibition or activation) is engaged first (Kok, 1999). Moreover, at least in the area of research on selective attention, there is behavioral evidence that irrelevant information is not passively ignored but instead is actively suppressed (Posner and Cohen, 1984; Tipper, 1985; Tipper and Cranston, 1985). The same is likely to be true for the inhibition of movements, which are not merely the consequence of activating antagonist muscles to stop an already commenced action (Coxon et al., 2006). Thus, although the use of the term inhibition has been challenged when referred to the suppression of cognitive content such as during selective attention or memory retrieval, the possibility of active inhibition of motor responses is usually widely accepted (Breese, 1899; MacLeod et al., 2003).

Cognitive inhibition, in its more restrictive meaning, has been defined as *"... the stopping or overriding of a mental process, in whole or in part, with or without intention"* (MacLeod, 2007), as opposed to

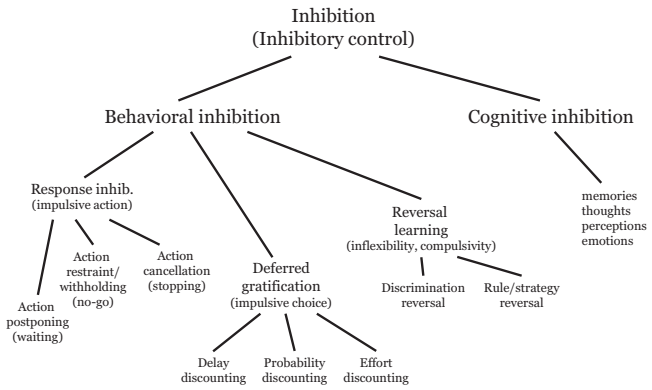

Fig. 4. The diagram depicts a possible subdivision between behavioral and cognitive inhibition with corresponding behavioral tasks that have been used to measure different subtypes of impulsive behavior. In response inhibition paradigms, actions have to be postponed until a go signal appears (waiting), withheld/restrained when an unexpected no-go signal is presented instead of a go signal or canceled when a stop-signal appears after the beginning of the response. On the other hand, in paradigms measuring impulsive choice is the urge to obtain immediate reward that should be inhibited in order to obtain larger rewards after a certain amount of time or effort. In reversal learning paradigms, the strong association between response and outcome has to be overcome when contingencies changes without explicit signals. Response-outcome contingencies can be deterministic or probabilistic.

the inhibition of manifest behavior. The relationship between inhibition of mental processes and of physical responses is not yet entirely clear (but see Fig. 4 for a tentative classification of inhibitory processes). Harnishfeger (Harnishfeger, 1995; Kipp, 2005) invokes a sharp distinction between cognitive and motor forms of inhibition – the first mediating the control of cognitive contents and attentional processes, the second relating to overt behavior such as response inhibition and delayed gratification. According to this view, cognitive inhibition strictly refers to mental processes such as when during the attentional processing of stimuli we have to inhibit the irrelevant ones (Friedman and Miyake, 2004; Nigg, 2000), although this phenomenon is often referred to as 'resistance to interference' or simply 'interference control' (Klein and Taylor, 1994; Tipper, 1992). By these means, other cognitive and behavioral processes are facilitated, with the consequence of enabling dynamic adjustments of goal-oriented actions as well as reducing interference from irrelevant distracting stimuli. Similarly, memory is facilitated by the ability to inhibit or suppress irrelevant information (Conway and Engle, 1994; Desimone and Duncan, 1995; Levy and Anderson, 2002; Miller and Cohen, 2001) and, more in general, intelligence too was considered by many to be positively correlated with inhibitory capacity (Dempster, 1991; Thurstone, 1924), but see (Friedman et al., 2006; Miyake et al., 2000). Diamond et al. pointed out that there are two ways in which inhibition can be involved in thinking: the first is the case in which inhibition of movements favors thinking by removing competing activities and the second is the possibility that inhibition is an essential part of the thinking process itself. They conclude their chapter on 'Inhibitory processes in thinking' by writing that "*... we are ready to give serious consideration to the position which was stated by Wundt in 1902, and to recognize the need for inhibitory elements in the thinking process...*" and that "*... there is no reason whatever to give one of these processes* [excitation or inhibition] *preferential status over the other, in constructing hypothesis about behavior, and about that portion of behavior which we call thinking.*" (Diamond et al., 1963, p. 178).

According to MacLeod the most important features of cognitive inhibition are mental withholding and reduced performance but, since the former is inferred from the latter, this creates confusion when trying to define cognitive inhibition. It is for this reason that he recommends theorists to provide a personal meaningful definition of the term inhibition as well as a set of criteria for considering a behavioral phenomenon to involve inhibition (MacLeod, 2007). Thus, although cognitive inhibition is more difficult to study compared to motor inhibition, due to the absence of overt behavioral measures, several studies have investigated differences and similarities between these two phenomena. Such studies usually adopt two different versions of the same go/no-go paradigm where in the 'motor' version subjects are required to press a button during go trial and refrain to respond on no-go trials, whereas in the 'cognitive' version subjects have to silently count only the go stimuli (which are randomly intermixed with no-go cues) or to just imagine a motor response or its inhibition to the same task stimuli. Investigation of ERPs revealed that no-go components were similar in the cognitive and motor versions of the task (Bruin and Wijers, 2002; Burle et al., 2004; Pfefferbaum et al., 1985; Smith et al., 2012; Wang et al., 2002). Intentional inhibition of memory content has been demonstrated using the think/no-think paradigm (Anderson and Green, 2001), although others (Bulevich et al., 2006) have considered these findings as deriving from some form of 'retroactive inhibition' (or interference) (Hilgard, 1953). Also brain imaging studies have often found overlapping foci of activity for both cognitive and motor inhibition paradigms (Anderson et al., 2004; Aron et al., 2004; Cohen and Lieberman, 2010; Dillon and Pizzagalli, 2007; Nakata et al., 2008, 2009; Tabibnia et al., 2011), although inhibition of verbal material may be predominantly left-lateralized (e.g., Jonides et al., 1998). Memory content, instead is inhibited by the right dorsolateral PFC, which suppresses memory retrieval by decreasing hippocampus activation (Benoit and Anderson, 2012). Further support to the notion that cognitive and motor inhibition shares overlapping brain networks comes from the findings that psychiatric and neurological patients usually are impaired in tasks assessing inhibition of motor responses as well as inhibition of cognitive material (Barkley, 1997; Chamberlain et al., 2006a; Clark et al., 2007; Conway and Fthenaki, 2003; D'Esposito et al., 1999; Jonides et al., 1998; Michael et al., 2006; Temel et al., 2005; Thompson-Schill et al., 2002).

In agreement with Skaggs (1929), in the reminder of this review we will consider 'inhibitions of impulses to act' at the nexus between the decision of inhibiting an action and the act of inhibition itself, which can be measured for example when an expected or pre-potent action is not performed or takes more time than usual. Of course, *response inhibition* involves motor-related brain areas more extensively than purely cognitive inhibition does and, most of times, is *voluntary* or involving some degree of consciousness. Limiting our discussion to the inhibition of observable *motor* behavior allows the objective measurement of the latency and efficiency of underlying cognitive and physiological processes in the intact organism. Moreover, by measuring observable indices of inhibitory processes we can study the behavioral and functional consequences of their failure in the healthy and pathological brain. In this way, response inhibition serves as an endophenotype, or 'proxy', for the study of impulsivity and its neurobiological underpinnings with important implications for a range of psychiatric disorders (Almasy and Blangero, 2001; Aron, 2007; Aron and Poldrack, 2005; Hutton and Ettinger, 2006). Another advantage of this approach is that a variety of behavioral tasks used to assess behavioral inhibition in humans can be readily adapted to be used in laboratory animals. Accordingly, motor inhibition is studied in the laboratory most often by means of tasks involving pre-potent responses to certain frequent stimuli and the need to suddenly inhibit those responses upon the unexpected presentation of infrequent stop cues. For example, in the theoretical formulation of Barkley (1997), inhibition can be assessed by tasks requiring the suppression of

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

a pre-potent response, stopping an ongoing response or interference control. He also defined 'pre-potent response' as "*... that response for which immediate reinforcement (positive or negative) is available or has been previously associated with that response.*" (pp. 67–68). Thus, in the remainder of this review we will mainly deal with the phenomenon of motor (or response) inhibition, which is part of the broader concept of cognitive control; more specifically, its observable behavioral manifestation in situations that involve the inhibition of an overt motor act.

2. Failure of the inhibitory processes: impulsivity

> "If the centres of inhibition, and thereby the faculty of attention, are weak, or present impulses unusually strong, volition is impulsive rather than deliberate". (Ferrier, 1876, p. 287).

Impulsivity [or impulsiveness] is generally regarded as a consequence of impaired executive functioning. More specifically, an impulsive action is determined by the co-occurrence of dysfunctional inhibitory processes and strong 'impulsions' (or impulses), plus being triggered and modulated by dispositional and situational variables (Hofmann et al., 2009; Metcalfe and Mischel, 1999). Without a strong desire, urge or habit there would be no need for inhibition, whereas fully functional inhibitory processes would prevent the impulsive act (see Fig. 5 for comparison with compulsivity). Impulsive traits characterize many psychiatric conditions such as attention deficit/hyperactivity disorder (ADHD; Nigg, 2001), drug addiction (Jentsch and Taylor, 1999) and schizophrenia (Gut-Fayand et al., 2001).

In ADHD children impulsivity is often manifested as the inability to wait in a variety of situations and as the tendency to interrupt others' conversations, or to respond before the end of the question (American Psychiatric Association, 1994). Also the attentional deficits shown by ADHD patients may potentially be the consequence of the inability to inhibit irrelevant thoughts and/or the manifestation of inappropriate emotions, which interfere with focused cognitive processing. Impulsivity is so pervasive in the behavior of ADHD children that the father of British pediatrics Sir George Frederick Still (1868–1941) described them as having little inhibitory volition (Still, 1902). Similarly, contemporary theorists recognize the centrality of poor behavioral inhibition in this disorder (Barkley, 1990, 1997; Nigg, 2001; Quay, 1988; Schachar et al., 1995). Childhood impulsivity is also a central aspect of theories of delinquency (John et al., 1994), antisocial behavior (Luengo et al., 1994; Moffitt, 1993) and predicts early-onset criminal conduct (Tremblay et al., 1994). Impulsivity is often described also as the main behavioral characteristic of drug abusers (Jentsch and Taylor, 1999; Olmstead, 2006; Perry and Carroll, 2008; Verdejo-Garcia et al., 2008; Volkow et al., 2002) and, in schizophrenics, is generally associated with worse clinical outcomes and constitutes a risk factor for the development of violence, drug addiction and suicidal behavior (Dumais et al., 2011; Gut-Fayand et al., 2001). Finally, OCD patients display profound inability to inhibit intrusive thoughts and compulsive behaviors (Chamberlain et al., 2005).

Deficient inhibitory control may also negatively affect the lives of healthy adult individuals. Fuster (2008; p. 128) wrote that "*Defective inhibition is maladaptive, not only because it allows the execution of purposeless or unproductive acts but also because some of those acts may short-circuit the attainment of goals...*". This sentence well describes the way inhibitory deficits may negatively affect the career goals and social relationships during adulthood. However, not all impulsive behaviors are disadvantageous and a certain degree of 'loss of control' may have adaptive implications (Block, 2002). Dickman (1990) pointed out the existence of 'functional' impulsivity which may have adaptive value in certain situations, whereas Harnishfeger and Bjorklund (1994) suggested that Q6 inefficient inhibition may characterize the creative mind which is able to find novel relations among events or non-obvious solutions to problems. For example, impulsive individuals show superior performance compared to non-impulsive individuals in situations when there is short time available to make a decision or when facing very easy-to-solve problems (Dickman, 1985; Dickman and Meyer, 1988). At the level of social dynamics, impulsive traits in a minority of individuals can prove adaptive to the society which they belong to by increasing the exploration of new behavioral possibilities, while confining the relative risks to a restricted sample of subjects (Williams and Taylor, 2006). In higher mammals, the ability to exert inhibitory control over automatic reflexes and conditioned responses has been suggested to have evolved to allow slower cognitive processes to guide behavior in certain circumstances (Jentsch and Taylor, 1999; Robbins, 1996).

2.1. Subtypes of impulsive behavior

Several researchers have proposed different taxonomies for subdividing the complex behavioral phenotype of impulsivity (e.g., Barkley, 1997; Evenden, 1999; Eysenck and Eysenck, 1977; Gerbing et al., 1987; Nigg, 2001; Patton et al., 1995). Generally,

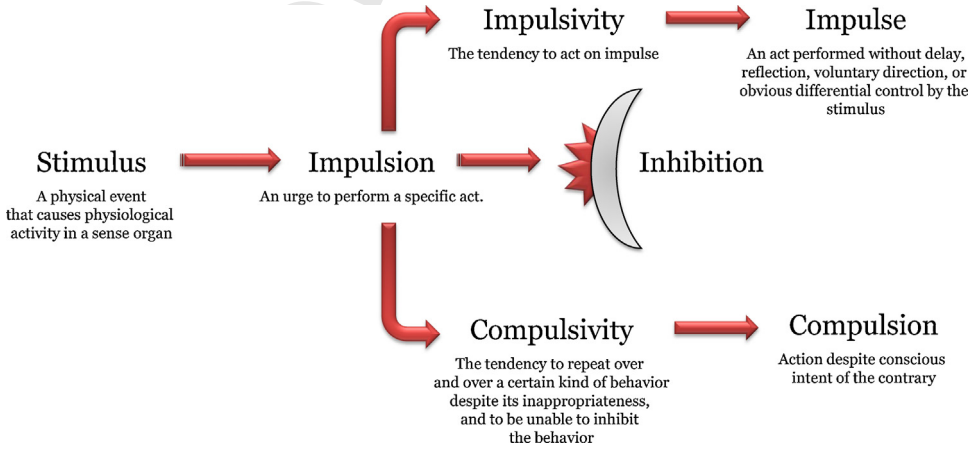

Fig. 5. In susceptible individuals certain stimuli may activate strong urges or desires that are not appropriate in a given environment or for the current state, goals or plans of the organism. Functional inhibitory processes may keep those urges under control whereas strong impulses and deficient inhibition will results in impulsive or compulsive acts or thoughts. Current models of drug addiction sustain that both (or a gradual transition between) impulsivity and compulsivity characterize the pathological behavior in Q37 drug abuse (Dalley et al., 2011; Koob and Volkow, 2010; Volkow et al., 2011).
Definitions are adapted or directly quoted from English and English (1958).

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

impulsivity has been defined as the inability to withhold or stop a response or a thought in the face of negative consequences; preference for a small immediate reward versus a larger but delayed one; acting without forethought or before all necessary information is available; novelty/sensation-seeking and an increased propensity to engage in risky behaviors. These definitions are not exhaustive and clearly cover a broad range of behaviors that not always correlate with each other and sometimes are even conceptually incompatible. For instance, it is not clear how the spontaneous and unplanned behavior without consideration of possible negative consequences required by some definitions of impulsivity may result in the planning activity of sensation-seekers pursuing risky behaviors such as parachuting or skydiving. One possibility is that two broad types of impulsive behavior can be described: a slower form involving deliberation and the fulfillment of desires despite considering negative consequences, and a fast one without enough forethought about the possible negative outcomes (De Young, 2010; Strack and Deutsch, 2004; Swann et al., 2002). This distinction can be readily assimilated to the framework of dual mechanisms theories of cognitive control, which generally hold that two distinct 'operating modes' are at play to regulate thoughts and actions: one is a *reactive* mechanism which transiently reactivate task goals and is triggered by contextual cues in a bottom-up fashion; the other mechanism is *proactive* and entails a sustained representation of goal-relevant information in order to bias cognitive processes and behavioral responses (Braver, 2012). Recently this view has been applied to response inhibition paradigms (Aron, 2010) and may explain why assessing both types of inhibitory processes in the same subjects results in more powerful diagnostic capacity (Solanto et al., 2001) and partially dissociable neural networks (see below).

In the cognitive neuroscience literature, these two forms of behavioral inhibition have been described with different names by researchers, such as 'cool' versus 'hot', 'top-down' versus 'bottom-up', 'stopping' versus 'waiting', 'action restraint' versus 'action cancellation' and 'motor' versus 'choice' impulsivity (Castellanos et al., 2006; Eagle et al., 2008a; Lawrence et al., 2008; Metcalfe and Mischel, 1999; Nigg, 2005; Robinson et al., 2009; Roiser et al., 2009; Schachar et al., 2007; Teasdale et al., 1998; Urcelay and Dalley, 2012). Results from dedicated behavioral tasks have shown that these two forms of inhibition are partially dissociable at the behavioral level in healthy subjects (Reynolds et al., 2006), ADHD patients (Solanto et al., 2001) and animal models (Baarendse and Vanderschuren, 2012; Robinson et al., 2009; Torregrossa et al., 2012). However, this distinction between different subtypes of impulsive behaviors is to be considered more quantitative than qualitative, with the different behavioral tasks measuring distinct but interrelated forms of impulsivity, also depending on the involvement of affective processes. Accordingly, the most commonly accepted subdivision of impulsivity in operational terms is between the inhibition of ongoing or pre-potent motor responses (e.g., withholding, stopping or postponing a response) on one hand, and of motivational and affectively charged processes (e.g., deferring gratification) on the other (Ainslie, 2001; Castellanos et al., 2006; Harnishfeger, 1995; Nigg, 2005; Winstanley et al., 2006; Zelazo and Mueller, 2002). Somewhat in between these two families of behavioral tasks, reversal learning paradigms entail unexpected changes in stimulus/reward contingencies and represent a potentially powerful tool for the study of cognitive flexibility and compulsive behavior.

2.2. Assessing impulsivity

Impulsivity conceived as a personality trait can be measured in a number of ways in humans, for example by self-report questionnaires, such as the Barratt impulsivity scale, or by observing behavior in natural settings (Achenbach and Edelbrock, 1979; Barratt and Patton, 1983; Eysenck, 1993; Eysenck and Eysenck, 1975; Gray, 1972; Kendall and Wilcox, 1979; Patton et al., 1995). Impulsivity has had an important place in the study of human personality since Heymans's three-dimensional model of temperament (Van der Werff and Verster, 1987) and impulsivity-related items are included in the majority, if not all, self-report personality inventories. In Eysenck's work impulsivity gradually became a core feature of the personality trait of extraversion and subsequently was considered central to arousal-based theories of cognitive performance (Barratt, 1985; Revelle, 1997). However, impulsive traits as measured by self-report questionnaires do not often correlate with behavioral measures of impulsivity (e.g., O'Keefe, 1975; Reynolds et al., 2006; Stanford and Barratt, 1996; White et al., 1994), with the exception of delay discounting rates which have been shown to exhibit long term stability (Kirby, 2009). This difference may be due to the very nature of delay discounting tasks in that the choice between the egg today or the chicken tomorrow is based on both past experience and future expectations (Ainslie, 2001), which concur to form a stable representation of the 'self'. However, a recent study which made use of principal component analysis found that impulsive action, impulsive choice and self reported impulsivity loaded on three independent factors, similar to studies in animals where impulsive choice and impulsive action measures were not correlated (Broos et al., 2012).

The relatively low reliability of 'executive' tasks in humans is well known (Denckla, 1996; Rabbitt, 1997) and may depend on the strategies adopted by the subjects to solve the same problem, which are likely to change both between subjects and on different testing occasions. Alternative explanations for the inconsistency between questionnaires and laboratory tasks of impulsive behavior may invoke the multidimensional nature of the impulsivity construct (Evenden, 1999; Gerbing et al., 1987) or that impulsive tendencies are not stable within individuals and may vary depending on the state of the subject, such as the level of anxiety, desire and anger (Wingrove and Bond, 1997). In this respect, the use of both questionnaires and multiple behavioral measures may help discriminating between 'trait impulsivity' (stable personality characteristic) and 'state impulsivity' which is temporarily determined by environmental variables. Finally, most cognitive tasks, including those explicitly devised as a measure of behavioral inhibition, suffer from what is called 'impurity problem' (Burgess, 1997), because successful performance requires the contribution of several factors other than impulse control. Conversely, many tasks assessing executive cognitive functions such as shifting and updating may tap as well on inhibitory processes (Miyake et al., 2000). Thus, for example, although impulsivity is conceptually different from compulsivity, behavioral measures used to assess one or the other will involve some form of behavioral/cognitive inhibition (Fineberg et al., 2010; Robbins et al., 2012).

Although less work has been done to define the psychometrics and construct validity of behavioral tests of impulsivity, they present some advantages compared to self-report questionnaires, such as objectivity and less contamination from past life events. Laboratory tests are more objective because the behavior is rated by the experimenter on the basis of observable data and is not defined by lexical categories that may have different meanings for different subjects and in different cultural contexts. They are also less biased by the subject's self-perception and closer to biological models of impulsivity. Moreover, the possibility of using analogous behavioral tasks in humans and laboratory animals greatly expands the range of applications and allows faster and more in-depth genetic, pharmacological and neurological manipulations. Importantly, many of these tasks have demonstrated a good level of correspondence between studies in humans and other

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

animals in terms of performance, brain areas involved and effects of pharmacological or environmental interventions. Modern neuroscience research makes use of several laboratory tasks that measure distinct and complementary operational definitions of impulsivity in humans and other animals, according to the multi-faceted nature of this concept (Eagle et al., 2008a; Evenden, 1999; Logan et al., 1984; Mitchell, 2004; Rachlin and Green, 1972; Robbins, 2007; Winstanley et al., 2006). However, as stated above, our discussion will focus predominantly on tasks measuring motor response inhibition, although they will be compared with other behavioral paradigms such as delay discounting and reversal learning.

2.3. Response inhibition

The go/no-go paradigm and the SST are the prototypical tasks used to measure the ability to inhibit a pre-potent response. The SST can be regarded as an elaboration of the go/no-go paradigm (Newman et al., 1985) and, although these two behavioral measures correlate positively in normal subjects (Reynolds et al., 2006), important differences also exist on both behavioral and neural grounds. The main difference between SST and go/no-go paradigms is represented by the timing of presentation of the stop cue relative to the go stimulus. In go/no-go tasks the signal that triggers the inhibitory processes is presented unexpectedly in place of, or simultaneously to, the go signal, whereas in the SST the go cue always precedes the stop-signal. This means that they measure the inhibition of a planned response ('*action restraint*') or the inhibition of an already started action ('*action cancellation*'), respectively (Eagle et al., 2008a; Schachar et al., 2007). Thus both SST and the go/no-go task involve two different sub-tasks: one requires a fast 'go' response, which has to be inhibited on a subset of trials that require a 'stop' (or 'no-go') response. As we will note below, another important difference between the two tasks is represented by the possibility the SST offers to measure the *latency* of the inhibitory processes as well as their *efficacy*.

Dual-task interference has been investigated in a variety of situations ranging from simple reaction time tasks to very complex combination of stimuli (Pashler, 1994). At the turn of the 20th century many investigators were interested in understanding the nature of reaction times and the phenomenon of the 'psychological refractory period' (Craik, 1948; Vince and Welford, 1967; Welford, 1967) which is known to cause an increase in the reaction time to the second of two stimuli presented in rapid succession, as the processing related to the first stimulus would interfere with the response to the second (Helson and Steger, 1962; Vince, 1948). In some cases, the second stimulus was a stop-signal which instructs the subject to modify or stop the response to the primary stimulus on that trial (e.g., Henry and Harrison, 1961). Interestingly, it transpired that responses to stop-signals and stop-change signals (where the subject has to inhibit one response and to switch to another action) were not affected as much as other kind of responses by the 'cognitive bottleneck' of the refractory period, a finding that influenced modern theories of attention (Logan and Cowan, 1984; but see Brebner, 1968; Horstmann, 2003). The task version introduced by Lappin and Eriksen in 1966, was very similar to the response inhibition paradigms used nowadays. The primary task required the subjects to quickly respond to the presentation of one of two lights horizontally aligned. Sometimes, following the first by some delay, the second light was illuminated and the subject had to stop the planned response to the first one (Lappin and Eriksen, 1966). In their experiments, Lappin and Eriksen asked to what extent they could modulate the asynchrony between the two stimuli without impairing the inhibitory response to the second one. They found that the probability of inhibiting the response to the first light decreases as a function of the asynchrony between the two stimuli. Moreover, they were the first to observe that the probability of inhibition increases with slower reaction times to the first stimulus and, for this reason, subjects tend to delay the go response in order to improve their chances of inhibition given a stop-signal, especially when a delay makes it harder to stop (Lappin and Eriksen, 1966).

The modern version of the SST consists of a primary *go* task, which is usually a choice reaction time task where subjects have to respond, for example, by pressing a button with the index finger when presented with an arrow pointing left and by pressing a different button with the middle finger when the stimulus is an arrow pointing right. On a subset of trials, the go stimulus is followed shortly by a stop-signal, which could be visual (e.g., arrow pointing upward) or auditory (tone). The task this time is to *stop* the planned or ongoing response to the go stimulus. Subjects are instructed to try to respond as fast as they can to the go signal without slowing down their response in order to anticipate the occurrence of a stop trial. They are also told to attempt to refrain from responding on all stop trials, although sometimes they will not be able to do so. In fact, typically the probability of inhibition is high when the stop-signal is presented close to the beginning of the go response or shortly after, but becomes lower the longer the delay between the go and the stop-signal. Stop trials are presented randomly in order to make their appearance unpredictable to the subject. Similarly, different stop-signal delays (SSDs) should be presented in random sequence to prevent the subjects from developing a strategy to increase their chances to correctly stop a response (Logan, 1994), which is probably what happened in the study of Lappin and Eriksen (1966) where the same delay was used within a session (although intermixed with no-delay stop trials).

An important advance in the field was the formulation of the 'race' model (see Logan and Cowan, 1984; Logan, 1994; Verbruggen and Logan, 2009), which allows measurement of the *latency* of the inhibition of virtually every kind of movement. The race model caused an exponential increase in SST studies, principally because of the generality of the model, its relative ease of use and, importantly, because of the possibility it gives to empirically measure the latency of the covert response to a stop-signal (stop-signal reaction time; SSRT) which, otherwise, could not be observed directly (see Band et al., 2003; Verbruggen and Logan, 2008, 2009 for reviews). This model can be readily applied to studies in rodents and results obtained with the rodent version are often similar to that obtained in human subjects (Eagle et al., 2008a; Feola et al., 2000). In our laboratory we have used a version of the stop task for rats with fixed delays, which are based on the average speed of the animal during go trials; however, dynamically tracking the speed of the go response or of the stop accuracy in order to set SSDs according to the subject's performance is also feasible.

Limb movements and key presses are the actions most commonly employed in response inhibition experiments although any action can be used with these procedures. However, different movements may involve distinct neural pathways, which complicates the comparability of the results from different studies (Band and van Boxtel, 1999; Boucher et al., 2007; Hanes and Schall, 1996). A very popular version involves the countermanding of saccadic movements to peripheral stimuli after the presentation of a stop-signal (Lisberger et al., 1975; Schall and Boucher, 2007), and has been successfully used in experiments with non-human primates (Emeric et al., 2007; Hanes and Schall, 1996). Inhibition of hand and eye movements is accomplished by partially overlapping (Heinen et al., 2006; Hodgson et al., 2007; Isoda and Hikosaka, 2007) neural systems probably operating according to the same principles (Logan and Irwin, 2000). In this case, the comparison of response inhibition in different motor modalities has helped the distinction between downstream modality-specific brain areas

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

and prefrontal areas operating upstream and independently from the motor system engaged (Hodgson et al., 2007; Leung and Cai, 2007). A number of studies in humans have explored the inhibition of continuous actions such as speaking (Ladefoged et al., 1973; Levelt, 1983), typing (Logan, 1982; Long, 1976; Rabbitt, 1978), tracking (Morein-Zamir et al., 2004), squeezing (de Jong et al., 1990), arm movements (Henry and Harrison, 1961), but also making judgments (Logan, 1983), thinking (Morein-Zamir et al., 2010) and solving arithmetic problems (Zbrodoff and Logan, 1986). Each paradigm has its own advantages and drawbacks depending on the main focus of the study. For example, the sudden inhibition of typing for a skilled typist can be harder than it is for a normal person due to the intervention of automatic processes and long practiced behavioral sequences in the primary task.

Both visual and auditory stop-signals have been used in response inhibition experiments. Auditory stop-signals have been found to increase the speed and the efficiency of the stopping process (Ramautar et al., 2006a; van der Schoot et al., 2005), probably because the auditory neural transmission pathway has less synapses compared to the visual one (Elliott, 1968; Goldstone, 1968). A different explanation would be that auditory stop-signals and visual go cues do not compete for shared resources decreasing the amount of interference between stop and go responses (Wickens and Kessel, 1980). However, the opposite findings have been reported in SST experiments employing saccade inhibition rather than manual responses with visual stop-signal eliciting faster SSRTs (Armstrong and Munoz, 2003; Cabel et al., 2000; Morein-Zamir and Kingstone, 2006). This can be due to the fact that the countermanding of saccadic movements concerns visual areas such as the frontal eye fields (FEF) and the superior colliculi (Hanes et al., 1998; Munoz and Wurtz, 1993a,b) which are the same regions that are responsible for visual fixation, thus introducing an automatic 'bottom-up' component in the subjects' performance (Boucher et al., 2007; Cabel et al., 2000; Schall and Thompson, 1999). The salience and the relative probability of the stop-signal can also influence the race between go and stop processes (Armstrong and Munoz, 2003; Morein-Zamir and Kingstone, 2006; Ramautar et al., 2006b; van den Wildenberg and van der Molen, 2004; van der Schoot et al., 2005). Louder stop-signal tones (80 db) have been found to produce shorter SSRTs as compared with quieter tones (60 db) (Morein-Zamir and Kingstone, 2006; van der Schoot et al., 2005), compatible with the hypothesis that loud sounds are able to elicit 'immediate arousal' which causes a direct activation of the motor system (Posner et al., 1976; Sanders, 1998) and/or a stronger orienting response (Lynn, 1966). The probability of the occurrence of stop-signals is also an important parameter because it can bias subject's performance towards the go or the stop response. Infrequent stop-signals produce faster go responses that are more difficult to inhibit leading to slower inhibition (Ramautar et al., 2004, 2006b).

3. Neural substrates of response inhibition

> "The centres of inhibition being thus the essential factor of attention, constitute the organic basis of all the higher intellectual faculties. And in proportion to their development we should expect a corresponding intellectual power". (Ferrier, 1876, p. 287)

The investigation of the neural substrates of response inhibition has been pursued using a variety of techniques and approaches. Animal models offer the possibility of testing the effects of drugs and discrete brain lesions on impulsive behavior, but also the genetic basis of diseases characterized by deficient response inhibition. For many psychiatric conditions, inhibitory deficits are likely to derive from more generalized impairments in cognitive control and often are not the most compelling feature of the disease, while they are considered to be central in drug addiction and ADHD (Pattij and Vanderschuren, 2008; Volkow et al., 2004). Deficits in response inhibition, for example, predict alcohol and drug abuse in humans (Nigg et al., 2006; Rubio et al., 2008) and in animal models of drug addiction (Belin et al., 2008; Dalley et al., 2007), and are expressed also in the close relatives of ADHD individuals (Chamberlain and Sahakian, 2007; Slaats-Willemse et al., 2003). Research on patients diagnosed with ADHD, obsessive-compulsive disorder (OCD), schizophrenia, drug addicted individuals and their unaffected siblings suggests that deficits in response inhibition are potentially inheritable characteristics and therefore promising candidate endophenotypes for genetic investigation (Aron and Poldrack, 2005; Chamberlain et al., 2007b; Ersche et al., 2012; Vink et al., 2006). Consequently, a deeper understanding of the mechanisms behind inhibitory control deficits may open new doors, not only for the diagnosis, treatment and prevention of psychiatric diseases, but also for the improvement of life conditions in the general population.

3.1. Neuropharmacological studies

Response inhibition is facilitated in humans and laboratory animals by drugs commonly used for the treatment of ADHD (see Table 2) (Solanto, 1998; Spencer et al., 2001), although for some drugs – especially psychostimulants – the therapeutic effects are sometime dependent on baseline performance (de Wit et al., 2000; Eagle and Robbins, 2003; Eagle et al., 2007; Feola et al., 2000). These differences in response to psychostimulant administration probably depend on the genetic background of the individuals (e.g., Dlugos et al., 2009; Hamidovic et al., 2010a,b; Mattay et al., 2003). Especially dopamine (DA) D2 receptor availability seems to play an important role in determining the effects of psychostimulants (Dalley et al., 2007; Volkow et al., 1999a,b). On the other hand, the speeding effect of the stimulant drug methylphenidate on stopping is not blocked by the DA D1/D2 receptor antagonist α-flupenthixol in rats (Eagle et al., 2007), suggesting that there are also non-dopaminergic mechanisms determining individual differences in the behavioral effects of this class of drugs. In children with ADHD, increasing dopaminergic neurotransmission by L-dopa administration does not influence stopping an ongoing action, while the tricyclic antidepressant desipramine – which inhibits the reuptake of norepinephrine (NE) and serotonin (5-HT) – increased stopping success rate (Overtoom et al., 2003). The same study found that methylphenidate, but not L-dopa or desipramine, improved the speed and efficacy of the go response. Moreover bupropion, which acts principally by blocking DA reuptake but also as noradrenergic and nicotinic receptor antagonist (Fryer and Lukas, 1999; Slemmer et al., 2000), has no effect on the speed of response inhibition (Acheson and de Wit, 2008). The effects of methylphenidate and amphetamine on impulsivity and response inhibition are not yet fully understood. These drugs, not only increase DA extracellular levels in the brain, but also those of histamine and they preferentially release NE at low, therapeutic doses (Horner et al., 2007; Koob and Bloom, 1988; Kuczenski and Segal, 1997), especially in the PFC.

The relatively selective NE reuptake inhibitor atomoxetine improves response inhibition in both rats and humans (Eagle et al., 2008a). This effect does not appear to depend on baseline performance since it speeds SSRT in normal rats (Robinson et al., 2008) and humans (Chamberlain et al., 2006b; but see also Nandam et al., 2011) as well as in ADHD patients (Chamberlain et al., 2007a). The exact mechanism of atomoxetine's beneficial action is still unclear but it may involve increased NE and DA function in the PFC (Bymaster et al., 2002; Chamberlain et al., 2009; Levy, 2008). Guanfacine, a selective α2-adrenoceptor agonist, which diminishes ascending noradrenergic activity (Fresquet et al.,

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Table 2
Selection of studies in laboratory animals reporting the effects of various drugs of abuse and therapeutic drugs on impulsivity as measured by some of the most widely used behavioral paradigms: reversal learning, delay discounting, go/no-go and stop task. The table does not make distinctions between different species, strains, sexes, baseline levels of impulsivity or version of the task. Studies involving developmental investigations of drug effects (i.e., prenatal or neonatal administration) are not included in the table. The reader is referred to the cited studies for more detailed information. Abbreviations: rep./chr./s.a., repeated administration/chronic administration/self administration; alc. pref., alcohol-preferring; SSRIs, selective serotonin reuptake inhibitors; ↓ decrease in impulsivity; ↑ increase in impulsivity; ↔ no effects on impulsivity; ? unknown; multiple symbols signifies that the effects of the drug may depend on the version of the task used or on differences in subjects background.

Substance of abuse	Reversal learning	Delay discounting	Go/no-go	Stop task
Cocaine acute	↑(Jentsch et al., 2002)	?	↑(Paine and Olmstead, 2004) ↔(Paine et al., 2003)	?
rep./chr./s.a.	↑(Krueger et al., 2009; Porter et al., 2011; Stalnaker et al., 2007)	↑(Anker et al., 2009; Paine et al., 2003; Roesch et al., 2007; Simon et al., 2007)		↑(Liu et al., 2009)
Amphetamine acute	↓(Weiner and Feldon, 1986)	↓(Baarendse and Vanderschuren, 2012; Bizot et al., 2011; Floresco et al., 2008; van Gaalen et al., 2006)	↑(Blackburn and Hevenor, 1996)	↓(Feola et al., 2000)
	↑(Idris et al., 2005; McLean et al., 2010)	↑(Cardinal et al., 2000; Evenden and Ryan, 1996)	↓↑(Doty and Ferguson-Segall, 1987)	↔(Eagle and Robbins, 2003)
rep./chr./s.a.		↔(Wooters and Bardo, 2011)	↔(Loos et al., 2010)	
	↓(Russig et al., 2003) ↔(Featherstone et al., 2008)	↔(Slezak et al., 2012)	?	?
Methamphetamine acute	↓(Kulig and Calhoun, 1972) ↔(Kosheleff et al., 2012)	↓(Richards et al., 1999)	↓(Moschak et al., 2012)	?
rep./chr./s.a.	↑(Groman et al., 2012; Izquierdo et al., 2010) ↔(Kosheleff et al., 2012; Parsegian et al., 2011)	↑(Richards et al., 1999)	?	?
Morphine acute	↑(Galizio et al., 2006)	↑(Kieres et al., 2004; Pattij et al., 2009)	↔(Befort et al., 2011)	↔(Pattij et al., 2009)
rep./chr./s.a.	?	↑(Harvey-Lewis et al., 2012; Maguire et al., 2012)	?	?
Heroin acute	?	?	?	?
rep./chr./s.a.	↓(Ranaldi et al., 2009)	↑(Schippers et al., 2012) ↔(Harty et al., 2011)	?	?
Alcohol acute	↑↔(Cain et al., 2002)	↑(Olmstead et al., 2006; Poulos et al., 1998; Tomie et al., 1998)	?	↑(Feola et al., 2000)
	↑(Obernier et al., 2002)			
rep./chr./s.a.	↑(Badanich et al., 2011; Kuzmin et al., 2012)	?	?	?
alc. pref. animals	?	↑(Oberlin and Grahame, 2009; Wilhelm and Mitchell, 2008)	↑(Wilhelm et al., 2007)	?
Nicotine acute	↔(Allison and Shoaib, 2013)	↑(Dallery and Locey, 2005; Kolokotroni et al., 2011; Mendez et al., 2012)	↑(Kolokotroni et al., 2012)	↑(Bari and Robbins, unpub.)
rep./chr./s.a.	↓(Besheer and Bevins, 2000) ↔(Allison and Shoaib, 2013)	↑(Dallery and Locey, 2005) ↔(Counotte et al., 2009)	↑(Kolokotroni et al., 2011)	↑(Kirshenbaum et al., 2011)
Therapeutic drugs	Reversal learning	Delay discounting	Go/no-go	Stop task
Methylphenidate	↓↑(Handley and Calhoun, 1978) ↓(Seu et al., 2009)	↓(Bizot et al., 2011; van Gaalen et al., 2006) ↓↔(Bizot et al., 2007; Perry et al., 2008; Slezak and Anderson, 2011)	?	↑↓(Eagle et al., 2007)
Atomoxetine	↓(Seu et al., 2009)	↓(Bizot et al., 2011; Robinson et al., 2008) ↔(Baarendse and Vanderschuren, 2012)	?	↓(Robinson et al., 2008)
Modafinil	↓(Beracochea et al., 2003)	?	?	↓(Eagle et al., 2007)
SSRIs	↓(Bari et al., 2010; Brigman et al., 2010)	↓(Loiseau et al., 2005; Thiebot et al., 1985) ↔(Baarendse and Vanderschuren, 2012; Evenden and Ryan, 1996)	?	↔(Bari et al., 2009)

Table 2 (*Continued*)

Substance of abuse	Reversal learning	Delay discounting	Go/no-go	Stop task
Benzodiazepines	↑(Galizio et al., 2006)	↑(Bert et al., 2006; Eppolito et al., 2011; Thiebot et al., 1985) ↓(Evenden and Ryan, 1996) ↔(Maguire et al., 2012)	↑(Cole, 1990; Cole and Michaleski, 1986; Sokolic and McGregor, 2007)	↑(Bari and Robbins, unpub.)

Aron, A. R., Behrens, T. E., Smith, S., Frank, M. J. and Poldrack, R. A. (2007) Triangulating a cognitive control network using diffusion-weighted magnetic resonance imaging (MRI) and functional MRI. *J Neurosci* **27,** 3743-3752.
Dalley, J. W., Everitt, B. J. and Robbins, T. W. (2011) Impulsivity, compulsivity, and top-down cognitive control. *Neuron* **69,** 680-694.
Duann, J. R., Ide, J. S., Luo, X. and Li, C. S. (2009) Functional connectivity delineates distinct roles of the inferior frontal cortex and presupplementary motor area in stop signal inhibition. *J Neurosci* **29,** 10171-10179.
Freud, S. (1895) Project for a Scientific Psychology. In: *The standard edition of the complete psychological work of Sigmund Freud (1953)*. Ed. J. Strachey. The Hogart Press and the Institute of Psycho-Analysis: London.
Koob, G. F. and Volkow, N. D. (2010) Neurocircuitry of addiction. *Neuropsychopharmacology* **35,** 217-238.
Poldrack, R. A., Mumford, J. A. and Nichols, T. E. (2011) *Handbook of functional MRI data analysis*. Cambridge University Press.
Volkow, N. D., Wang, G. J., Fowler, J. S., Tomasi, D. and Telang, F. (2011) Addiction: beyond dopamine reward circuitry. *Proc Natl Acad Sci U S A* **108,** 15037-15042.
Allison, C. and Shoaib, M. (2013) Nicotine improves performance in an attentional set shifting task in rats. *Neuropharmacology* **64,** 314-320.
Anker, J. J., Perry, J. L., Gliddon, L. A. and Carroll, M. E. (2009) Impulsivity predicts the escalation of cocaine self-administration in rats. *Pharmacol Biochem Behav* **93,** 343-348.
Baarendse, P. J. and Vanderschuren, L. J. (2012) Dissociable effects of monoamine reuptake inhibitors on distinct forms of impulsive behavior in rats. *Psychopharmacology (Berl)* **219,** 313-326.
Badanich, K. A., Becker, H. C. and Woodward, J. J. (2011) Effects of chronic intermittent ethanol exposure on orbitofrontal and medial prefrontal cortex-dependent behaviors in mice. *Behav Neurosci* **125,** 879-891.
Bari, A., Eagle, D. M., Mar, A. C., Robinson, E. S. and Robbins, T. W. (2009) Dissociable effects of noradrenaline, dopamine, and serotonin uptake blockade on stop task performance in rats. *Psychopharmacology (Berl)* **205,** 273-283.
Bari, A., Theobald, D. E., Caprioli, D., Mar, A. C., Aidoo-Micah, A., Dalley, J. W. and Robbins, T. W. (2010) Serotonin modulates sensitivity to reward and negative feedback in a probabilistic reversal learning task in rats. *Neuropsychopharmacology* **35,** 1290-1301.
Befort, K., Mahoney, M. K., Chow, C., Hayton, S. J., Kieffer, B. L. and Olmstead, M. C. (2011) Effects of delta opioid receptors activation on a response inhibition task in rats. *Psychopharmacology (Berl)* **214,** 967-976.
Beracochea, D., Celerier, A., Peres, M. and Pierard, C. (2003) Enhancement of learning processes following an acute modafinil injection in mice. *Pharmacol Biochem Behav* **76,** 473-479.
Bert, B., Harms, S., Langen, B. and Fink, H. (2006) Clomipramine and selegiline: do they influence impulse control? *Journal of veterinary pharmacology and therapeutics* **29,** 41-47.
Besheer, J. and Bevins, R. A. (2000) Nicotine enhances acquisition of a T-maze visual discrimination: assessment of individual differences. *Behav Pharmacol* **11,** 613-620.
Bizot, J. C., Chenault, N., Houze, B., Herpin, A., David, S., Pothion, S. and Trovero, F. (2007) Methylphenidate reduces impulsive behaviour in juvenile Wistar rats, but not in adult Wistar, SHR and WKY rats. *Psychopharmacology (Berl)* **193,** 215-223.
Bizot, J. C., David, S. and Trovero, F. (2011) Effects of atomoxetine, desipramine, d-amphetamine and methylphenidate on impulsivity in juvenile rats, measured in a T-maze procedure. *Neurosci Lett* **489,** 20-24.
Blackburn, J. R. and Hevenor, S. J. (1996) Amphetamine disrupts negative patterning but does not produce configural association deficits on an alternative task. *Behavioural brain research* **80,** 41-49.
Brigman, J. L., Mathur, P., Harvey-White, J., Izquierdo, A., Saksida, L. M., Bussey, T. J., Fox, S., Deneris, E., Murphy, D. L. and Holmes, A. (2010) Pharmacological or genetic inactivation of the serotonin transporter improves reversal learning in mice. *Cereb Cortex* **20,** 1955-1963.
Cain, D. P., Finlayson, C., Boon, F. and Beiko, J. (2002) Ethanol impairs behavioral strategy use in naive rats but does not prevent spatial learning in the water maze in pretrained rats. *Psychopharmacology (Berl)* **164,** 1-9.
Cardinal, R. N., Robbins, T. W. and Everitt, B. J. (2000) The effects of d-amphetamine, chlordiazepoxide, alpha-flupenthixol and behavioural manipulations on choice of signalled and unsignalled delayed reinforcement in rats. *Psychopharmacology (Berl)* **152,** 362-375.
Cole, S. O. (1990) Diazepam-induced impairment of a go–no-go successive discrimination. *Behavioral and neural biology* **53,** 371-377.
Cole, S. O. and Michaleski, A. (1986) Dose-dependent impairment in the performance of a go–no-go successive discrimination by chlordiazepoxide. *Psychopharmacology (Berl)* **88,** 184-186.
Counotte, D. S., Spijker, S., Van de Burgwal, L. H., Hogenboom, F., Schoffelmeer, A. N., De Vries, T. J., Smit, A. B. and Pattij, T. (2009) Long-lasting cognitive deficits resulting from adolescent nicotine exposure in rats. *Neuropsychopharmacology* **34,** 299-306.
Dallery, J. and Locey, M. L. (2005) Effects of acute and chronic nicotine on impulsive choice in rats. *Behav Pharmacol* **16,** 15-23.
Doty, R. L. and Ferguson-Segall, M. (1987) Odor detection performance of rats following d-amphetamine treatment: a signal detection analysis. *Psychopharmacology (Berl)* **93,** 87-93.
Eagle, D. M. and Robbins, T. W. (2003) Inhibitory control in rats performing a stop-signal reaction-time task: effects of lesions of the medial striatum and d-amphetamine. *Behav Neurosci* **117,** 1302-1317.
Eagle, D. M., Tufft, M. R., Goodchild, H. L. and Robbins, T. W. (2007) Differential effects of modafinil and methylphenidate on stop-signal reaction time task performance in the rat, and interactions with the dopamine receptor antagonist cis-flupenthixol. *Psychopharmacology* **192,** 193-206.
Eppolito, A. K., France, C. P. and Gerak, L. R. (2011) Effects of acute and chronic flunitrazepam on delay discounting in pigeons. *J Exp Anal Behav* **95,** 163-174.
Evenden, J. L. and Ryan, C. N. (1996) The pharmacology of impulsive behaviour in rats: the effects of drugs on response choice with varying delays of reinforcement. *Psychopharmacology (Berl)* **128,** 161-170.
Featherstone, R. E., Rizos, Z., Kapur, S. and Fletcher, P. J. (2008) A sensitizing regimen of amphetamine that disrupts attentional set-shifting does not disrupt working or long-term memory. *Behav Brain Res* **189,** 170-179.
Feola, T. W., de Wit, H. and Richards, J. B. (2000) Effects of d-amphetamine and alcohol on a measure of behavioral inhibition in rats. *Behavioral neuroscience* **114,** 838-848.
Floresco, S. B., Tse, M. T. and Ghods-Sharifi, S. (2008) Dopaminergic and glutamatergic regulation of effort- and delay-based decision making. *Neuropsychopharmacology* **33,** 1966-1979.
Galizio, M., Miller, L., Ferguson, A., McKinney, P. and Pitts, R. C. (2006) Olfactory repeated discrimination reversal in rats: effects of chlordiazepoxide, dizocilpine, and morphine. *Behav Neurosci* **120,** 1175-1179.
Groman, S. M., Lee, B., Seu, E., James, A. S., Feiler, K., Mandelkern, M. A., London, E. D. and Jentsch, J. D. (2012) Dysregulation of D(2)-mediated dopamine transmission in monkeys after chronic escalating methamphetamine exposure. *J Neurosci* **32,** 5843-5852.
Handley, G. W. and Calhoun, W. H. (1978) The effects of methylphenidate on repeated acquisition of serial discrimination reversals. *Psychopharmacology (Berl)* **57,** 115-117.
Harty, S. C., Whaley, J. E., Halperin, J. M. and Ranaldi, R. (2011) Impulsive choice, as measured in a delay discounting paradigm, remains stable after chronic heroin administration. *Pharmacol Biochem Behav* **98,** 337-340.
Harvey-Lewis, C., Perdrizet, J. and Franklin, K. B. (2012) The effect of morphine dependence on impulsive choice in rats. *Psychopharmacology (Berl)* **223,** 477-487.
Idris, N. F., Repeto, P., Neill, J. C. and Large, C. H. (2005) Investigation of the effects of lamotrigine and clozapine in improving reversal-learning impairments induced by acute phencyclidine and D-amphetamine in the rat. *Psychopharmacology (Berl)* **179,** 336-348.
Izquierdo, A., Belcher, A. M., Scott, L., Cazares, V. A., Chen, J., O'Dell, S. J., Malvaez, M., Wu, T. and Marshall, J. F. (2010) Reversal-specific learning impairments after a binge regimen of methamphetamine in rats: possible involvement of striatal dopamine. *Neuropsychopharmacology* **35,** 505-514.
Jentsch, J. D., Olausson, P., De La Garza, R., 2nd and Taylor, J. R. (2002) Impairments of reversal learning and response perseveration after repeated, intermittent cocaine administrations to monkeys. *Neuropsychopharmacology* **26,** 183-190.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Table 2 *(Continued)*

Kieres, A. K., Hausknecht, K. A., Farrar, A. M., Acheson, A., de Wit, H. and Richards, J. B. (2004) Effects of morphine and naltrexone on impulsive decision making in rats. *Psychopharmacology (Berl)* **173,** 167-174.
Kirshenbaum, A. P., Jackson, E. R., Brown, S. J., Fuchs, J. R., Miltner, B. C. and Doughty, A. H. (2011) Nicotine-induced impulsive action: sensitization and attenuation by mecamylamine. *Behav Pharmacol* **22,** 207-221.
Kolokotroni, K. Z., Rodgers, R. J. and Harrison, A. A. (2011) Acute nicotine increases both impulsive choice and behavioural disinhibition in rats. *Psychopharmacology (Berl)* **217,** 455-473.
Kolokotroni, K. Z., Rodgers, R. J. and Harrison, A. A. (2012) Effects of chronic nicotine, nicotine withdrawal and subsequent nicotine challenges on behavioural inhibition in rats. *Psychopharmacology (Berl)* **219,** 453-468.
Kosheleff, A. R., Rodriguez, D., O'Dell, S. J., Marshall, J. F. and Izquierdo, A. (2012) Comparison of single-dose and extended methamphetamine administration on reversal learning in rats. *Psychopharmacology (Berl).*
Krueger, D. D., Howell, J. L., Oo, H., Olausson, P., Taylor, J. R. and Nairn, A. C. (2009) Prior chronic cocaine exposure in mice induces persistent alterations in cognitive function. *Behav Pharmacol* **20,** 695-704.
Kulig, B. M. and Calhoun, W. H. (1972) Enhancement of successive discrimination reversal learning by methamphetamine. *Psychopharmacologia* **27,** 233-240.
Kuzmin, A., Liljequist, S., Meis, J., Chefer, V., Shippenberg, T. and Bakalkin, G. (2012) Repeated moderate-dose ethanol bouts impair cognitive function in Wistar rats. *Addict Biol* **17,** 132-140.
Liu, S., Heitz, R. P. and Bradberry, C. W. (2009) A touch screen based Stop Signal Response Task in rhesus monkeys for studying impulsivity associated with chronic cocaine self-administration. *Journal of neuroscience methods* **177,** 67-72.
Loiseau, F., Le Bihan, C., Hamon, M. and Thiebot, M. H. (2005) Antidepressant-like effects of agomelatine, melatonin and the NK1 receptor antagonist GR205171 in impulsive-related behaviour in rats. *Psychopharmacology (Berl)* **182,** 24-32.
Loos, M., Staal, J., Schoffelmeer, A. N., Smit, A. B., Spijker, S. and Pattij, T. (2010) Inhibitory control and response latency differences between C57BL/6J and DBA/2J mice in a Go/No-Go and 5-choice serial reaction time task and strain-specific responsivity to amphetamine. *Behav Brain Res* **214,** 216-224.
Maguire, D. R., Li, J. X. and France, C. P. (2012) Impulsivity and drugs of abuse: A juice-reinforced operant procedure for determining within-session delay discounting functions in rhesus monkeys. *J Pharmacol Toxicol Methods.*
McLean, S. L., Neill, J. C., Idris, N. F., Marston, H. M., Wong, E. H. and Shahid, M. (2010) Effects of asenapine, olanzapine, and risperidone on psychotomimetic-induced reversal-learning deficits in the rat. *Behav Brain Res* **214,** 240-247.
Mendez, I. A., Gilbert, R. J., Bizon, J. L. and Setlow, B. (2012) Effects of acute administration of nicotinic and muscarinic cholinergic agonists and antagonists on performance in different cost-benefit decision making tasks in rats. *Psychopharmacology (Berl).*
Moschak, T. M., Stang, K. A., Phillips, T. J. and Mitchell, S. H. (2012) Behavioral inhibition in mice bred for high vs. low levels of methamphetamine consumption or sensitization. *Psychopharmacology (Berl)* **222,** 353-365.
Oberlin, B. G. and Grahame, N. J. (2009) High-Alcohol Preferring Mice Are More Impulsive Than Low-Alcohol Preferring Mice as Measured in the Delay Discounting Task. *Alcoholism, clinical and experimental research.*
Obernier, J. A., White, A. M., Swartzwelder, H. S. and Crews, F. T. (2002) Cognitive deficits and CNS damage after a 4-day binge ethanol exposure in rats. *Pharmacol Biochem Behav* **72,** 521-532.
Olmstead, M. C., Hellemans, K. G. and Paine, T. A. (2006) Alcohol-induced impulsivity in rats: an effect of cue salience? *Psychopharmacology* **184,** 221-228.
Paine, T. A., Dringenberg, H. C. and Olmstead, M. C. (2003) Effects of chronic cocaine on impulsivity: relation to cortical serotonin mechanisms. *Behavioural brain research* **147,** 135-147.
Paine, T. A. and Olmstead, M. C. (2004) Cocaine disrupts both behavioural inhibition and conditional discrimination in rats. *Psychopharmacology* **175,** 443-450.
Parsegian, A., Glen, W. B., Jr., Lavin, A. and See, R. E. (2011) Methamphetamine self-administration produces attentional set-shifting deficits and alters prefrontal cortical neurophysiology in rats. *Biol Psychiatry* **69,** 253-259.
Pattij, T., Schetters, D., Janssen, M. C., Wiskerke, J. and Schoffelmeer, A. N. (2009) Acute effects of morphine on distinct forms of impulsive behavior in rats. *Psychopharmacology (Berl)* **205,** 489-502.
Perry, J. L., Stairs, D. J. and Bardo, M. T. (2008) Impulsive choice and environmental enrichment: effects of d-amphetamine and methylphenidate. *Behav Brain Res* **193,** 48-54.
Porter, J. N., Olsen, A. S., Gurnsey, K., Dugan, B. P., Jedema, H. P. and Bradberry, C. W. (2011) Chronic cocaine self-administration in rhesus monkeys: impact on associative learning, cognitive control, and working memory. *J Neurosci* **31,** 4926-4934.
Poulos, C. X., Parker, J. L. and Le, D. A. (1998) Increased impulsivity after injected alcohol predicts later alcohol consumption in rats: evidence for "loss-of-control drinking" and marked individual differences. *Behav Neurosci* **112,** 1247-1257.
Ranaldi, R., Egan, J., Kest, K., Fein, M. and Delamater, A. R. (2009) Repeated heroin in rats produces locomotor sensitization and enhances appetitive Pavlovian and instrumental learning involving food reward. *Pharmacol Biochem Behav* **91,** 351-357.
Richards, J. B., Sabol, K. E. and de Wit, H. (1999) Effects of methamphetamine on the adjusting amount procedure, a model of impulsive behavior in rats. *Psychopharmacology (Berl)* **146,** 432-439.
Robinson, E. S., Eagle, D. M., Mar, A. C., Bari, A., Banerjee, G., Jiang, X., Dalley, J. W. and Robbins, T. W. (2008) Similar effects of the selective noradrenaline reuptake inhibitor atomoxetine on three distinct forms of impulsivity in the rat. *Neuropsychopharmacology* **33,** 1028-1037.
Roesch, M. R., Takahashi, Y., Gugsa, N., Bissonette, G. B. and Schoenbaum, G. (2007) Previous cocaine exposure makes rats hypersensitive to both delay and reward magnitude. *J Neurosci* **27,** 245-250.
Russig, H., Durrer, A., Yee, B. K., Murphy, C. A. and Feldon, J. (2003) The acquisition, retention and reversal of spatial learning in the morris water maze task following withdrawal from an escalating dosage schedule of amphetamine in wistar rats. *Neuroscience* **119,** 167-179.
Schippers, M. C., Binnekade, R., Schoffelmeer, A. N., Pattij, T. and De Vries, T. J. (2012) Unidirectional relationship between heroin self-administration and impulsive decision-making in rats. *Psychopharmacology (Berl)* **219,** 443-452.
Seu, E., Lang, A., Rivera, R. J. and Jentsch, J. D. (2009) Inhibition of the norepinephrine transporter improves behavioral flexibility in rats and monkeys. *Psychopharmacology (Berl)* **202,** 505-519.
Simon, N. W., Mendez, I. A. and Setlow, B. (2007) Cocaine exposure causes long-term increases in impulsive choice. *Behavioral neuroscience* **121,** 543-549.
Slezak, J. M. and Anderson, K. G. (2011) Effects of acute and chronic methylphenidate on delay discounting. *Pharmacol Biochem Behav* **99,** 545-551.
Slezak, J. M., Krebs, C. A. and Anderson, K. G. (2012) A within-subject analysis of d-amphetamine exposure on delay discounting in rats. *Pharmacol Biochem Behav* **102,** 502-506.
Sokolic, L. and McGregor, I. S. (2007) Benzodiazepines impair the acquisition and reversal of olfactory go/no-go discriminations in rats. *Behav Neurosci* **121,** 527-534.
Stalnaker, T. A., Roesch, M. R., Calu, D. J., Burke, K. A., Singh, T. and Schoenbaum, G. (2007) Neural correlates of inflexible behavior in the orbitofrontal-amygdalar circuit after cocaine exposure. *Ann N Y Acad Sci* **1121,** 598-609.
Thiebot, M. H., Le Bihan, C., Soubrie, P. and Simon, P. (1985) Benzodiazepines reduce the tolerance to reward delay in rats. *Psychopharmacology* **86,** 147-152.
Tomie, A., Aguado, A. S., Pohorecky, L. A. and Benjamin, D. (1998) Ethanol induces impulsive-like responding in a delay-of-reward operant choice procedure: impulsivity predicts autoshaping. *Psychopharmacology (Berl)* **139,** 376-382.
van Gaalen, M. M., van Koten, R., Schoffelmeer, A. N. and Vanderschuren, L. J. (2006) Critical involvement of dopaminergic neurotransmission in impulsive decision making. *Biol Psychiatry* **60,** 66-73.
Weiner, I. and Feldon, J. (1986) Reversal and nonreversal shifts under amphetamine. *Psychopharmacology (Berl)* **89,** 355-359.
Wilhelm, C. J. and Mitchell, S. H. (2008) Rats bred for high alcohol drinking are more sensitive to delayed and probabilistic outcomes. *Genes, brain, and behavior* **7,** 705-713.
Wilhelm, C. J., Reeves, J. M., Phillips, T. J. and Mitchell, S. H. (2007) Mouse lines selected for alcohol consumption differ on certain measures of impulsivity. *Alcoholism, clinical and experimental research* **31,** 1839-1845.
Wooters, T. E. and Bardo, M. T. (2011) Methylphenidate and fluphenazine, but not amphetamine, differentially affect impulsive choice in spontaneously hypertensive, Wistar-Kyoto and Sprague-Dawley rats. *Brain Res* **1396,** 45-53.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

2007; Jarrott et al., 1982), generally slows SST performance and impairs stop accuracy in the rat at high doses (Bari et al., 2009) and when infused directly in the dorsomedial PFC (Bari et al., 2011a), while it had no effect on healthy volunteers at the dose tested by Muller et al. (2005). Conversely, systemic administration of the selective α2-adrenoceptor antagonist atipamezole (Bari and Robbins, 2013) or atomoxetine infusion in the rat dorsomedial PFC improve stopping, whereas blocking DA receptors in the same area selectively impairs the go response (Bari et al., 2011a). Taken together, these results strongly suggest that atomoxetine improves response inhibition via noradrenergic modulation of PFC neurons, although the exact mechanism is yet not known. One possibility is that increased NE release in cortical areas facilitates attention to task-related stimuli (Cubillo et al., 2013) and optimizes the redistribution of neural activation between different brain areas in fast-changing contexts, similar to its role in neurovascular coupling (Bekar et al., 2012).

The wake-promoting agent modafinil has been shown to improve response inhibition in healthy volunteers (Turner et al., 2003; Zack and Poulos, 2009), ADHD patients (Turner et al., 2004a) and rats (Eagle et al., 2007), but not in Huntington's disease (Blackwell et al., 2008) or schizophrenic patients (Turner et al., 2004b). Its mechanisms of action on cognition have not yet been fully elucidated, although they seem to be mediated primarily by catecholaminergic neurotransmission in cortical areas (see Ballon and Feifel, 2006; Minzenberg and Carter, 2007; Scoriels et al., 2013 for reviews). Similar to methylphenidate, modafinil-mediated improvements in response inhibition in rats were not altered by DA D1/D2 antagonist co-administration, suggesting that mechanisms other than dopaminergically mediated ones are responsible for such improvements (Eagle et al., 2007). It has been proposed that modafinil modulates the firing properties of the locus coeruleus – the only source of forebrain NE – causing a shift from a tonic to a phasic mode of neuronal firing (Minzenberg et al., 2008), which is regarded as a neurophysiological correlate of focused attention (Aston-Jones et al., 1999).

Although the important role for noradrenergic neurotransmission in response inhibition has been confirmed by several studies, the specific cognitive processes affected by this modulatory neurotransmitter are still a matter of debate. It is possible that elevated noradrenergic tone enhances inhibitory processes through gain modulation of neurons in multiple brain regions (Aston-Jones et al., 2000; Berridge and Waterhouse, 2003) facilitating both stop-signal detection and the transmission of the stop command to output motor regions. On the other hand, the LC phasic response has been shown to be time-locked to the task-appropriate behavioral response rather than to the stimulus itself (Clayton et al., 2004; Rajkowski et al., 2004). LC neurons are phasically activated by unexpected or behaviorally relevant stimuli and thus their activation being more closely related to the behavioral output suggests that the LC is involved in the actuation of decisions based on task rules. Accordingly, LC phasic activation and the resulting increase in forebrain NE release is hypothesized to facilitate the appropriate behavioral response to imperative stimuli (Aston-Jones and Cohen, 2005b; Nieuwenhuis, 2010). Finally, since the noradrenergic system is involved in sustained attention and in the orienting response to stimuli, the attentional demand of the task used should be taken into account when interpreting the effects of noradrenergic manipulation on response inhibition.

Particular attention has been devoted to the scalp-recorded P300 component of ERPs during response inhibition tasks, which is thought to be generated by phasic LC activation (Nieuwenhuis et al., 2005), although it is not clear yet whether this component reflects inhibitory processes, conflict monitoring or the orienting response to salient stimuli (Bekker et al., 2005b; Dimoska and Johnstone, 2007; Dimoska et al., 2006; Huster et al., 2010; Johnstone et al., 2007; Nieuwenhuis et al., 2010). Moreover, the electrophysiological activity of noradrenergic neurons in the LC is strongly modulated by drugs that improve response inhibition such as methylphenidate (Devilbiss and Berridge, 2006) and atomoxetine (Bari and Aston-Jones, 2013) which have been suggested to improve communication within and between brain areas important for executive control (Arnsten and Dudley, 2005; Bari and Aston-Jones, 2013; Gamo and Arnsten, 2011; Gamo et al., 2010; Robbins and Arnsten, 2009). In sum, the LC-NE system is a good candidate as a key modulator of fast inhibitory processes possibly acting at different levels such as stimulus detection, behavioral orienting, attentional shifting and conflict detection (Aston-Jones and Cohen, 2005a; Aston-Jones et al., 1999; Berridge and Waterhouse, 2003; Bouret and Sara, 2005; Corbetta and Shulman, 2002; Sara, 2009; Yu and Dayan, 2005). Although mediating the enhancement of different cognitive processes and the 'amplification' of relevant stimuli, the specific contribution of the LC-NE system to response inhibition is still unknown. However, converging evidence suggests that it may facilitate not only stimulus detection (Aston-Jones and Bloom, 1981; Robbins and Everitt, 1982), but also the rearrangement of cognitive and neural resources (Corbetta et al., 2008; Hermans et al., 2011; Sara and Bouret, 2012) to allow executive-oriented shifts of attention and behavior.

The serotonergic system seems to have a marginal role, if any, in SST inhibition because 5-HT depletion or administration of the selective serotonin reuptake inhibitors (SSRI) do not alter the SSRT in humans or rats (Bari et al., 2009; Chamberlain et al., 2006b; Clark et al., 2005; Cools et al., 2005; Eagle et al., 2009; Nandam et al., 2011; Overtoom et al., 2009), although a possible interaction between 5-HT levels and individuals' history of alcoholism in the ability to stop a response has been reported (Crean et al., 2002). One study described improved response inhibition following MDMA intoxication. The authors suggested a possible link with 5-HT neurotransmission for this effect (Ramaekers and Kuypers, 2006), similar to the case of desipramine effects in ADHD children (Overtoom et al., 2003). Methylphenidate administration has no effect on extracellular levels of 5-HT in the rat brain, which suggests that its beneficial effects on impulsivity are independent of 5-HT neurotransmission (Kuczenski and Segal, 1997). The serotonergic system, however, plays an important role in action withholding and deferring gratification (Dalley and Roiser, 2012; Eagle et al., 2008a), probably affecting the motivational significance of the pre-potent action to be inhibited on the basis of future reward or punishment (Homberg, 2012; Miyazaki et al., 2012; Soubrié, 1986). Other aspects of impulsive behavior that are linked to 5-HT and to the genetic polymorphysms affecting 5-HT neurotransmission are aggression and suicidal tendencies (Coccaro et al., 2011; Ferrari et al., 2005; Heinz et al., 2011; Pavlov et al., 2012). However, the effect of genetic or early environmental variables affecting the 5-HT system should be interpreted with caution, given the important neurotrophic role of 5-HT and its strong impact on other neuromodulator systems and brain connectivity during development. Future studies using selective pharmacological agents acting on 5-HT receptors may more effectively define the role of 5-HT neurotransmission in response inhibition.

Recent studies have investigated the role of cholinergic neurotransmission in response inhibition and found baseline-dependent effects. Thus, activation of nicotinic receptors improved SSRT in high-impulsive subjects and ADHD patients, while blockade of the same receptors impaired inhibitory performance in normal volunteers (Potter et al., 2012; Potter and Newhouse, 2008). However, it is known that cholinergic stimulation increases cognitive performance by enhancing attentional levels (Sarter and

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Paolone, 2011) and mice lacking nicotinic receptor β2-subunit in dorsal prefrontal areas show impaired attention (Guillem et al., 2011). These and other results (e.g., Bekker et al., 2005a; Harati et al., 2008) suggest that the cholinergic agonists may improve performance during response inhibition tasks by boosting attentional levels, but probably have no direct effect on inhibitory processes. Other drugs such as benzodiazepines (Acheson et al., 2006; Fillmore et al., 2001; but see Reynolds et al., 2004), cannabinoids (McDonald et al., 2003; Pattij et al., 2007; Ramaekers et al., 2009, 2006) and alcohol (de Wit et al., 2000; Feola et al., 2000; Loeber and Duka, 2009; Mulvihill et al., 1997) have been consistently shown to impair SSRT. Caffeine is without effect in healthy individuals, although it may enhance sustained attention (Tieges et al., 2009). Finally, opioids (Pattij et al., 2009; Zacny and de Wit, 2009) and anti-histaminergic drugs (Theunissen et al., 2006) do not alter response inhibition as measured by the SST.

High-impulsive rats, which have difficulty at inhibiting their response while waiting for the appearance of a stimulus in the 5-choice serial reaction time task, display lower levels of the D2/3 subtype of dopamine receptors in the ventral striatum and acquire more readily cocaine self-administration, compared to low impulsive subjects (Dalley et al., 2007). Moreover, recent studies have shown that blocking D2 receptors in the dorsal striatum negatively affects SST performance (Eagle et al., 2011) but normalizes impulsive behavior in the 5-CSRTT when infused into the nucleus accumbens (Pezze et al., 2009). On the other hand, systemic or PFC D2 receptor antagonism does not affect impulsivity in the rodent SST (Bari et al., 2011a; Bari and Robbins, 2013) or in the 5-CSRTT (Granon et al., 2000; van Gaalen et al., 2006a). In humans, Hamidovic et al. (2009) found that in subjects carrying a DRD2 polymorphism associated with a slow SSRT, amphetamine speeded stopping performance, while it had the opposite effect on subjects with a different polymorphism associated with fast SSRTs under placebo conditions. Similarly, in humans and other animals, dopamine D2 receptors located in the striatum are a critically important link between impulsivity and drug addiction (Volkow et al., 2007). Recently the DA D2 receptor agonist cabergoline has been shown to improve SSRT in healthy volunteers (Nandam et al., 2013), although the interpretation of these effects is complicated by the affinity of this drug for other receptors.

Taken together, these results suggest an important role for prefrontal noradrenergic neurotransmission in the inhibition of an already initiated response (Eagle et al., 2008a; Robbins and Arnsten, 2009), whereas DA appears to modulate motor readiness for both inhibition and activation, potentially at the level of the striatum (Bari et al., 2009; Brown and Robbins, 1991; Eagle et al., 2011; Ghahremani et al., 2012; Lange et al., 1992), and both NE and DA influence error monitoring and performance adjustment (Bari and Robbins, 2013; Chevrier and Schachar, 2010; de Bruijn et al., 2004; Nandam et al., 2013; Riba et al., 2005). Finally, 5-HT might contribute to more affective forms of inhibition and/or '*waiting*' behavior (Eagle et al., 2008a) when gains have to be weighed against losses. The studies described above represent important advancements towards the definition of the pathological neural substrates of diseases characterized by impulsivity and/or the propensity to develop compulsive behavior and addictions. A challenge for future research will be the dissociation of inhibition from attention and shifting at the behavioral level so to better define the role of different neurotransmitter systems in cognitive control.

3.2. Cortical mechanisms of response inhibition

Luria (1966) proposed that the frontal lobes serve to regulate behavior according to current goals and that patients with damage in those areas are unable to follow task instructions, although they correctly understand their meaning. Behavioral inhibition is dependent on the integrity of the frontal lobes and is strongly impaired in patients and animals with frontal lesions (Brutkowski and Mempel, 1961; Drewe, 1975a,b; Mishkin, 1964; Stanley and Jaynes, 1949). From the results of his experiments on monkeys, Mishkin concluded that "*... frontal lesions produce abnormal difficulty in suppressing whatever response normally prevails in a given situation.*" (Mishkin et al., 1962), whereas others defined PFC lesion effects in dogs as disinhibition of inhibitory reflexes (Brutkowski et al., 1956; Konorski, 1961). However, impulsive behavior is not the only consequence of frontal damage and it has long been recognized that another preponderant characteristic of animals bearing frontal lesions is a high level of distractibility (e.g., Kluver, 1933; Konorski and Lawicka, 1964) and 'hyperreactivity' (Rosvold and Mishkin, 1961). In this regard Konorski wrote that "*The higher level of control* [by the frontal cortex] *would tend to inhibit the orienting reaction in order to allow attention to be shifted, to be increased or decreased depending on the significance of the stimulus.*" (Konorski and Lawicka, 1964, p. 293). Current models of inhibitory control acknowledge the critical contribution of prefrontal and pre-motor areas to response inhibition and consider the orienting reaction to be modulated by a brain stem-cortical circuit which is sensitive to environmental variables, as well as to the current goals of the organism (Nieuwenhuis et al., 2010; Sara and Bouret, 2012). This 'flexible' orienting reaction may thus represent the necessary step towards successful control of voluntary or automatic responses.

In general, executive control is thought to operate in a hierarchical manner with the PFC having a leading role over lower-level structures (Brooks, 1986; Fuster, 1989; Norman and Shallice, 1986; Robbins, 1996; Stuss, 1992). Moreover, depending on the specific task, different cortical and subcortical regions are involved in ancillary processes such as sustained attention, conflict detection and online representation of task rules. Cortical areas most often involved in response inhibition tasks according to fMRI and lesion studies include the pre-SMA, SMA (Mostofsky et al., 2003; Simmonds et al., 2008), pre-motor cortex (Picton et al., 2007; Watanabe et al., 2002), parietal cortex (Menon et al., 2001; Rubia et al., 2001) ventrolateral PFC and insula (Boehler et al., 2010; Swick et al., 2008). Activation of the *right* inferior frontal cortex (IFC) and the adjacent insula has been consistently linked to response inhibition (Aron et al., 2004; Garavan et al., 2006, 1999; Kelly et al., 2004; Konishi et al., 1998), although activation is sometimes observed bilaterally (e.g., Cai and Leung, 2011; Menon et al., 2001; Watanabe et al., 2002). However, the insular cortex may be involved in interference resolution when conflicting responses are activated (Bunge et al., 2002a,b; Wager et al., 2005) or, more generally, in maintaining high levels of motivation and top-down control during behavioral tasks (Dosenbach et al., 2008). On the other hand, parietal activation may be related to the visuospatial attentional demands of the task (Rubia et al., 2001), because of its involvement in sensorimotor integration (Grafton et al., 1992), whereas the pre-motor region is known to control motor excitability of the contralateral limbs independently from motor area 1 (M1; Gerschlager et al., 2001; Rizzo et al., 2004).

The dorsolateral PFC displays high levels of activity during response inhibition tasks (Fassbender et al., 2004; Garavan et al., 2006; Hester et al., 2004; Menon et al., 2001), but this area is probably more involved in maintaining task rules 'on-line' (Levy and Goldman-Rakic, 2000; Petrides, 2000) as its activation has been related to the increased working memory load in some studies (Mostofsky et al., 2003; Simmonds et al., 2008). In general, the dorsolateral PFC is thought to exert executive control on motivational and emotional behaviors (Delgado et al., 2008), rather than on motor responses. Li et al. (2006) isolated cerebral areas

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

responsible for response inhibition from those concerned with signal monitoring and post-response processes. In their study, the superior and pre-central gyri, which are part of the SMA, were considered as being specifically involved in stopping a response because they were more active in subjects with fast SSRT and the degree of such activation was correlated with the speed of response inhibition. Moreover, motor inhibition has been produced by direct electrical stimulation of the pre-SMA in monkeys (Isoda and Hikosaka, 2007) and humans (Fried et al., 1991; Luders et al., 1988). Accordingly, deficits in response inhibition have been observed after temporary inactivation of the pre-SMA (Chen et al., 2009) and damage to medial prefrontal portions of the brain overlapping with it (Floden and Stuss, 2006; Nachev et al., 2007). However the SMA is also involved in response initiation (Dinner and Luders, 1995; Kawashima et al., 1996) and selection (Rowe et al., 2010) as well as inhibition (Nachev et al., 2005), whereas more executive forms of stopping may be carried out by other structures (Rubia et al., 2001). Patients with lesions including the SMA, the pre-motor area and the motor subdivision of the anterior cingulate cortex (ACC) show prolonged reaction times and increased number of omissions to the go stimulus (Fellows and Farah, 2005b; Picton et al., 2007; Stuss et al., 2002), which is suggestive of a more general role in motor behavior and response selection for these regions (e.g., Ball et al., 1999; Humberstone et al., 1997; Mostofsky and Simmonds, 2008). Finally FEFs, also belonging to the SMA and critically involved in saccade countermanding tasks (Stuphorn and Schall, 2006), play an important role in the monitoring of behavior (Stuphorn et al., 2000).

Many reports of impaired performance in go/no-go tasks have identified the medial sector of the PFC as being responsible for such deficits (e.g., Drewe, 1975b; Godefroy and Rousseaux, 1996; Leimkuhler and Mesulam, 1985; Verfaellie and Heilman, 1987). These results are supported by fMRI and PET studies in humans which highlight a possible role of ACC in response inhibition (Casey et al., 1997b; Garavan et al., 1999; Kawashima et al., 1996; Rubia et al., 2001). Among the different functions that have been ascribed to the human ACC are 'attention-for-action' (Posner et al., 1988), response selection (Bench et al., 1992; Corbetta et al., 1991; Paus et al., 1993), error detection (Carter et al., 1998; Gemba et al., 1986) conflict monitoring (Botvinick et al., 2001) anticipation (Murtha et al., 1996) and working memory (Petit et al., 1998). Moreover, the human ACC has been proposed to subserve motor control by facilitating appropriate responses and inhibiting inappropriate ones especially in fast-changing contexts (Paus et al., 1993). Although primate ACC is considered one of the main limbic structures, it has both motor functions and access to autonomic information, which are integrated in order to select the appropriate behavioral output (Devinsky et al., 1995; Vogt et al., 1992). The ACC projects directly to the spinal cord (Biber et al., 1978; Dum and Strick, 1991), to several nuclei of the basal ganglia (Kunishio and Haber, 1994; Muller-Preuss and Jurgens, 1976; Yeterian and Van Hoesen, 1978) and possesses reciprocal connections with motor and supplementary motor areas (Devinsky et al., 1995), which place it in an ideal position for goal-directed response control.

Although lesions of the ACC impair the voluntary suppression of eye and arm movements (Goldberg et al., 1981; Paus et al., 1991), its role in the intact brain has been subsequently demonstrated to be more concerned with conflict monitoring, error detection and the allocation of attentional resources (Botvinick et al., 2001; Braver et al., 2001; Carter et al., 2000; Kiehl et al., 2000; Menon et al., 2001; Paus, 2001; Ridderinkhof et al., 2004; Rubia et al., 2003; Rushworth et al., 2004) rather than with response inhibition *per se* (Fellows and Farah, 2005b). Prominent computational models of cognitive control propose that the ACC signals to other brain areas the presence of conflict and the necessity of increased executive control over behavioral output (Brown and Braver, 2005; Cohen et al., 2004), whereas others emphasize its role in action selection according to the principles of reinforcement learning theories (Holroyd and Coles, 2002). In rats, dorsomedial prefrontal cortex lesion or its temporary inactivation impair response inhibition in the SST (Bari et al., 2011a), 5-CSRTT (Muir et al., 1996; Paine et al., 2011; Passetti et al., 2002) and in the lever holding task (Narayanan et al., 2006) without affecting sensory, motivational and non-inhibitory motor processes. Interestingly, the rat medial prefrontal cortex may also exhibit a certain degree of right lateralization, similar to humans, when behavioral inhibition has to be exerted (Sullivan and Gratton, 2002).

Another sector of the PFC, the orbitofrontal cortex (OFC), does not seem to play a central role in tasks requiring motor inhibition in humans (Swick et al., 2008), but see (Horn et al., 2003). However, a recent study on a large non-clinical sample of adolescents distinguished two main brain networks differently involved during SST inhibition related to sub-clinical ADHD symptoms or drug use. The authors showed that OFC hypoactivity during response inhibition characterizes the neural phenotype of adolescents who made use of alcohol, nicotine or illicit substances, whereas hypoactivation of a right frontal-basal ganglia network was observed in subjects with ADHD-related symptoms (Whelan et al., 2012). These results suggest that hypofunction of distinct fronto-cortical networks, although having different pathophysiological origins, may converge on similar behavioral manifestations of deficient response inhibition, probably selectively acting on affective ('hot') or executive processes ('cold'). Decreasing serotonergic tone by tryptophan depletion in humans has been found to affect the activity of the OFC during response inhibition (Rubia et al., 2005), although no behavioral effects were observed, which is in keeping with data from experiments in rats (Eagle et al., 2009). Moreover, the OFC has been implicated in the SST performance of rats, with OFC lesions slowing SSRTs (Eagle et al., 2008b) and infusions of atomoxetine in this area improving general SST performance (Bari et al., 2011a). One crucial difference with other prefrontal areas which are more directly implicated in action inhibition may lay in the relatively specific involvement of the OFC in computations regarding affectively relevant stimuli and their value, as opposed to the evaluation of actions and their implementation/inhibition based on internal goals (Rudebeck et al., 2008), which may be preferentially handled by more dorsal areas of the PFC. Impaired action- or stimulus-related inhibitory processes, will both result in impulsivity, but with different, although sometimes partially overlapping, behavioral manifestations.

Important differences have also been observed between brain activation patterns during SST and go/no-go tasks. Although both tasks tap inhibitory processes and impulsive subjects are impaired on both measures, they have been partially dissociated anatomically and pharmacologically (Eagle et al., 2008a; Schachar et al., 2007; Swick et al., 2011). Rubia et al. (2001) contrasted patterns of brain activation elicited by SST and go/no-go task and concluded that performance in the former is more related to right-sided activations, whilst a bilateral activation is seen during no-go inhibition. These authors hypothesized that the main difference between the two tasks is in the degree of response selection involved, which is higher in go/no-go tasks whilst on the other hand, inhibition is more difficult in the SST. Different results were obtained by two other studies that used both SST and go/no-go task on the same subjects. When common activations to both tasks were analyzed, one study found a predominant activation of the right middle frontal gyrus (Zheng et al., 2008), whereas the other found bilateral IFG activation in addition to right middle frontal gyrus and left insula foci of activity (McNab et al., 2008). Finally, a recent meta-analysis obtained contrasting findings to those of Rubia et al. (2001), with right-lateralized foci of activity during go/ Q8 no-go and bilateral patterns during SST, although this study found

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

larger contribution of the insula compared to the IFG to response inhibition (Swick et al., 2011). These discrepant findings highlight the need for further investigation on the different types of response inhibition, a direction that has been recently undertaken by several groups. One notable example is the distinction between the fast interruption of ongoing activity and the tonic withholding of action tendencies (e.g., Aron, 2010; Eagle et al., 2008a), which have been discussed here previously.

In summary, given the number of different processes necessary for successful response inhibition, both in real life and in the laboratory (e.g., stimulus/conflict detection, sustained attention, attentional shifting, error monitoring and so on), it seems reasonable that a complex circuit is involved. It is probably the interaction between IFC and pre-SMA (plus subcortical and brain stem nuclei; see below) that allows the successful inhibition of a pre-potent motor response (Aron, 2010; Sharp et al., 2010), a conclusion that is corroborated by connectivity and causality studies (Fig. 6; Aron et al., 2007; Duann et al., 2009; Pandya et al., 1981; Vogt and Pandya, 1987). More lesion studies are needed to confirm neuroimaging results and to clearly establish the role of specific brain areas in response inhibition tasks, although functional recovery, poor specificity of the lesion and heterogeneity of the experimental sample may limit the power of such studies in humans. Moreover, it is often impossible to exclude the contribution to the deficit observed of damaged fibers of passage in the affected area, which would influence the effective communication within brain networks. These and other limitations can be overcome, with the obvious caveats, by the use of animal models (Bari et al., 2011b; Winstanley et al., 2006). Although comparisons regarding the homology of brain areas between humans and rodents has to be made carefully (Preuss, 1995), strong parallels can sometimes be drawn from what is known about the anatomical and functional homology between brain structures in different species (Robbins, 1998; Uylings et al., 2003).

3.3. Subcortical contribution to response inhibition

Q9 De Jong et al. (1995, 1990) proposed the existence of two inhibitory processes. A *selective* one, to stop only some actions but not others that are active at the same time, and a *non-selective* one to stop all active response processes. They suggested that the first has its locus of action upstream from M1, while the second operates 'peripherally' via midbrain regions. They based these conclusions on the analysis of lateralized readiness potentials, which reflect the activation of the motor cortex, and electromyographic activity, which is related to muscle activation. Band and van Boxtel (1999) criticized the conclusions of De Jong et al. (1995) because they were based on assumptions that are difficult to validate and involved psychophysiological measures of dubious interpretation, concluding that there was no evidence for a post-motor cortex locus of inhibition. Instead, they support the hypothesis of a single central inhibitory mechanism in the frontal cortex, although acknowledging the possibility of an important contribution of the basal ganglia and the thalamus, based on theories derived from Skinner and Yingling's (1977) model of sensory gating. Similarly, in Brunia's model, the role of the thalamus is to allow motor information – elaborated through the interaction between PFC and basal ganglia – to reach M1 in order to execute the response; the occurrence of a stop cue would close the thalamic 'gate' inhibiting the response (Brunia, 1993).

According to prominent views regarding the neural substrates of stopping an ongoing response, cortical areas involved in response inhibition send a stop command to basal ganglia structures which, in turn, 'intercept' the go response, thus decreasing the excitability of M1 (Greenhouse et al., 2011b). One important recipient of cortical stopping commands is the subthalamic nucleus (STN) which is directly connected to pre-SMA and IFG (Fig. 6; Aron et al., 2007; Inase et al., 1999). Cortico-basal ganglia projections reaching the STN are part of the so-called *hyperdirect* pathway (Nambu et al., 2002) and allow for fast inhibition of ongoing actions by increasing inhibitory signals from the globus pallidus, to which the STN strongly projects, thus inhibiting the output from the basal ganglia (Alexander and Crutcher, 1990; Parent and Hazrati, 1995). Several lines of investigation have established the involvement of the STN in response inhibition (Aron and Poldrack, 2006; Forstmann et al., 2012; Frank, 2006; Hikosaka and Isoda, 2010; Li et al., 2008; Munakata et al., 2011). These include studies in Parkinson's disease

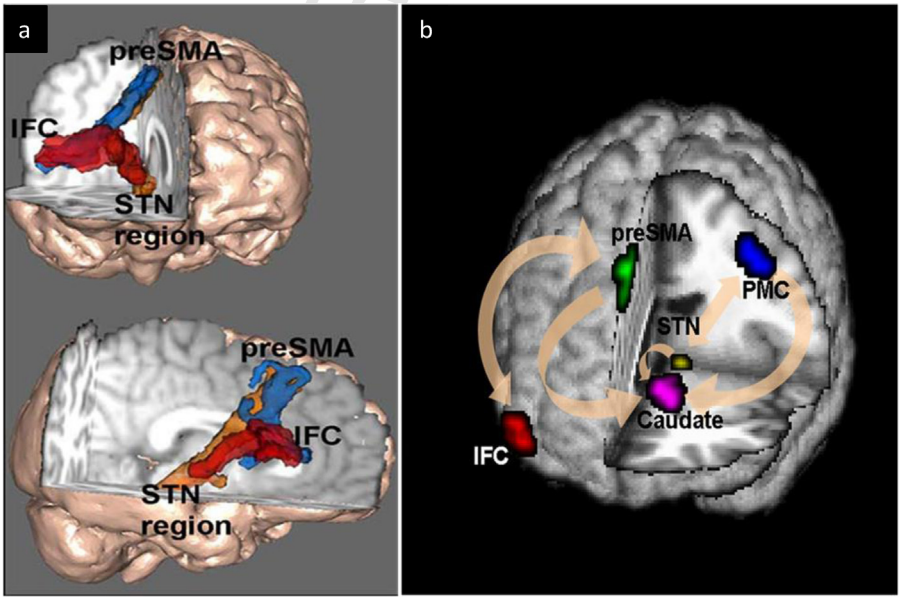

Fig. 6. a) 3-D rendering of a diffusion-weighted tractography analysis of the network involved in SST inhibition showing white matter tracts between structures (Aron et al., 2007). b) Granger causality analysis results showing functional connectivity between cortical and subcortical areas during response inhibition (Duann et al., 2009). But see Q38 Poldrack et al. (2011, Chap. 8) for a criticism of the Granger analysis of fMRI data. Reproduced with permission. Abbreviations: preSMA, pre-supplementary motor area; IFC, inferior frontal cortex; STN, subthalamic nucleus; PMC, primary motor cortex. Reproduced with permission.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

patients during intra- or post-surgical electrophysiological recordings (Ray et al., 2012) or stimulation of this nucleus (Ballanger et al., 2009; Mirabella et al., 2012; Obeso et al., 2011; van den Wildenberg et al., 2006), but also studies in rats (Eagle et al., 2008b) and monkeys (Isoda and Hikosaka, 2008).

The involvement of the *indirect* cortico-striatal pathway in response inhibition is more controversial. Neuroimaging studies do not allow strong predictions about the role of the striatum in response inhibition and early symptomatic Huntington's disease patients bearing a consistent degeneration of striatal neurons do not display inhibitory deficits (Greenhouse et al., 2011b). Nonetheless the striatum is an important part of the fronto-striatal loop involved in motor control (Alexander and Crutcher, 1990) and is known to participate in response inhibition (Boehler et al., 2010; Ghahremani et al., 2012; Jahfari et al., 2011; Li et al., 2008). One possibility is that striatal neurons are involved in selective suppression mechanisms, thus increasing the likelihood of both canceling and restraining a response, in accordance with neuroimaging evidence (Aron, 2010; Jahfari et al., 2009; Vink et al., 2005) and rodent studies (Eagle and Robbins, 2003; Eagle et al., 2011). Recent research has been able to differentiate between global and selective inhibitory mechanisms (Aron, 2010) by using more sophisticated techniques (e.g., Badry et al., 2009; Greenhouse et al., 2011a; Majid et al., 2012). It has been hypothesized that a *reactive* mechanism would stop all ongoing responses through the hyperdirect pathway, whereas *proactive* inhibition would act more selectively with the involvement of the striatum (Aron, 2010) via dopaminergic modulation in this area (Boehler et al., 2011; Eagle et al., 2011).

3.4. The controversy concerning IFG and cognitive control

The IFC lays anterior to the pre-central sulcus and inferior to the inferior frontal sulcus. It includes BA 44 (posterior, pars opercularis), 45 (medial, pars triangularis), and 47/12 (anterior, pars orbitalis) of the human brain and encompasses the inferior frontal gyrus (IFG; Petrides and Pandya, 2002), which is found to be activated by a broad range of tasks (Aron et al., 2004; Duncan and Owen, 2000). Many neuroimaging studies point to the *right* IFG as the main locus of inhibitory control in both go/no-go and SST paradigms (e.g., Aron et al., 2004; Buchsbaum et al., 2005; Menon et al., 2001; Nakata et al., 2008; Rubia et al., 2003). In keeping with these data, patients with cortical damage including the area of the right IFG show prolonged SSRT proportional to the extent of the lesion (Aron et al., 2003) and atomoxetine modulates this same area during response inhibition in normal subjects (Chamberlain et al., 2009). Moreover, disruption of neural activity in the area of the IFG by transcranial magnetic stimulation (TMS) prolongs SSRT (Chambers et al., 2006) and the magnitude of IFG activation correlates with individual differences in response inhibition (Aron et al., 2007). Another set of evidence regarding the role of the IFG in inhibitory control derives from studies in ADHD patients, who are notoriously impulsive and impaired in response inhibition tasks such as stop-signal (Schachar and Logan, 1990), stop-change (Schachar et al., 1995) and go/no-go (Trommer et al., 1988) paradigms. This patient population shows cortical activation patterns compatible with abnormal right IFG functioning (Bunge et al., 2002a; Casey et al., 1997a; Castellanos et al., 1996; Cubillo et al., 2010; Dickstein et al., 2006; Durston et al., 2004; Overtoom et al., 2002; Rubia et al., 2010; Sowell et al., 2003).

However, not all the evidence converges on the primary role of the right IFG in response inhibition. For example, some lesion studies failed to find response inhibition impairments in patients with brain damage including the right IFG (Dimitrov et al., 2003; Floden and Stuss, 2006; Picton et al., 2007), whereas patients with damage in the *left* IFG are impaired in the go/no-go task (Swick et al., 2008). Consequently, despite the extensive evidence on the involvement of the IFG in response inhibition tasks, there is no consensus yet around the specific process regulated by this area and the degree of lateralization of its hypothesized function. The IFG has been hypothesized to serve disparate functions including attentional orienting (Chao et al., 2009; Corbetta and Shulman, 2002), resolution of stimulus conflict (Wendelken et al., 2009) or the monitoring of behavior (Kringelbach and Rolls, 2004; Walton et al., 2004). Similarly, other authors linked activation in the IFG during the SST to signal monitoring and post-response processing (Li et al., 2006) according to its putative role in affective processing (Fulbright et al., 2001; Nomura et al., 2003). The attentional account for the role of the IFG (Corbetta et al., 2008; Corbetta and Shulman, 2002) is supported by studies that compared brain activation in response to unexpected stimuli and stopping *per se* (Sharp et al., 2010).

More general roles have been subsequently proposed for the IFG, namely the fast adaptation of response (Dodds et al., 2010) and/or attentional control (Hampshire et al., 2010) in a changing environment, allowing the response to salient stimuli that are relevant to the task at hand (Corbetta and Shulman, 2002; Yamasaki et al., 2002). These two hypotheses are supported by a number of studies in which activation of the IFG increased as additional control had to be exerted over one's actions (Chikazoe et al., 2009; Dodds et al., 2010; Hampshire et al., 2010), and in studies where attending to task-relevant stimuli did not require any kind of response inhibition and, sometimes, not even a response (Bor et al., 2003; Duncan and Owen, 2000; Hampshire et al., 2008, 2009; Hon et al., 2006; Linden et al., 1999; Nakamura et al., 1999; Passingham et al., 2000), respectively. Thus, it has been proposed that the IFC integrates attentional and response control via its connections with sensory- and motor-related brain networks (Dodds et al., 2010) representing a nexus between stimulus-driven and goal-oriented behavior (Hampshire et al., 2010). Finally, the recent attribution of 'limbic' functions to the STN (Baunez and Lardeux, 2011) and its strong connections with the IFG, fits the hypothesis of a limbic-executive hub in the IFC. An even more general view hypothesizes the involvement of the right IFG in the updating or reprogramming of action plans (Mars et al., 2007) in response to behaviorally relevant stimuli, but not for the detection of such stimuli, thus ruling out the attentional explanation (Verbruggen et al., 2010, 2008).

It is possible that distinct subregions of the right IFC are differentially involved in attention (dorsal part; the inferior frontal junction; IFJ) and response inhibition (ventral/posterior part) (Chikazoe et al., 2009; Levy and Wagner, 2011; Verbruggen et al., 2010), thus conciliating the two main streams of hypothesis regarding the function of this brain area. Verbruggen and colleagues observed dissociable effects by reversibly disrupting neural activity in different parts of the IFC. Thus, interfering with right IFG activity disrupted response inhibition but also response updating, whereas the impairment seen after inactivation of the inferior frontal junction was related to the detection of stimulus change (Verbruggen et al., 2010) consistently with previous studies (Downar et al., 2001; Vossel et al., 2009). Accordingly, a recent meta-analysis compared fMRI results between studies that used response inhibition tasks (SST and go/no-go) or reflexive reorienting of attention and found dissociable patterns of activation in the right IFC (Levy and Wagner, 2011). Thus, the IFJ may serve the orienting to unexpected or behaviorally relevant stimuli, the pars opercularis seems to contribute to the update of action plans and the pars triangularis may aid selection between alternative plans when there is high uncertainty. These important results may help clarifying the reason why incongruent evidence have been obtained by neuroimaging studies, which are characterized by limited spatial and temporal resolution and by the merely correlative nature of the data obtained.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

A role for the *left* IFG (Broca's area) has also been investigated during response inhibition tasks and found to be involved by some (Botvinick et al., 2001; Durston et al., 2002; Fassbender et al., 2004; Novick et al., 2005; Picton et al., 2007; Swick et al., 2008; Watanabe et al., 2002), but not other studies (e.g., Aron et al., 2003; Chambers et al., 2007; Clark et al., 2007). Some authors have attributed an important role in rule maintenance and retrieval to the left portion of the IFC (e.g., Bunge et al., 2003) suggesting that this region may help enforcing the semantic information associated with the inhibitory cue (Poldrack et al., 1999; Thompson-Schill et al., 1997), which can be encoded differently in different subjects. For instance, subjects may rely on verbal instructions as received by the experimenter or on more abstract rules when a stop-signal is detected. This possibility, together with subtle differences in task instructions, types of stimuli and the frequency of stop/no-go trials, may explain the competing findings regarding the lateralization of IFG activation during response inhibition.

4. Comparison with choice impulsivity and reversal learning

> "Whenever choice appears in any form – as rivalry between appetites which cannot be simultaneously satisfied, as a perceived meaning attached to an ambiguous stimulus, as a planned decision between two courses of action, as a symbolic fulfillment of an unsuspected wish – it always involves an element of inhibition". (Diamond et al., 1963; p. 145)

As previously discussed, two other families of behavioral tasks have been used to measure behavioral inhibition in clinical and preclinical settings: (1) extinction and reversal learning paradigms, where inhibition is operationally defined as the ability to inhibit a response previously rewarded but now punished (or no longer rewarded); (2) delay, effort or probability discounting tasks (broadly defined as decision-making paradigms) where the subject has to choose between actions that are more rewarding in the long run – thus postponing gratification – and actions that result in immediate, smaller reward. Whilst implicating behavioral inhibition, the first class of tests actually measures an aspect of behavior more akin to compulsivity and perseveration rather than impulsivity *per se*. Decision-making paradigms have been often exploited for the study of impulsive behavior, drug addiction and psychopathology, especially with regards to animal models (Bari, 2010; Bari and Robbins, 2011; Bari et al., 2011b; Belin et al., 2009; Olmstead, 2006). Other behavioral tasks largely used in animals that measure response inhibition in forms sometimes referred to as 'waiting' impulsivity include the 5-CSRTT, the lever holding task and the differential reinforcement of low rate of responding procedure, which have been described elsewhere (Bari et al., 2008; Bari and Robbins, 2011; Robbins, 2002).

4.1. Delay discounting

In everyday life impulsive individuals momentarily value the positive consequences of their actions more than the objective advantage of avoiding the punishment deriving from those actions. In turn, the anticipation of the reward may cause an impulsive 'state' where the immediate gratification is preferred over delayed advantages in terms of better outcomes or punishment avoidance. This kind of poor decision-making is well described by the state that Bechara and colleagues called 'myopia for the future' and is usually seen in patients with ventromedial frontal lobe damage (Bechara et al., 1994, 2000). Impulsive decision-making can be assessed by delay discounting tasks where impulsive behavior is defined as the tendency to choose immediate smaller rewards over larger but postponed ones (Ainslie, 1975, 2001; Madden and Bickel, 2009; Rachlin, 2000) and this family of tasks is usually said to measure '(intertemporal) choice impulsivity'. Thus, for example, a subject may prefer to receive $100 immediately instead of choosing to receive $300 in 1 year time. Related behavioral tests include probability and effort-based decision-making tasks, which have been discussed elsewhere (Floresco and Magyar, 2006; Green and Myerson, 2010; Salamone et al., 2012).

The function best describing delay discounting behavior is most often hyperbolic rather than exponential (Ainslie, 1975; Strotz, 1956) and presents similarity across different species (Green and Myerson, 2004; Mazur, 1987; McKerchar et al., 2009; Reynolds and Schiffbauer, 2004). Since the rate of discounting is not linear and varies among subjects, delay discounting tasks have adopted an adjusting-delay procedure to find the delay at which the large and the smaller amount of reward would be valued equally, namely the 'indifference point' (Mazur, 1987). A similar method for finding the indifference point – the adjusting-amount procedure (Richards et al., 1997) – has yielded the same discounting rates as the adjusting-delay one (Green et al., 2007). As noted before, delay discounting rates are very stable over time in the same individuals and strongly related to the genetic background (Anokhin et al., 2011; Kirby, 2009; Ohmura et al., 2006) in both humans (Eisenberg et al., 2007) and rodents (Anderson and Woolverton, 2005; Isles et al., 2004; Madden et al., 2008; Wilhelm and Mitchell, 2009). Similar to other paradigms, individual differences in reward sensitivity and feedback evaluation may contribute to the discounting rate observed in intertemporal choice decision-making. Thus, although one of the prominent views is to consider steep discounting rates as a failure to inhibit immediate desires which lead to suboptimal long term consequences, some authors give more importance to the lack of forethought that characterizes this kind of impulsive behavior.

In normal subjects, the value of rewards is usually a function of the delay to their delivery. However, the impact of delay is stronger in impulsive individuals and in several psychiatric disorders (Peters and Buchel, 2011). In general, addictions are characterized by the immediate fulfillment of pre-potent desires without consideration for the negative consequences of one's behavior. Thus, is not surprising that in pathologies such as drug addiction (Bickel and Marsch, 2001; Bickel et al., 2008; Coffey et al., 2003; Kirby et al., 1999; Monterosso et al., 2007; Petry, 2001a), obesity (Epstein et al., 2008; Fields et al., 2011; Weller et al., 2008) and compulsive gambling (Ledgerwood et al., 2009; Petry, 2001b; Reynolds, 2006) patients display higher rates of delay discounting, because although drugs, food and the prospect of winning money are highly rewarding in the immediate situation, they all can have serious negative consequences on the long run (see Bickel et al., 2012 for review). Another phenomenon predicted by delay discounting models and observed especially in addicted individuals is 'preference reversal', which causes these patient populations to relapse (or 'lose control') to the unwanted behavior as a function of its proximity, despite the previous commitment to abstaining from it (Ainslie, 2001; Kirby and Herrnstein, 1995; O'Brien et al., 2006). Impulsive choice in delay discounting tasks has been found to be increased in opiate (Madden et al., 1997), alcohol (Petry, 2001a), methamphetamine (Monterosso et al., 2007) and tobacco (Baker et al., 2003) dependent individuals. These results suggest that poor decision-making may predate drug use in these subjects, but direct evidence in humans is still scarce. Experiments in laboratory animals have shown that rats that discount more delayed, but bigger rewards, display higher rates of cocaine intake (Anker et al., 2009; Perry et al., 2005) and reinstatement of cocaine- (Perry et al., 2008) or nicotine-seeking (Diergaarde et al., 2008). Finally, similarly to human drug addicted individuals, chronic administration of most drugs of abuse in animal models causes an increase in impulsive choice as measured by delay discounting tasks (see Table 2) (see Setlow et al., 2009 for review).

The type of behavioral inhibition required in delay discounting tasks has probably little to do with response inhibition paradigms

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

that involve the fast withdrawal of a motor response. It is likely that more affectively charged cognitive processes are at play when deciding whether to delay gratification or not, compared to standard response inhibition paradigms. Although impulsivity measures from response inhibition and delay discounting tasks do not seem to correlate in the majority of studies, they represent complementary measures that cover a broader area of the impulsivity construct (Broos et al., 2012; Rogers et al., 2010; Solanto et al., 2001) and are similarly modulated by 'anti-impulsivity' drugs such as atomoxetine, methylphenidate and amphetamine in both humans and rats (de Wit et al., 2002; Robinson et al., 2008; Winstanley et al., 2006). Animal studies have shown that lesions of the ventral portion of the striatum (Cardinal et al., 2001) or specific regions within the OFC (Mar et al., 2011; Mobini et al., 2002) increase impulsivity in the delay discounting procedure, thus confirming the involvement of a more 'limbic' circuitry in this 'hot' type of behavioral inhibition (Cardinal et al., 2004; Metcalfe and Mischel, 1999). Moreover, neurons in the monkey OFC show a pattern of activity negatively correlated to delay and positively correlated to reward magnitude, thus encoding for variations in subjective values (Roesch and Olson, 2005). On the contrary, lesion of the subthalamic nucleus decreases impulsive choice (Uslaner and Robinson, 2006; Winstanley et al., 2005). Finally, selective dopaminergic (Koffarnus et al., 2011; van Gaalen et al., 2006b) and serotonergic (Bizot et al., 1999; Evenden and Ryan, 1999) compounds have been shown to modulate discounting rates when administered acutely.

In humans, at least three brain networks have been associated with delay discounting. These are (1) a ventral cortico-striatal network including medial OFC and ventral striatum determining individual differences in reward value, (2) a lateral prefrontal-cingulate network comprising lateral OFC, cingulate cortex, dorsolateral and ventrolateral PFC implicated in conflict detection and behavioral inhibition, and (3) a medial temporal-hippocampus network for prospective evaluation of future outcomes (McClure et al., 2004; Monterosso et al., 2007; Peters and Buchel, 2011). Related views have linked brain activity in ventral striatum, OFC, and cingulate cortex to the subjective value of immediate and delayed outcomes (Kable and Glimcher, 2007). Thus, in general, the mesocorticolimbic dopaminergic pathway including medial prefrontal, OFC and ventral striatal projections, which subserve motivational and emotional processes, seems to play a major role in choice impulsivity. Accordingly, several reports have shown abnormal activation and dopaminergic regulation of this circuit in ADHD individuals (Plichta et al., 2009; Rubia et al., 2009; Volkow et al., 2009), which display steeper discounting rates compared to healthy subjects (Bitsakou et al., 2009; Paloyelis et al., 2010; Solanto et al., 2001). These results are consistent with theories that emphasize motivational deficits and delay aversion in patients with ADHD (Nigg and Casey, 2005; Sagvolden et al., 2005; Sonuga-Barke, 2002).

In contrast to response inhibition studies reviewed above, 5-HT neurotransmission seems more related to the *waiting* component of inhibitory control (Miyazaki et al., 2012), where motivational and affective processes have larger impact on behavior. Thus, 5-HT depletion increases impulsive choice (Bizot et al., 1999; Denk et al., 2005; Mobini et al., 2000; Schweighofer et al., 2008; Wogar et al., 1993a,b), and 5-HT extracellular content in the dorsal raphé has been found to increase when animals have to wait for a reward to be delivered (Miyazaki et al., 2011a,b). Overall, these and the neuroanatomical studies reviewed above suggest that 5-HT may signal the proximity and/or likelihood of the reward (Doya, 2002; Tanaka et al., 2004) especially in OFC, where the final computation regarding the subjective value of different options is executed (Padoa-Schioppa and Cai, 2011; Schoenbaum et al., 2011; Wallis, 2012). Finally, as we will see better below, another role for the 5-HT system, probably in conjunction with different subregions within the OFC (Mar et al., 2011; Rudebeck and Murray, 2011; Wallis, 2007), is to signal negative feedback (Cools et al., 2008; Daw et al., 2002; Deakin and Graeff, 1991).

4.2. Reversal learning

Many different variants of reversal learning paradigms have been extensively used in humans and other animals for the study of cognitive constructs such as flexibility, impulsivity and compulsivity (Izquierdo and Jentsch, 2012). Although heavily relying on learning and cognitive flexibility, and potentially assessing compulsive behavior, deficient performance on reversal learning paradigms has been shown to be tightly related to impulsivity (e.g., Franken et al., 2008; Romer et al., 2009). In a standard reversal learning procedure the subject is usually faced with the possibility of choosing between two distinct stimuli/responses, only one of which is deemed 'correct', thus leading to reward. Once the subject has learned the stimulus-reward association, the experimenter reverses the contingencies without notice and the subject has to amend the behavior accordingly by trial and error. Analysis of reversal learning performance may reveal two aspects of impulsive behavior that are not readily displayed by subjects during response inhibition or delay discounting tasks. The first is the ability to inhibit responding to previously rewarded (but now punished) stimuli, a tendency to which is seen immediately after contingency reversals and that requires disengaging from an established behavioral/attentional set in order to adapt to the new stimulus-reward association (see Izquierdo and Jentsch, 2012; Kehagia et al., 2010 for reviews). The second pertains to reward/punishment sensitivity.

Deficits in reversal learning performance in normal subjects are often masked by the relatively simplicity of the task, which is bound to cause ceiling effects in the behavioral data. A more sensitive measure of reversal learning deficits can be obtained by 'degrading' stimulus-reward contingencies and introducing spurious feedback as in probabilistic reversal learning (PRL) paradigms. These are more difficult tasks because of the need to integrate reinforcement history over several trials and to regulate responding to local reinforcement. Thus, PRL performance may reveal another aspect of impulsive behavior, namely the sensitivity to negative feedback (e.g., punishment or lack of reward) which is obtained by assessing the probability of switching to the alternative stimulus after receiving punishment on preceding trials (i.e., lose-shift). Conversely, reward sensitivity can be measured in the PRL task by taking into account the propensity of the subjects to choose again the stimulus that have been rewarded on preceding trials (i.e., win-stay). These 'affective' components of reversal learning performance have been shown to depend on DA and 5-HT transmission (Bari et al., 2010; Chamberlain et al., 2006b; Evers et al., 2005; Swainson et al., 2000) and hypothesized to involve prediction error processing in fronto-striatal circuitries (Clarke et al., 2008; Cools et al., 2002).

Sensitivity to punishment is, of course, very relevant for the study of impulsivity and relates to those pathological aspects of behavior which are conserved despite negative consequences, such as drug abuse or criminal conduct. Accordingly, the negligible impact that prospective negative outcomes have on impulsive decision-making is an important aspect of behavioral inhibition as exemplified by the definition of impulsivity given by Moeller et al. (2001): "*... a predisposition towards rapid, unplanned reactions to internal or external stimuli without regard to the negative consequences of these reactions to themselves or others*". Conversely, exaggerated reaction to punishment is observed in depressed patients, leading to inadequate responses to negative feedback and helpless behavior that are typical of this clinical condition (Beats

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

et al., 1996; Elliott et al., 1996; Murphy et al., 2003; Steffens et al., 2001). On the other hand, high reward sensitivity is a critical aspect of those impulsive behaviors characterized by risk/sensation-seeking and addictions. The opposite is true for depressed patients who display blunted reaction to positively charged stimuli (Der-Avakian and Markou, 2012; Nestler and Carlezon, 2006). Thus, in the PRL, rodents bearing near-total depletion of brain 5-HT display a transient increase in negative feedback sensitivity, whereas pharmacological or genetic manipulation that increase extracellular 5-HT availability, have been shown to increase win-stay behavior and decrease negative feedback sensitivity (Bari et al., 2010; Ineichen et al., 2012), mirroring results obtained in healthy volunteers after SSRI administration (Norbury et al., 2009).

OFC lesion impairs reversal learning causing perseverative behavior, across species. Mice (Bissonette et al., 2008), rats (Chudasama and Robbins, 2003), monkeys (Dias et al., 1996; Jones and Mishkin, 1972; Rudebeck and Murray, 2008) and humans (Fellows and Farah, 2005a; Hornak et al., 2004; Rolls et al., 1994) display intact initial discrimination but impaired reversal learning after damage to the OFC, but not to dorsomedial or lateral cortices. Reversal performance engages bilateral OFC activation as revealed by imaging studies (O'Doherty et al., 2001) and is impaired in clinical subjects with OCD (Remijnse et al., 2006) or ADHD (Itami and Uno, 2002) diagnoses, revealing the possible involvement of OFC malfunction in these disorders. Moreover, exposure to drugs of abuse causes reversal deficits and perseverative tendencies in both humans (Ersche et al., 2008) and rats (Izquierdo et al., 2010; Jentsch et al., 2002; Schoenbaum et al., 2004), which can be ameliorated by DA D2/3 agonist administration in chronic stimulant abusers (Ersche et al., 2011).

In monkeys, successful reversal learning performance depends on intact serotonergic, but not dopaminergic, transmission in the OFC (Clarke et al., 2007). The opposite is true in the monkey caudate nucleus (Clarke et al., 2011) where DA D2 receptor levels correlate with performance during reversal learning and sensitivity to positive, but not negative feedback within the task (Groman et al., 2011). Rodents with cortical forebrain 5-HT depletion display impaired performance on a variety of reversal learning paradigms (Lapiz-Bluhm et al., 2009; Masaki et al., 2006), whereas increased 5-HT extracellular content improves performance (Brigman et al., 2010; Lapiz-Bluhm et al., 2009). Although 5-HT and DA seem to have an important role in reversal performance, probably acting at different levels in the brain, manipulation of the noradrenergic system have been also effective on reversal tasks (Seu et al., 2009), possibly affecting the 'shifting of attention' component of the task (Lapiz et al., 2007; Lapiz and Morilak, 2006; McGaughy et al., 2008). For example, blocking NE reuptake (thus increasing its extracellular levels) improves performance of adolescent rats and reverses the negative effects of noradrenergic deafferentation in adult rats on attentional set shifting, but the same treatment had no effect on simple reversal learning (Cain et al., 2011; Newman et al., 2008).

It is worth noting that also successful performance on shifting tasks is dependent on inhibitory processes, according to prominent views (Allport et al., 1994) but see also Wylie and Allport (2000). In summary, reversal learning tasks can reveal important aspects regarding the wider construct of impulsivity. Reward and negative feedback sensitivity, together with the capacity of shifting the focus of attention to more profitable options are central to many definitions of impulsive behavior. However, impairments in reversal learning are often perseverative in nature with the subject choosing to respond according to the old rule despite negative outcomes. While these can be considered inhibitory deficits in the short term, the recurring nature of the maladaptive response is better described as compulsive, rather than impulsive.

5. Summary, conclusions and future perspectives

> "I have nothing to say on the nature of the inhibitory process. I would urge, however, that here, as in all other cases, we should distinguish between the psychical and the physical; we cannot legitimately speak of any mental states as inhibitory of any physical processes, any more than we can speak of them as producing movements. I have long urged that controlling as well as directive action is displayed throughout the nervous system." (Jackson, 1931b, p. 481)

The aim of the first part of the present review was to offer an historical perspective of the major concepts of inhibition, emphasizing their importance for the development of different areas of scientific investigation spanning from neural inhibition to self-control. In the second part we focused much of our discussion on a specific act of control, namely response inhibition and the way it can be used as a measure of impulsive behavior. Response inhibition paradigms such as the go/no-go task and the SST do not measure pure forms of inhibition, but they require a series of ancillary cognitive processes which have in common the final operation of successful response inhibition. This lack of specificity is not necessarily detrimental to the heuristic and scientific value of these behavioral tasks. In everyday life, adaptive inhibition requires a multitude of interrelated processes such as the monitoring of behavior, sustained attention, conflict detection and others, before the inhibition of the planned (or ongoing) course of action is put in place and the behavior adjusted according to the new goal-oriented plans. Accordingly, we have discussed the place of inhibition among other 'executive functions'. As it transpired, more research is needed to better define their functional interrelation. Finally we gave a general overview of the neurobiological underpinnings of response inhibition and discussed the comparison with other forms of behavioral inhibition as measured by delay discounting and reversal learning tasks. Efforts aimed at dissociating different forms of inhibition, and of executive functions in general, at the behavioral and neural levels will improve significantly our understanding of brain mechanisms in health and pathology.

The historical introduction offers an overview of the different concepts of inhibition that in part mirror modern distinctions described later in the paper. We discussed many of the different uses and meanings of the concept of inhibition with a special emphasis on response control. This will hopefully help future theoretical conceptualization and experiment planning, and will facilitate communication among researchers. Similarly, we hope that the work of many scientists cited in this review will stimulate the reader to explore diversified fields of knowledge so to acquire a multidisciplinary point of view, which can give unexpected insights and guide future experiments. In fact, the use of different terminology in related disciplines to describe the same phenomenon may hinder the exchange of ideas among scientists or students. For example, the concept of inhibition is often broadly referred to as 'self-control' in psychology and pertains to manifest behavior as well as to thoughts and emotions (e.g., Cohen and Lieberman, 2010; Hare et al., 2009; Hofmann et al., 2012; Muraven et al., 2006). A broad field of investigation such the study of inhibitory processes would benefit from the use of shared terminology, but this can only be possible after a better definition of their behavioral and neural correlates. Many of the theoretical constructions of impulsivity and disinhibitory syndromes date back to the pre-neuroimaging era or are stated in purely cognitive or behavioral terms. It is timely to combine psychological theorizing, multivariate statistical analysis and modern neuroscientific investigation techniques in order to understand the fundamental basis of inhibitory control.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Our discussion on behavioral measures of impulsivity progressively focused on those regarding the 'cold' end of the behavioral inhibition continuum, mostly because fast response cancellation (as required by stop-signal paradigms) is closer to biological models and presumably involves relatively less intervening cognitive and affective mechanisms. These forms of response inhibition are put in place by the organism in response to external countermanding signals. At the other end of the continuum, behavioral inhibition in delay discounting tasks is enforced by internal commands, which are based on subjective goals and values, thus entailing more affective ('hot') processes and limbic brain structures. Finally, different from imperative stop-signals and subjective evaluation of long term consequences, impulsive/compulsive behavior in reversal learning paradigms depends on the subject's sensitivity to – and interpretation of – external (positive or negative) cues. These subtypes of behavioral inhibition also differ regarding the process that need to be inhibited, namely a motor response in the SST and go/no-go task, the immediate fulfillment of a strong desire in impulsive choice paradigms, or an habitual stimulus–response association in reversal learning tasks.

An old advertisement on TV used to claim that "power is nothing without control". Among the many ways in which our brain controls its own activity and overt behavior, inhibitory processes are among the most important both in everyday life and during emergency situations. This is because, as Ursin wrote, *"We have to stop whatever we are doing in order to start any new action"* and *"Inhibition is indeed a most important faculty for our abilities to make choices, and for our freedom of choice"* (Ursin, 2005, pp. 1059, 1064).

Research on the behavioral and neural basis of impulsivity and inhibition may profoundly change the way we understand and treat many psychiatric disorders. Enormous advances have been made in the theoretical and clinical definition of addiction and ADHD with the result of more focused investigation of the neuroanatomical basis of impulsive behavior in these pathologies. In general, results obtained testing animal models usually concord with results obtained in human subjects. This is very important for biomedical research, given the obvious limitations of human testing and the possibility of exerting tighter experimental control in studies involving animal models. Future studies will have to focus not only on the neurobiological basis of impulsive behavior, but also strive to better characterize inhibitory processes, including their relationship with other executive functions and general intelligence (g).

The present review, although extensive, is not meant to be exhaustive. Several other aspects of behavioral inhibition and impulsivity have been purposely left out from the present discussion, but for each of them dedicated excellent reviews can be found elsewhere. We have also briefly mentioned some types of inhibition that have been variously defined as automatic or unconscious such as inhibition of return (Posner and Cohen, 1984), negative priming (Neill, 1977; Tipper, 2001), interference inhibition (Dempster and Corkill, 1999; Dyer and Severance, 1973; Stroop, 1935) and the interesting relationship between inhibitory processes and memory (Anderson and Spellman, 1995; Chiu et al., 2012; Zacks and Hasher, 1994) or the developmental aspects of inhibitory processes (Blakemore and Robbins, 2012; Harnishfeger and Bjorklund, 1944; Michel and Anderson, 2009). Moreover, our discussion repeatedly touched upon various aspects of the tight relation between inhibition and attentional control (Kok, 1999; Moran and Desimone, 1985), although this was not the focus of the present review; this argument is vast and not yet well explored, but definitely very important for the understanding of cognitive processes and the way they work together. Other topics that have been discussed only briefly include computational models, saccade inhibition tasks and electrophysiological correlates (including ERPs) of behavioral inhibition.

Many unanswered questions about the nature of impulsive behavior remain and warrant further investigation. Moreover, the brain circuitry implicated in response inhibition is still lacking clear definition, as well as the specification of its different modes of function in various environmental situations and in pathologies characterized by impulsive behavior. For example, do the pre-SMA and the IFG facilitate the inhibition of pre-potent responses or they simply favor the representation of alternative courses of action? When pathological impulsivity is the consequence of emotional dysregulation or of aberrant cognitive operations? Can lapses in inhibitory control (e.g., relapse to drug use, violent aggression) be successfully treated by behavioral or pharmacological therapies? Much has to be done for us to be able to answer these questions and improvements in animal models and imaging techniques will be very helpful. An important step would be to devise behavioral task that are less affected by the 'impurity' problem and in which performance is dependent mainly on the cognitive construct under examination, but this may be illusory.

Uncited Reference

Q11

Sharp et al. (2013).

Acknowledgments

The authors would like to thankfully acknowledge the work of two anonymous reviewers for their valuable comments. AB was supported by an MRC U.K. Studentship. The review was completed within the Behavioural and Clinical Neuroscience Institute, supported by a joint award from the MRC and Wellcome Trust. Dedicated to the memory of our friend and colleague Daina Economidou.

References

Achenbach, T.M., Edelbrock, C.S., 1979. The child behavior profile: II. Boys aged 12-16 and girls aged 6-11 and 12-16. Journal of Consulting and Clinical Psychology 47, 223–233.

Acheson, A., de Wit, H., 2008. Bupropion improves attention but does not affect impulsive behavior in healthy young adults. Experimental and Clinical Psychopharmacology 16, 113–123.

Acheson, A., Reynolds, B., Richards, J.B., de Wit, H., 2006. Diazepam impairs behavioral inhibition but not delay discounting or risk taking in healthy adults. Experimental and Clinical Psychopharmacology 14, 190–198.

Ainslie, G., 1975. Specious reward: a behavioral theory of impulsiveness and impulse control. Psychological Bulletin 82, 463–496.

Ainslie, G., 2001. Breakdown of Will. Cambridge University Press, New York, NY.

Alderson, R.M., Rapport, M.D., Hudec, K.L., Sarver, D.E., Kofler, M.J., 2010. Competing core processes in attention-deficit/hyperactivity disorder (ADHD): do working memory deficiencies underlie behavioral inhibition deficits? Journal of Abnormal Child Psychology 38, 497–507.

Alexander, G.E., Crutcher, M.D., 1990. Functional architecture of basal ganglia circuits: neural substrates of parallel processing. Trends in Neurosciences 13, 266–271.

Allport, A., Styles, E.A., Hsieh, S., 1994. Shifting intentional set: exploring the dynamic control of tasks. In: Umilta, C., Moscovitch, M. (Eds.), Attenion and Performance XV: Conscious and Nonconscious Information Processing. Bradford Publishers, Cambridge.

Almasy, L., Blangero, J., 2001. Endophenotypes as quantitative risk factors for psychiatric disease: rationale and study design. American Journal of Medical Genetics 105, 42–44.

American Psychiatric Association Ed, 1994. Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), 4th ed. American Psychiatric Association, Washington, DC.

Anderson, K.G., Woolverton, W.L., 2005. Effects of clomipramine on self-control choice in Lewis and Fischer 344 rats. Pharmacology, Biochemistry, and Behavior 80, 387–393.

Anderson, M.C., Green, C., 2001. Suppressing unwanted memories by executive control. Nature 410, 366–369.

Anderson, M.C., Ochsner, K.N., Kuhl, B., Cooper, J., Robertson, E., Gabrieli, S.W., Glover, G.H., Gabrieli, J.D., 2004. Neural systems underlying the suppression of unwanted memories. Science (New York, N.Y.) 303, 232–235.

Anderson, M.C., Spellman, B.A., 1995. On the status of inhibitory mechanisms in cognition: memory retrieval as a model case. Psychological Review 102, 68–100.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Anker, J.J., Perry, J.L., Gliddon, L.A., Carroll, M.E., 2009. Impulsivity predicts the escalation of cocaine self-administration in rats. Pharmacology, Biochemistry, and Behavior 93, 343–348.
Anokhin, A.P., Golosheykin, S., Grant, J.D., Heath, A.C., 2011. Heritability of delay discounting in adolescence: a longitudinal twin study. Behavior Genetics 41, 175–183.
Anstie, F.E., 1864. Stimulants and Narcotics. Macmillan, London.
Armstrong, I.T., Munoz, D.P., 2003. Inhibitory control of eye movements during oculomotor countermanding in adults with attention-deficit hyperactivity disorder. Experimental Brain Research 152, 444–452.
Arnsten, A.F., Dudley, A.G., 2005. Methylphenidate improves prefrontal cortical cognitive function through alpha2 adrenoceptor and dopamine D1 receptor actions: relevance to therapeutic effects in Attention Deficit Hyperactivity Disorder. Behavioral and Brain Functions 1, 2.
Aron, A.R., 2007. The neural basis of inhibition in cognitive control. Neuroscientist 13, 214–228.
Aron, A.R., 2010. From reactive to proactive and selective control: developing a richer model for stopping inappropriate responses. Biological Psychiatry 69, e55–e68.
Aron, A.R., Behrens, T.E., Smith, S., Frank, M.J., Poldrack, R.A., 2007. Triangulating a cognitive control network using diffusion-weighted magnetic resonance imaging (MRI) and functional MRI. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 27, 3743–3752.
Aron, A.R., Fletcher, P.C., Bullmore, E.T., Sahakian, B.J., Robbins, T.W., 2003. Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. Nature Neuroscience 6, 115–116.
Aron, A.R., Poldrack, R.A., 2005. The cognitive neuroscience of response inhibition: relevance for genetic research in attention-deficit/hyperactivity disorder. Biological Psychiatry 57, 1285–1292.
Aron, A.R., Poldrack, R.A., 2006. Cortical and subcortical contributions to stop signal response inhibition: role of the subthalamic nucleus. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 26, 2424–2433.
Aron, A.R., Robbins, T.W., Poldrack, R.A., 2004. Inhibition and the right inferior frontal cortex. Trends in Cognitive Sciences 8, 170–177.
Aston-Jones, G., Bloom, F.E., 1981. Norepinephrine-containing locus coeruleus neurons in behaving rats exhibit pronounced responses to non-noxious environmental stimuli. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 1, 887–900.
Aston-Jones, G., Cohen, J.D., 2005a. Adaptive gain and the role of the locus coeruleus-norepinephrine system in optimal performance. The Journal of Comparative Neurology 493, 99–110.
Aston-Jones, G., Cohen, J.D., 2005b. An integrative theory of locus coeruleus-norepinephrine function: adaptive gain and optimal performance. Annual Review of Neuroscience 28, 403–450.
Aston-Jones, G., Rajkowski, J., Cohen, J., 1999. Role of locus coeruleus in attention and behavioral flexibility. Biological Psychiatry 46, 1309–1320.
Aston-Jones, G., Rajkowski, J., Cohen, J., 2000. Locus coeruleus and regulation of behavioral flexibility and attention. Progress in Brain Research 126, 165–182.
Baarendse, P.J., Vanderschuren, L.J., 2012. Dissociable effects of monoamine reuptake inhibitors on distinct forms of impulsive behavior in rats. Psychopharmacology 219, 313–326.
Badry, R., Mima, T., Aso, T., Nakatsuka, M., Abe, M., Fathi, D., Foly, N., Nagiub, H., Nagamine, T., Fukuyama, H., 2009. Suppression of human cortico-motoneuronal excitability during the Stop-signal task. Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology 120, 1717–1723.
Baker, F., Johnson, M.W., Bickel, W.K., 2003. Delay discounting in current and never-before cigarette smokers: similarities and differences across commodity, sign, and magnitude. Journal of Abnormal Psychology 112, 382–392.
Ball, T., Schreiber, A., Feige, B., Wagner, M., Lucking, C.H., Kristeva-Feige, R., 1999. The role of higher-order motor areas in voluntary movement as revealed by high-resolution EEG and fMRI. NeuroImage 10, 682–694.
Ballanger, B., van Eimeren, T., Moro, E., Lozano, A.M., Hamani, C., Boulinguez, P., Pellecchia, G., Houle, S., Poon, Y.Y., Lang, A.E., Strafella, A.P., 2009. Stimulation of the subthalamic nucleus and impulsivity: release your horses. Annals of Neurology 66, 817–824.
Ballon, J.S., Feifel, D., 2006. A systematic review of modafinil: Potential clinical uses and mechanisms of action. The Journal of Clinical Psychiatry 67, 554–566.
Band, G.P., van Boxtel, G.J., 1999. Inhibitory motor control in stop paradigms: review and reinterpretation of neural mechanisms. Acta Psychologica 101, 179–211.
Band, G.P., van der Molen, M.W., Logan, G.D., 2003. Horse-race model simulations of the stop-signal procedure. Acta Psychologica 112, 105–142.
Bari, A., 2010. ADHD: animal models. In: Stolerman, I.P. (Ed.), Encyclopedia of Psychopharmacology. Springer-Verlag, Berlin, pp. 170–175.
Bari, A., Aston-Jones, G., 2013. Atomoxetine modulates spontaneous and sensory-evoked discharge of locus coeruleus noradrenergic neurons. Neuropharmacology 64, 53–64.
Bari, A., Dalley, J.W., Robbins, T.W., 2008. The application of the 5-choice serial reaction time task for the assessment of visual attentional processes and impulse control in rats. Nature Protocols 3, 759–767.
Bari, A., Eagle, D.M., Mar, A.C., Robinson, E.S., Robbins, T.W., 2009. Dissociable effects of noradrenaline, dopamine, and serotonin uptake blockade on stop task performance in rats. Psychopharmacology 205, 273–283.
Bari, A., Mar, A.C., Theobald, D.E., Elands, S.A., Oganya, K.C., Eagle, D.M., Robbins, T.W., 2011a. Prefrontal and monoaminergic contributions to stop-signal task performance in rats. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 31, 9254–9263.
Bari, A., Robbins, T.W., 2011. Animal models of ADHD. Current Topics in Behavioral Neuroscience 7, 149–185.
Bari, A., Robbins, T.W., 2013. Noradrenergic versus dopaminergic modulation of impulsivity, attention and monitoring behaviour in rats performing the stop-signal task: Possible relevance to ADHD. Psychopharmacology.
Bari, A., Robbins, T.W., Dalley, J.W., 2011b. Impulsivity. In: Olmstead, M.C. (Ed.), Animal Models of Drug Addicition. Humana Press, New York, pp. 379–402.
Bari, A., Theobald, D.E., Caprioli, D., Mar, A.C., Aidoo-Micah, A., Dalley, J.W., Robbins, T.W., 2010. Serotonin modulates sensitivity to reward and negative feedback in a probabilistic reversal learning task in rats. Neuropsychopharmacology 35, 1290–1301.
Barkley, R.A., 1990. A critique of current diagnostic criteria for attention deficit hyperactivity disorder: clinical and research implications. Journal of Developmental and Behavioral Pediatrics: JDBP 11, 343–352.
Barkley, R.A., 1997. Behavioral inhibition, sustained attention, and executive functions: constructing a unifying theory of ADHD. Psychological Bulletin 121, 65–94.
Barratt, E.S., 1985. Impulsiveness subtraits: arousal and information processing. In: Spence, J.T., Izard, C.E. (Eds.), Motivation, Emotion and Personality. Elsevier Science, Amsterdam, pp. 137–146.
Barratt, E.S., Patton, J.H., 1983. Impulsivity: cognitive, behavioral, and psychophysiological correlates. In: Zuckerman, M. (Ed.), Biological Basis of Sensation Seeking, Impulsivity, and Anxiety. Erlbaum, Hillsdale NJ, pp. 77–116.
Baunez, C., Lardeux, S., 2011. Frontal cortex-like functions of the subthalamic nucleus. Frontiers in Systematic Neuroscience 5, 83.
Beats, B.C., Sahakian, B.J., Levy, R., 1996. Cognitive performance in tests sensitive to frontal lobe dysfunction in the elderly depressed. Psychological Medicine 26, 591–603.
Bechara, A., Damasio, A.R., Damasio, H., Anderson, S.W., 1994. Insensitivity to future consequences following damage to human prefrontal cortex. Cognition 50, 7–15.
Bechara, A., Tranel, D., Damasio, H., 2000. Characterization of the decision-making deficit of patients with ventromedial prefrontal cortex lesions. Brain 123 (Pt 11) 2189–2202.
Bekar, L.K., Wei, H.S., Nedergaard, M., 2012. The locus coeruleus-norepinephrine network optimizes coupling of cerebral blood volume with oxygen demand. Journal of Cerebral Blood Flow and Metabolism: Official Journal of the International Society of Cerebral Blood Flow and Metabolism 32, 2135–2145.
Bekker, E.M., Bocker, K.B., Van Hunsel, F., van den Berg, M.C., Kenemans, J.L., 2005a. Acute effects of nicotine on attention and response inhibition. Pharmacology, Biochemistry, and Behavior 82, 539–548.
Bekker, E.M., Overtoom, C.C., Kooij, J.J., Buitelaar, J.K., Verbaten, M.N., Kenemans, J.L., 2005b. Disentangling deficits in adults with attention-deficit/hyperactivity disorder. Archives of General Psychiatry 62, 1129–1136.
Belin, D., Bari, A., Besson, M., Dalley, J.W., 2009. Multi-disciplinary investigations of impulsivity in animal models of attention-deficit hyperactivity disorder and drug addiction vulnerability. In: Granon, S. (Ed.), Endophenotypes of Psychiatric and Neurodegenerative Disorders in Rodent Models. Transworld Research, London.
Belin, D., Mar, A.C., Dalley, J.W., Robbins, T.W., Everitt, B.J., 2008. High impulsivity predicts the switch to compulsive cocaine-taking. Science 320, 1352–1355.
Bell, J., Bell, C., 1827. Anatomy and Physiology of the Human Body. Collins & Co, New York.
Bench, C.J., Friston, K.J., Brown, R.G., Scott, L.C., Frackowiak, R.S., Dolan, R.J., 1992. The anatomy of melancholia – focal abnormalities of cerebral blood flow in major depression. Psychological Medicine 22, 607–615.
Benoit, R.G., Anderson, M.C., 2012. Opposing mechanisms support the voluntary forgetting of unwanted memories. Neuron 76, 450–460.
Berridge, C.W., Waterhouse, B.D., 2003. The locus coeruleus-noradrenergic system: modulation of behavioral state and state-dependent cognitive processes. Brain Research. Brain Research Reviews 42, 33–84.
Biber, M.P., Kneisley, L.W., LaVail, J.H., 1978. Cortical neurons projecting to the cervical and lumbar enlargements of the spinal cord in young and adult rhesus monkeys. Experimental Neurology 59, 492–508.
Bickel, W.K., Jarmolowicz, D.P., Mueller, E.T., Koffarnus, M.N., Gatchalian, K.M., 2012. Excessive discounting of delayed reinforcers as a trans-disease process contributing to addiction and other disease-related vulnerabilities: emerging evidence. Pharmacology & Therapeutics 134, 287–297.
Bickel, W.K., Marsch, L.A., 2001. Toward a behavioral economic understanding of drug dependence: delay discounting processes. Addiction 96, 73–86.
Bickel, W.K., Yi, R., Kowal, B.P., Gatchalian, K.M., 2008. Cigarette smokers discount past and future rewards symmetrically and more than controls: is discounting a measure of impulsivity? Drug and Alcohol Dependence 96, 256–262.
Bissonette, G.B., Martins, G.J., Franz, T.M., Harper, E.S., Schoenbaum, G., Powell, E.M., 2008. Double dissociation of the effects of medial and orbital prefrontal cortical lesions on attentional and affective shifts in mice. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 28, 11124–11130.
Bitsakou, P., Psychogiou, L., Thompson, M., Sonuga-Barke, E.J., 2009. Delay aversion in attention deficit/hyperactivity disorder: an empirical investigation of the broader phenotype. Neuropsychologia 47, 446–456.
Bizot, J., Le Bihan, C., Puech, A.J., Hamon, M., Thiebot, M., 1999. Serotonin and tolerance to delay of reward in rats. Psychopharmacology 146, 400–412.
Blackwell, A.D., Paterson, N.S., Barker, R.A., Robbins, T.W., Sahakian, B.J., 2008. The effects of modafinil on mood and cognition in Huntington's disease. Psychopharmacology 199, 29–36.
Blakemore, S.J., Robbins, T.W., 2012. Decision-making in the adolescent brain. Nature Neuroscience 15, 1184–1191.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Block, J., 2002. Personality as an Affect-Processing System: Toward an Integrative Theory. Lawrence Erlbaum, Mahwah, NJ.
Boehler, C.N., Appelbaum, L.G., Krebs, R.M., Hopf, J.M., Woldorff, M.G., 2010. Pinning down response inhibition in the brain-conjunction analyses of the Stop-signal task. NeuroImage 52, 1621–1632.
Boehler, C.N., Bunzeck, N., Krebs, R.M., Noesselt, T., Schoenfeld, M.A., Heinze, H.J., Munte, T.F., Woldorff, M.G., Hopf, J.M., 2011. Substantia nigra activity level predicts trial-to-trial adjustments in cognitive control. Journal of Cognitive Neuroscience 23, 362–373.
Bor, D., Duncan, J., Wiseman, R.J., Owen, A.M., 2003. Encoding strategies dissociate prefrontal activity from working memory demand. Neuron 37, 361–367.
Botvinick, M.M., Braver, T.S., Barch, D.M., Carter, C.S., Cohen, J.D., 2001. Conflict monitoring and cognitive control. Psychological Review 108, 624–652.
Boucher, L., Stuphorn, V., Logan, G.D., Schall, J.D., Palmeri, T.J., 2007. Stopping eye and hand movements: are the processes independent? Perception & Psychophysics 69, 785–801.
Bouret, S., Sara, S.J., 2005. Network reset: a simplified overarching theory of locus coeruleus noradrenaline function. Trends in Neurosciences 28, 574–582.
Bramwell, J.M., 1903. Hypnotism. Its history, Practice and Theory. J.B. Lippincott Company, Philadelphia.
Braver, T.S., 2012. The variable nature of cognitive control: a dual mechanisms framework. Trends in Cognitive Sciences 16, 106–113.
Braver, T.S., Barch, D.M., Gray, J.R., Molfese, D.L., Snyder, A., 2001. Anterior cingulate cortex and response conflict: effects of frequency, inhibition and errors. Cerebral Cortex 11, 825–836.
Brebner, J., 1968. Continuing and reversing the direction of responding movements: some exceptions to the so-called psychological refractory period. Journal of Experimental Psychology 78, 120–127.
Breese, B.B., 1899. On inhibition. Psychological Monographs 3, 1–65.
Brigman, J.L., Mathur, P., Harvey-White, J., Izquierdo, A., Saksida, L.M., Bussey, T.J., Fox, S., Deneris, E., Murphy, D.L., Holmes, A., 2010. Pharmacological or genetic inactivation of the serotonin transporter improves reversal learning in mice. Cerebral Cortex 20, 1955–1963.
Brooks, V.B. (Ed.), 1986. The Neural Basis of Motor Control. Oxford University Press, New York.
Broos, N., Schmaal, L., Wiskerke, J., Kostelijk, L., Lam, T., Stoop, N., Weierink, L., Ham, J., de Geus, E.J., Schoffelmeer, A.N., van den Brink, W., Veltman, D.J., de Vries, T.J., Pattij, T., Goudriaan, A.E., 2012. The relationship between impulsive choice and impulsive action: a cross-species translational study. PLoS One 7, e36781.
Brown, J.W., Braver, T.S., 2005. Learned predictions of error likelihood in the anterior cingulate cortex. Science (New York, N.Y.) 307, 1118–1121.
Brown, V.J., Robbins, T.W., 1991. Simple and choice reaction time performance following unilateral striatal dopamine depletion in the rat. Impaired motor readiness but preserved response preparation. Brain 114 (Pt 1B) 513–525.
Bruin, K.J., Wijers, A.A., 2002. Inhibition, response mode, and stimulus probability: a comparative event-related potential study. Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology 113, 1172–1182.
Brunia, C.H., 1993. Waiting in readiness: gating in attention and motor preparation. Psychophysiology 30, 327–339.
Q14 Brunton, T.L., 1883. On the nature of inhibition, and the action of drugs upon it. Nature 27 .
Brutkowski, S., 1965. Functions of prefrontal cortex in animals. Physiological Reviews 45, 721–746.
Q15 Brutkowski, S., Konorski, J., Lawicka, W., Stepien, I., Stepien, L., 1956. The effect of the removal of frontal polesof the cerebral cortex on motor conditioned reflexes in dogs. Acta Biol. Exp. (Warsaw) 17, 167–188.
Brutkowski, S., Mempel, E., 1961. Disinhibition of inhibitory conditioned responses following selective brain lesions in dogs. Science (New York, N.Y.) 134, 2040–2041.
Buchsbaum, B.R., Greer, S., Chang, W.L., Berman, K.F., 2005. Meta-analysis of neuroimaging studies of the Wisconsin card-sorting task and component processes. Human Brain Mapping 25, 35–45.
Bulevich, J.B., Roediger 3rd, H.L., Balota, D.A., Butler, A.C., 2006. Failures to find suppression of episodic memories in the think/no-think paradigm. Memory & Cognition 34, 1569–1577.
Bunge, S.A., Dudukovic, N.M., Thomason, M.E., Vaidya, C.J., Gabrieli, J.D., 2002a. Immature frontal lobe contributions to cognitive control in children: evidence from fMRI. Neuron 33, 301–311.
Bunge, S.A., Hazeltine, E., Scanlon, M.D., Rosen, A.C., Gabrieli, J.D., 2002b. Dissociable contributions of prefrontal and parietal cortices to response selection. NeuroImage 17, 1562–1571.
Bunge, S.A., Kahn, I., Wallis, J.D., Miller, E.K., Wagner, A.D., 2003. Neural circuits subserving the retrieval and maintenance of abstract rules. Journal of Neurophysiology 90, 3419–3428.
Burgess, M.A., 1997. Theory and methodology in executive function research. In: Rabbitt, P. (Ed.), Methodology of Frontal and Executive Function. Psychology Press, Hove, UK, pp. 81–116.
Burle, B., Vidal, F., Bonnet, M., 2004. Electroencephalographic nogo potentials in a no-movement context: the case of motor imagery in humans. Neuroscience Letters 360, 77–80.
Bymaster, F.P., Katner, J.S., Nelson, D.L., Hemrick-Luecke, S.K., Threlkeld, P.G., Heiligenstein, J.H., Morin, S.M., Gehlert, D.R., Perry, K.W., 2002. Atomoxetine increases extracellular levels of norepinephrine and dopamine in prefrontal cortex of rat: a potential mechanism for efficacy in attention deficit/hyperactivity disorder. Neuropsychopharmacology 27, 699–711.
Cabel, D.W., Armstrong, I.T., Reingold, E., Munoz, D.P., 2000. Control of saccade initiation in a countermanding task using visual and auditory stop signals. Experimental Brain Research 133, 431–441.
Cai, W., Leung, H.C., 2011. Rule-guided executive control of response inhibition: functional topography of the inferior frontal cortex. PLoS One 6, e20840.
Cain, R.E., Wasserman, M.C., Waterhouse, B.D., McGaughy, J.A., 2011. Atomoxetine facilitates attentional set shifting in adolescent rats. Developments in Cognitive Neuroscience 1, 552–559.
Cardinal, R.N., Pennicott, D.R., Sugathapala, C.L., Robbins, T.W., Everitt, B.J., 2001. Impulsive choice induced in rats by lesions of the nucleus accumbens core. Science (New York, N.Y.) 292, 2499–2501.
Cardinal, R.N., Winstanley, C.A., Robbins, T.W., Everitt, B.J., 2004. Limbic corticostriatal systems and delayed reinforcement. Annals of the New York Academy of Sciences 1021, 33–50.
Carter, C.S., Braver, T.S., Barch, D.M., Botvinick, M.M., Noll, D., Cohen, J.D., 1998. Anterior cingulate cortex, error detection, and the online monitoring of performance. Science 280, 747–749.
Carter, C.S., Macdonald, A.M., Botvinick, M., Ross, L.L., Stenger, V.A., Noll, D., Cohen, J.D., 2000. Parsing executive processes: strategic vs evaluative functions of the anterior cingulate cortex. Proceedings of the National Academy of Sciences of the United States of America 97, 1944–1948.
Casey, B.J., Castellanos, F.X., Giedd, J.N., Marsh, W.L., Hamburger, S.D., Schubert, A.B., Vauss, Y.C., Vaituzis, A.C., Dickstein, D.P., Sarfatti, S.E., Rapoport, J.L., 1997a. Implication of right frontostriatal circuitry in response inhibition and attention-deficit/hyperactivity disorder. Journal of the American Academy of Child and Adolescent Psychiatry 36, 374–383.
Casey, B.J., Trainor, R., Giedd, J., Vauss, Y., Vaituzis, C.K., Hamburger, S., Kozuch, P., Rapoport, J.L., 1997b. The role of the anterior cingulate in automatic and controlled processes: a developmental neuroanatomical study. Developmental Psychobiology 30, 61–69.
Castellanos, F.X., Giedd, J.N., Marsh, W.L., Hamburger, S.D., Vaituzis, A.C., Dickstein, D.P., Sarfatti, S.E., Vauss, Y.C., Snell, J.W., Lange, N., Kaysen, D., Krain, A.L., Ritchie, G.F., Rajapakse, J.C., Rapoport, J.L., 1996. Quantitative brain magnetic resonance imaging in attention-deficit hyperactivity disorder. Archives of General Psychiatry 53, 607–616.
Castellanos, F.X., Sonuga-Barke, E.J., Milham, M.P., Tannock, R., 2006. Characterizing cognition in ADHD: beyond executive dysfunction. Trends in Cognitive Sciences 10, 117–123.
Chamberlain, S.R., Blackwell, A.D., Fineberg, N.A., Robbins, T.W., Sahakian, B.J., 2005. The neuropsychology of obsessive compulsive disorder: the importance of failures in cognitive and behavioural inhibition as candidate endophenotypic markers. Neuroscience and Biobehavioral Reviews 29, 399–419.
Chamberlain, S.R., Del Campo, N., Dowson, J., Muller, U., Clark, L., Robbins, T.W., Sahakian, B.J., 2007a. Atomoxetine improved response inhibition in adults with attention deficit/hyperactivity disorder. Biological Psychiatry 62, 977–984.
Chamberlain, S.R., Fineberg, N.A., Blackwell, A.D., Robbins, T.W., Sahakian, B.J., 2006a. Motor inhibition and cognitive flexibility in obsessive-compulsive disorder and trichotillomania. The American Journal of Psychiatry 163, 1282–1284.
Chamberlain, S.R., Fineberg, N.A., Menzies, L.A., Blackwell, A.D., Bullmore, E.T., Robbins, T.W., Sahakian, B.J., 2007b. Impaired cognitive flexibility and motor inhibition in unaffected first-degree relatives of patients with obsessive-compulsive disorder. The American Journal of Psychiatry 164, 335–338.
Chamberlain, S.R., Hampshire, A., Muller, U., Rubia, K., Del Campo, N., Craig, K., Regenthal, R., Suckling, J., Roiser, J.P., Grant, J.E., Bullmore, E.T., Robbins, T.W., Sahakian, B.J., 2009. Atomoxetine modulates right inferior frontal activation during inhibitory control: a pharmacological functional magnetic resonance imaging study. Biological Psychiatry 65, 550–555.
Chamberlain, S.R., Muller, U., Blackwell, A.D., Clark, L., Robbins, T.W., Sahakian, B.J., 2006b. Neurochemical modulation of response inhibition and probabilistic learning in humans. Science (New York, N.Y.) 311, 861–863.
Chamberlain, S.R., Sahakian, B.J., 2007. The neuropsychiatry of impulsivity. Current Opinion in Psychiatry 20, 255–261.
Chambers, C.D., Bellgrove, M.A., Gould, I.C., English, T., Garavan, H., McNaught, E., Kamke, M., Mattingley, J.B., 2007. Dissociable mechanisms of cognitive control in prefrontal and premotor cortex. Journal of Neurophysiology 98, 3638–3647.
Chambers, C.D., Bellgrove, M.A., Stokes, M.G., Henderson, T.R., Garavan, H., Robertson, I.H., Morris, A.P., Mattingley, J.B., 2006. Executive brake failure following deactivation of human frontal lobe. Journal of Cognitive Neuroscience 18, 444–455.
Chao, H.H., Luo, X., Chang, J.L., Li, C.S., 2009. Activation of the pre-supplementary motor area but not inferior prefrontal cortex in association with short stop signal reaction time – an intra-subject analysis. BMC Neuroscience 10, 75.
Chen, C.Y., Muggleton, N.G., Tzeng, O.J., Hung, D.L., Juan, C.H., 2009. Control of prepotent responses by the superior medial frontal cortex. NeuroImage 44, 537–545.
Chevrier, A., Schachar, R.J., 2010. Error detection in the stop signal task. NeuroImage. Q16
Chikazoe, J., Jimura, K., Asari, T., Yamashita, K., Morimoto, H., Hirose, S., Miyashita, Y., Konishi, S., 2009. Functional dissociation in right inferior frontal cortex during performance of go/no-go task. Cerebral Cortex 19, 146–152.
Chiu, Y.C., Aron, A.R., Verbruggen, F., 2012. Response suppression by automatic retrieval of stimulus-stop association: evidence from transcranial magnetic stimulation. Journal of Cognitive Neuroscience 24, 1908–1918.
Chudasama, Y., Robbins, T.W., 2003. Dissociable contributions of the orbitofrontal and infralimbic cortex to pavlovian autoshaping and discrimination reversal learning: further evidence for the functional heterogeneity of the rodent frontal

cortex. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 23, 8771–8780.
Clark, L., Blackwell, A.D., Aron, A.R., Turner, D.C., Dowson, J., Robbins, T.W., Sahakian, B.J., 2007. Association between response inhibition and working memory in adult ADHD: a link to right frontal cortex pathology? Biological Psychiatry 61, 1395–1401.
Clark, L., Roiser, J.P., Cools, R., Rubinsztein, D.C., Sahakian, B.J., Robbins, T.W., 2005. Stop signal response inhibition is not modulated by tryptophan depletion or the serotonin transporter polymorphism in healthy volunteers: implications for the 5-HT theory of impulsivity. Psychopharmacology 182, 570–578.
Clarke, H.F., Hill, G.J., Robbins, T.W., Roberts, A.C., 2011. Dopamine, but not serotonin, regulates reversal learning in the marmoset caudate nucleus. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 31, 4290–4297.
Clarke, H.F., Robbins, T.W., Roberts, A.C., 2008. Lesions of the medial striatum in monkeys produce perseverative impairments during reversal learning similar to those produced by lesions of the orbitofrontal cortex. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 28, 10972–10982.
Clarke, H.F., Walker, S.C., Dalley, J.W., Robbins, T.W., Roberts, A.C., 2007. Cognitive inflexibility after prefrontal serotonin depletion is behaviorally and neurochemically specific. Cerebral Cortex 17, 18–27.
Clayton, E.C., Rajkowski, J., Cohen, J.D., Aston-Jones, G., 2004. Phasic activation of monkey locus ceruleus neurons by simple decisions in a forced-choice task. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 24, 9914–9920.
Coccaro, E.F., Sripada, C.S., Yanowitch, R.N., Phan, K.L., 2011. Corticolimbic function in impulsive aggressive behavior. Biological Psychiatry 69, 1153–1159.
Coffey, S.F., Gudleski, G.D., Saladin, M.E., Brady, K.T., 2003. Impulsivity and rapid discounting of delayed hypothetical rewards in cocaine-dependent individuals. Experimental and Clinical Psychopharmacology 11, 18–25.
Cohen, J.D., Aston-Jones, G., Gilzenrat, M.S., 2004. A system-level perspective on attention and cognitive control. In: Posner, M.I. (Ed.), Cognitive Neuroscience of Attention. Guilford, New York, pp. 71–90.
Cohen, J.R., Lieberman, M.D., 2010. The common neural basis of exerting self-control in multiple domains. In: Trope, Y., Hassin, R., Ochsner, K.R. (Eds.), Self-Control. Oxford UP, New York, pp. 141–160.
Conway, A.R., Engle, R.W., 1994. Working memory and retrieval: a resource-dependent inhibition model. Journal of Experimental Psychology. General 123, 354–373.
Conway, M.A., Fthenaki, A., 2003. Disruption of inhibitory control of memory following lesions to the frontal and temporal lobes. Cortex 39, 667–686.
Cools, R., Blackwell, A., Clark, L., Menzies, L., Cox, S., Robbins, T.W., 2005. Tryptophan depletion disrupts the motivational guidance of goal-directed behavior as a function of trait impulsivity. Neuropsychopharmacology 30, 1362–1373.
Cools, R., Clark, L., Owen, A.M., Robbins, T.W., 2002. Defining the neural mechanisms of probabilistic reversal learning using event-related functional magnetic resonance imaging. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 22, 4563–4567.
Cools, R., Roberts, A.C., Robbins, T.W., 2008. Serotoninergic regulation of emotional and behavioural control processes. Trends in Cognitive Sciences 12, 31–40.
Corbetta, M., Miezin, F.M., Dobmeyer, S., Shulman, G.L., Petersen, S.E., 1991. Selective and divided attention during visual discriminations of shape, color, and speed: functional anatomy by positron emission tomography. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 11, 2383–2402.
Corbetta, M., Patel, G., Shulman, G.L., 2008. The reorienting system of the human brain: from environment to theory of mind. Neuron 58, 306–324.
Corbetta, M., Shulman, G.L., 2002. Control of goal-directed and stimulus-driven attention in the brain. Nature Reviews. Neuroscience 3, 201–215.
Coxon, J.P., Stinear, C.M., Byblow, W.D., 2006. Intracortical inhibition during volitional inhibition of prepared action. Journal of Neurophysiology 95, 3371–3383.
Q17 Craik, K.J., 1948. Theory of the human operator in control systems; man as an element in a control system. Br. J. Psychol. Gen. Sect. 38, 142–148.
Crean, J., Richards, J.B., de Wit, H., 2002. Effect of tryptophan depletion on impulsive behavior in men with or without a family history of alcoholism. Behavioural Brain Research 136, 349–357.
Cubillo, A., Halari, R., Ecker, C., Giampietro, V., Taylor, E., Rubia, K., 2010. Reduced activation and inter-regional functional connectivity of fronto-striatal networks in adults with childhood Attention-Deficit Hyperactivity Disorder (ADHD) and persisting symptoms during tasks of motor inhibition and cognitive switching. Journal of Psychiatric Research 44, 629–639.
Cubillo, A., Smith, A.B., Barrett, N., Giampietro, V., Brammer, M., Simmons, A., Rubia,
Q18 K., 2013. Drug-specific laterality effects on frontal lobe activation of atomoxetine and methylphenidate in attention deficit hyperactivity disorder boys during working memory. Psychological Medicine 1–14.
D'Esposito, M., Postle, B.R., Jonides, J., Smith, E.E., 1999. The neural substrate and temporal dynamics of interference effects in working memory as revealed by event-related functional MRI. Proceedings of the National Academy of Sciences of the United States of America 96, 7514–7519.
Dalley, J.W., Fryer, T.D., Brichard, L., Robinson, E.S., Theobald, D.E., Laane, K., Pena, Y., Murphy, E.R., Shah, Y., Probst, K., Abakumova, I., Aigbirhio, F.I., Richards, H.K., Hong, Y., Baron, J.C., Everitt, B.J., Robbins, T.W., 2007. Nucleus accumbens D2/3 receptors predict trait impulsivity and cocaine reinforcement. Science 315, 1267–1270.
Dalley, J.W., Roiser, J.P., 2012. Dopamine, serotonin and impulsivity. Neuroscience 215, 42–58.
Daw, N.D., Kakade, S., Dayan, P., 2002. Opponent interactions between serotonin and dopamine. Neural Networks: the Official Journal of the International Neural Network Society 15, 603–616.
de Bruijn, E.R., Hulstijn, W., Verkes, R.J., Ruigt, G.S., Sabbe, B.G., 2004. Drug-induced stimulation and suppression of action monitoring in healthy volunteers. Psychopharmacology 177, 151–160.
De Jong, R., Coles, M.G.H., Logan, G.D., 1995. Strategies and mechanisms in nonselective and selective inhibitory motor control. Journal of Experimental Psychology: Human Perception and Performance 21, 498–511.
de Jong, R., Coles, M.G.H., Logan, G.D., Gratton, G., 1990. Searching for the point of no return: the control of response processes in speeded choice reaction performance. Journal of Experimental Psychology: Human Perception and Performance 16, 164–182.
de Wit, H., Crean, J., Richards, J.B., 2000. Effects of d-amphetamine and ethanol on a measure of behavioral inhibition in humans. Behavioral Neuroscience 114, 830–837.
de Wit, H., Enggasser, J.L., Richards, J.B., 2002. Acute administration of d-amphetamine decreases impulsivity in healthy volunteers. Neuropsychopharmacology 27, 813–825.
De Young, C.G., 2010. Impulsivity as a personality trait. In: Vohs, K.D., Baumeister, R.F. (Eds.), Handbook of Self-regulation: Research, Theory and Applications. second ed. Guilford Press, New York.
Deakin, J.F., Graeff, F.G., 1991. 5-HT and mechanisms of defence. Journal of Psychopharmacology 5, 305–315.
Delgado, J.M., 1964. Free behavior and brain stimulation. International Review of Neurobiology 6, 349–449.
Delgado, M.R., Gillis, M.M., Phelps, E.A., 2008. Regulating the expectation of reward via cognitive strategies. Nature Neuroscience 11, 880–881.
Dempster, F.N., 1991. Inhibitory processes: a neglected dimension of intelligence. Intelligence 15, 157–173.
Dempster, F.N., Corkill, A.J., 1999. Individual differences in susceptibility to interference and general cognitive ability. Acta Psychologica 101, 395–416.
Denckla, M.B., 1996. A theory and model of executive function: a neuropsychological perspective. In: Lyon, G.R., Krasnegor, N.A. (Eds.), Attention, Memory and Executive Function. Brookes, Baltimore, MD, pp. 263–278.
Denk, F., Walton, M.E., Jennings, K.A., Sharp, T., Rushworth, M.F., Bannerman, D.M., 2005. Differential involvement of serotonin and dopamine systems in cost-benefit decisions about delay or effort. Psychopharmacology 179, 587–596.
Der-Avakian, A., Markou, A., 2012. The neurobiology of anhedonia and other reward-related deficits. Trends in Neurosciences 35, 68–77.
Desimone, R., Duncan, J., 1995. Neural mechanisms of selective visual attention. Annual Review of Neuroscience 18, 193–222.
Devilbiss, D.M., Berridge, C.W., 2006. Low-dose methylphenidate actions on tonic and phasic locus coeruleus discharge. Journal of Pharmacology and Experimental Therapeutics 319, 1327–1335.
Devinsky, O., Morrell, M.J., Vogt, B.A., 1995. Contributions of anterior cingulate cortex to behaviour. Brain 118 (Pt 1) 279–306.
Diamond, S., Balvin, R.S., Diamond, F.R. (Eds.), 1963. Inhibition and Choice: A Neurobiological Approach to Problems of Plasticity in Behavior. Harpen & Row, New York.
Dias, R., Robbins, T.W., Roberts, A.C., 1996. Dissociation in prefrontal cortex of affective and attentional shifts. Nature 380, 69–72.
Dickman, S., 1985. Impulsivity and perception: individual differences in the processing of the local and global dimensions of stimuli. Journal of Personality and Social Psychology 48, 133–149.
Dickman, S.J., 1990. Functional and dysfunctional impulsivity: personality and cognitive correlates. Journal of Personality and Social Psychology 58, 95–102.
Dickman, S.J., Meyer, D.E., 1988. Impulsivity and speed-accuracy tradeoffs in information processing. Journal of Personality and Social Psychology 54, 274–290.
Dickstein, S.G., Bannon, K., Castellanos, F.X., Milham, M.P., 2006. The neural correlates of attention deficit hyperactivity disorder: an ALE meta-analysis. Journal of Child Psychology and Psychiatry, and Allied Disciplines 47, 1051–1062.
Diergaarde, L., Pattij, T., Poortvliet, I., Hogenboom, F., de Vries, W., Schoffelmeer, A.N., De Vries, T.J., 2008. Impulsive choice and impulsive action predict vulnerability to distinct stages of nicotine seeking in rats. Biological Psychiatry 63, 301–308.
Dillon, D.G., Pizzagalli, D.A., 2007. Inhibition of action, thought, and emotion: a Q19 selective neurobiological review. Appl Prev Psychol 12, 99–114.
Dimitrov, M., Nakic, M., Elpern-Waxman, J., Granetz, J., O'Grady, J., Phipps, M., Milne, E., Logan, G.D., Hasher, L., Grafman, J., 2003. Inhibitory attentional control in patients with frontal lobe damage. Brain and Cognition 52, 258–270.
Dimoska, A., Johnstone, S.J., 2007. Neural mechanisms underlying trait impulsivity in non-clinical adults: stop-signal performance and event-related potentials. Progress in Neuro-psychopharmacology & Biological Psychiatry 31, 443–454.
Dimoska, A., Johnstone, S.J., Barry, R.J., 2006. The auditory-evoked N2 and P3 components in the stop-signal task: indices of inhibition, response-conflict or error-detection? Brain and Cognition 62, 98–112.
Dinner, D.S., Luders, H.O., 1995. Human supplementary sensorimotor area. Electrical stimulation and movement-related potential studies. Advances in Neurology 66, 261–269, discussion 269-271.
Dlugos, A.M., Hamidovic, A., Palmer, A.A., de Wit, H., 2009. Further evidence of association between amphetamine response and SLC6A2 gene variants. Psychopharmacology 206, 501–511.
Dodds, C.M., Morein-Zamir, S., Robbins, T.W., 2010. Dissociating inhibition, attention, and response control in the frontoparietal network using functional magnetic resonance imaging. Cerebral Cortex 21, 1155–1165.

Dosenbach, N.U., Fair, D.A., Cohen, A.L., Schlaggar, B.L., Petersen, S.E., 2008. A dual-networks architecture of top-down control. Trends in Cognitive Sciences 12, 99–105.
Downar, J., Crawley, A.P., Mikulis, D.J., Davis, K.D., 2001. The effect of task relevance on the cortical response to changes in visual and auditory stimuli: an event-related fMRI study. NeuroImage 14, 1256–1267.
Doya, K., 2002. Metalearning and neuromodulation. Neural Networks: the Official Journal of the International Neural Network Society 15, 495–506.
Drewe, E.A., 1975a. An experimental investigation of Luria's theory on the effects of frontal lobe lesions in man. Neuropsychologia 13, 421–429.
Drewe, E.A., 1975b. Go – no go learning after frontal lobe lesions in humans. Cortex 11, 8–16.
Duann, J.R., Ide, J.S., Luo, X., Li, C.S., 2009. Functional connectivity delineates distinct roles of the inferior frontal cortex and presupplementary motor area in stop signal inhibition. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 29, 10171–10179.
Dum, R.P., Strick, P.L., 1991. The origin of corticospinal projections from the premotor areas in the frontal lobe. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 11, 667–689.
Dumais, A., Potvin, S., Joyal, C., Allaire, J.F., Stip, E., Lesage, A., Gobbi, G., Cote, G., 2011. Schizophrenia and serious violence: a clinical-profile analysis incorporating impulsivity and substance-use disorders. Schizophrenia Research 130, 234–237.
Duncan, J., Johnson, R., Swales, M., Freer, C., 1997. Frontal lobe deficits after head injury: unity and diversity of function. Cognitive Neuropsychology 14, 713–741.
Duncan, J., Owen, A.M., 2000. Common regions of the human frontal lobe recruited by diverse cognitive demands. Trends in Neurosciences 23, 475–483.
Dunkel, H.B., 1970. Herbart and Hebartianism: An Educational Ghost Story. Chicago University Press, Chicago.
Durston, S., Hulshoff Pol, H.E., Schnack, H.G., Buitelaar, J.K., Steenhuis, M.P., Minderaa, R.B., Kahn, R.S., van Engeland, H., 2004. Magnetic resonance imaging of boys with attention-deficit/hyperactivity disorder and their unaffected siblings. Journal of the American Academy of Child and Adolescent Psychiatry 43, 332–340.
Durston, S., Thomas, K.M., Worden, M.S., Yang, Y., Casey, B.J., 2002. The effect of preceding context on inhibition: an event-related fMRI study. NeuroImage 16, 449–453.
Dyer, F.N., Severance, L.J., 1973. Stroop interference with successive presentations of separate incongruent words and colors. Journal of Experimental Psychology 98, 438–439.
Eagle, D.M., Bari, A., Robbins, T.W., 2008a. The neuropsychopharmacology of action inhibition: cross-species translation of the stop-signal and go/no-go tasks. Psychopharmacology 199, 439–456.
Eagle, D.M., Baunez, C., Hutcheson, D.M., Lehmann, O., Shah, A.P., Robbins, T.W., 2008b. Stop-signal reaction-time task performance: role of prefrontal cortex and subthalamic nucleus. Cerebral Cortex 18, 178–188.
Eagle, D.M., Lehmann, O., Theobald, D.E., Pena, Y., Zakaria, R., Ghosh, R., Dalley, J.W., Robbins, T.W., 2009. Serotonin depletion impairs waiting but not stop-signal reaction time in rats: implications for theories of the role of 5-HT in behavioral inhibition. Neuropsychopharmacology 34, 1311–1321.
Eagle, D.M., Robbins, T.W., 2003. Inhibitory control in rats performing a stop-signal reaction-time task: effects of lesions of the medial striatum and d-amphetamine. Behavioral Neuroscience 117, 1302–1317.
Eagle, D.M., Tufft, M.R., Goodchild, H.L., Robbins, T.W., 2007. Differential effects of modafinil and methylphenidate on stop-signal reaction time task performance in the rat, and interactions with the dopamine receptor antagonist cis-flupenthixol. Psychopharmacology 192, 193–206.
Eagle, D.M., Wong, J.C., Allan, M.E., Mar, A.C., Theobald, D.E., Robbins, T.W., 2011. Contrasting roles for dopamine D1 and D2 receptor subtypes in the dorsomedial striatum but not the nucleus accumbens core during behavioral inhibition in the stop-signal task in rats. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 31, 7349–7356.
Egner, T., Hirsch, J., 2005. Cognitive control mechanisms resolve conflict through cortical amplification of task-relevant information. Nature Neuroscience 8, 1784–1790.
Eisenberg, D.T., Mackillop, J., Modi, M., Beauchemin, J., Dang, D., Lisman, S.A., Lum, J.K., Wilson, D.S., 2007. Examining impulsivity as an endophenotype using a behavioral approach: a DRD2 TaqI A and DRD4 48-bp VNTR association study. Behavioral and Brain Functions 3, 2.
Ellen, P., Powell, E.W., 1962. Effects of septal lesions on behavior generated by positive reinforcement. Experimental Neurology 6, 1–11.
Elliott, R., 1968. Simple visual and simple auditory reaction time: a comparison. Psychonomic Science 10, 335–336.
Elliott, R., Sahakian, B.J., McKay, A.P., Herrod, J.J., Robbins, T.W., Paykel, E.S., 1996. Neuropsychological impairments in unipolar depression: the influence of perceived failure on subsequent performance. Psychological Medicine 26, 975–989.
Emeric, E.E., Brown, J.W., Boucher, L., Carpenter, R.H., Hanes, D.P., Harris, R., Logan, G.D., Mashru, R.N., Pare, M., Pouget, P., Stuphorn, V., Taylor, T.L., Schall, J.D., 2007. Influence of history on saccade countermanding performance in humans and macaque monkeys. Vision Research 47, 35–49.
English, H.B., English, A.C., 1958. A Comprehensive Dictionary of Psychological and Psychoanalytic Terms: A Guide to Usage. David McKay Company, Inc., New York.
Epstein, L.H., Dearing, K.K., Temple, J.L., Cavanaugh, M.D., 2008. Food reinforcement and impulsivity in overweight children and their parents. Eating Behaviors 9, 319–327.
Ersche, K.D., Jones, P.S., Williams, G.B., Turton, A.J., Robbins, T.W., Bullmore, E.T., 2012. Abnormal brain structure implicated in stimulant drug addiction. Science (New York, N.Y.) 335, 601–604.
Ersche, K.D., Roiser, J.P., Abbott, S., Craig, K.J., Muller, U., Suckling, J., Ooi, C., Shabbir, S.S., Clark, L., Sahakian, B.J., Fineberg, N.A., Merlo-Pich, E.V., Robbins, T.W., Bullmore, E.T., 2011. Response perseveration in stimulant dependence is associated with striatal dysfunction and can be ameliorated by a D(2/3) receptor agonist. Biological Psychiatry 70, 754–762.
Ersche, K.D., Roiser, J.P., Robbins, T.W., Sahakian, B.J., 2008. Chronic cocaine but not chronic amphetamine use is associated with perseverative responding in humans. Psychopharmacology 197, 421–431.
Evenden, J.L., 1999. Varieties of impulsivity. Psychopharmacology 146, 348–361.
Evenden, J.L., Ryan, C.N., 1999. The pharmacology of impulsive behaviour in rats VI: the effects of ethanol and selective serotonergic drugs on response choice with varying delays of reinforcement. Psychopharmacology 146, 413–421.
Evers, E.A., Cools, R., Clark, L., van der Veen, F.M., Jolles, J., Sahakian, B.J., Robbins, T.W., 2005. Serotonergic modulation of prefrontal cortex during negative feedback in probabilistic reversal learning. Neuropsychopharmacology 30, 1138–1147.
Eysenck, H.J., 1947. Dimensions of Personality. Routledge & Kegan Paul, London.
Eysenck, H.J., 1993. The nature of impulsivity. In: McCown, W.G., Johnson, J.L., Sure, M.B. (Eds.), The Impulsive Client: Theory, Research, and Treatment. American Psychological Association, Washington DC.
Eysenck, H.J., Eysenck, S.B.G., 1975. Manual of the Eysenck Personality Questionnaire. Hodder & Stoughton, London.
Eysenck, S.B., Eysenck, H.J., 1977. The place of impulsiveness in a dimensional system of personality description. The British Journal of Social and Clinical Psychology 16, 57–68.
Fassbender, C., Murphy, K., Foxe, J.J., Wylie, G.R., Javitt, D.C., Robertson, I.H., Garavan, H., 2004. A topography of executive functions and their interactions revealed by functional magnetic resonance imaging. Brain Research. Cognitive Brain Research 20, 132–143.
Fellows, L.K., Farah, M.J., 2005a. Different underlying impairments in decision-making following ventromedial and dorsolateral frontal lobe damage in humans. Cerebral Cortex 15, 58–63.
Fellows, L.K., Farah, M.J., 2005b. Is anterior cingulate cortex necessary for cognitive control? Brain 128, 788–796.
Feola, T.W., de Wit, H., Richards, J.B., 2000. Effects of d-amphetamine and alcohol on a measure of behavioral inhibition in rats. Behavioral Neuroscience 114, 838–848.
Ferrari, P.F., Palanza, P., Parmigiani, S., de Almeida, R.M., Miczek, K.A., 2005. Serotonin and aggressive behavior in rodents and nonhuman primates: predispositions and plasticity. European Journal of Pharmacology 526, 259–273.
Ferrier, D., 1876. The Functions of the Brain. G. P. Putnam's Sons, New York.
Ferrier, D., 1878. The Goulstonian lectures of the localisation of cerebral disease. British Medical Journal I 397–402, 443–447.
Ferrier, D., 1886. The Functions of the Brain, 2nd ed. Putnam, New York.
Fields, S.A., Sabet, M., Peal, A., Reynolds, B., 2011. Relationship between weight status and delay discounting in a sample of adolescent cigarette smokers. Behavioural Pharmacology 22, 266–268.
Fillmore, M.T., Rush, C.R., Kelly, T.H., Hays, L., 2001. Triazolam impairs inhibitory control of behavior in humans. Experimental and Clinical Psychopharmacology 9, 363–371.
Fineberg, N.A., Potenza, M.N., Chamberlain, S.R., Berlin, H.A., Menzies, L., Bechara, A., Sahakian, B.J., Robbins, T.W., Bullmore, E.T., Hollander, E., 2010. Probing compulsive and impulsive behaviors, from animal models to endophenotypes: a narrative review. Neuropsychopharmacology 35, 591–604.
Floden, D., Stuss, D.T., 2006. Inhibitory control is slowed in patients with right superior medial frontal damage. Journal of Cognitive Neuroscience 18, 1843–1849.
Floresco, S.B., Magyar, O., 2006. Mesocortical dopamine modulation of executive functions: beyond working memory. Psychopharmacology 188, 567–585.
Forstmann, B.U., Keuken, M.C., Jahfari, S., Bazin, P.L., Neumann, J., Schafer, A., Anwander, A., Turner, R., 2012. Cortico-subthalamic white matter tract strength predicts interindividual efficacy in stopping a motor response. NeuroImage 60, 370–375.
Frank, M.J., 2006. Hold your horses: a dynamic computational role for the subthalamic nucleus in decision making. Neural Networks: the Official Journal of the International Neural Network Society 19, 1120–1136.
Franken, I.H., van Strien, J.W., Nijs, I., Muris, P., 2008. Impulsivity is associated with behavioral decision-making deficits. Psychiatry Research 158, 155–163.
French, G.M., 1959a. A deficit associated with hypermotility in monkeys with lesions of the dorsolateral frontal granular cortex. Journal of Comparative Physiology & Psychology 52, 25–28.
French, G.M., 1959b. Locomotor effects of regional ablations of frontal cortex in rhesus monkeys. Journal of Comparative Physiology & Psychology 52, 18–24.
Fresquet, N., Angst, M.J., Schleef, C., Gobaille, S., Sandner, G., 2007. Adrenergic drugs modify the level of noradrenaline in the insular cortex and alter extinction of conditioned taste aversion in rats. Behavioural Brain Research 178, 39–46.
Freud, S., 1959. Inhibitions, Symptoms and Anxiety (The Standard Edition). W.W. Norton & Company, Inc, New York.
Freud, S., 1966. Project for a Scientific Psychology, Standard ed. Hogarth, London.
Fried, I., Katz, A., McCarthy, G., Sass, K.J., Williamson, P., Spencer, S.S., Spencer, D.D., 1991. Functional organization of human supplementary motor cortex studied by electrical stimulation. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 11, 3656–3666.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Friedman, N.P., Miyake, A., 2004. The relations among inhibition and interference control functions: a latent-variable analysis. Journal of Experimental Psychology. General 133, 101–135.
Friedman, N.P., Miyake, A., Corley, R.P., Young, S.E., Defries, J.C., Hewitt, J.K., 2006. Not all executive functions are related to intelligence. Psychological Science: A Journal of the American Psychological Society 17, 172–179.
Friedman, N.P., Miyake, A., Young, S.E., Defries, J.C., Corley, R.P., Hewitt, J.K., 2008. Individual differences in executive functions are almost entirely genetic in origin. Journal of Experimental Psychology. General 137, 201–225.
Fryer, J.D., Lukas, R.J., 1999. Noncompetitive functional inhibition at diverse, human nicotinic acetylcholine receptor subtypes by bupropion, phencyclidine, and ibogaine. Journal of Pharmacology and Experimental Therapeutics 288, 88–92.
Fulbright, R.K., Troche, C.J., Skudlarski, P., Gore, J.C., Wexler, B.E., 2001. Functional MR imaging of regional brain activation associated with the affective experience of pain. AJR. American Journal of Roentgenology 177, 1205–1210.
Fuster, J.M. (Ed.), 1989. The Prefrontal Cortex. Anatomy, Physiology, and Neuropsychology of the Frontal Lobe. Raven Press, New York.
Fuster, J.M., 2008. The Prefrontal Cortex. Academic Press, London.
Gall, F.J. (Ed.), 1835. On the Functions of the Brain and on Each of its Parts. Marsh, Capen and Lyon, Boston, [Original work published 1822-1825].
Gamo, N.J., Arnsten, A.F., 2011. Molecular modulation of prefrontal cortex: rational development of treatments for psychiatric disorders. Behavioral Neuroscience 125, 282–296.
Gamo, N.J., Wang, M., Arnsten, A.F., 2010. Methylphenidate and atomoxetine enhance prefrontal function through alpha2-adrenergic and dopamine D1 receptors. Journal of the American Academy of Child and Adolescent Psychiatry 49, 1011–1023.
Garavan, H., Hester, R., Murphy, K., Fassbender, C., Kelly, C., 2006. Individual differences in the functional neuroanatomy of inhibitory control. Brain Research 1105, 130–142.
Garavan, H., Ross, T.J., Stein, E.A., 1999. Right hemispheric dominance of inhibitory control: an event-related functional MRI study. Proceedings of the National Academy of Sciences of the United States of America 96, 8301–8306.
Gaskell, W.H., 1886. The electrical changes in the quiescent cardiac muscle which accompany stimulation of the vagus nerve. The Journal of Physiology 7, 451–452.
Gemba, H., Sasaki, K., 1989. Potential related to no-go reaction of go/no-go hand movement task with color discrimination in human. Neuroscience Letters 101, 263–268.
Gemba, H., Sasaki, K., Brooks, V.B., 1986. 'Error' potentials in limbic cortex (anterior cingulate area 24) of monkeys during motor learning. Neuroscience Letters 70, 223–227.
Gerbing, D.W., Ahadi, S.A., Patton, J.H., 1987. Toward a conceptualization of impulsivity: components across the behavioral and self-report domains. Multivariate Behavioral Research 22, 357–379.
Gerschlager, W., Siebner, H.R., Rothwell, J.C., 2001. Decreased corticospinal excitability after subthreshold 1 Hz rTMS over lateral premotor cortex. Neurology 57, 449–455.
Ghahremani, D.G., Lee, B., Robertson, C.L., Tabibnia, G., Morgan, A.T., De Shetler, N., Brown, A.K., Monterosso, J.R., Aron, A.R., Mandelkern, M.A., Poldrack, R.A., London, E.D., 2012. Striatal dopamine D(2)/D(3) receptors mediate response inhibition and related activity in frontostriatal neural circuitry in humans. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 32, 7316–7324.
Godefroy, O., Rousseaux, M., 1996. Binary choice in patients with prefrontal or posterior brain damage. A relative judgement theory analysis. Neuropsychologia 34, 1029–1038.
Goldberg, G., Mayer, N.H., Toglia, J.U., 1981. Medial frontal cortex infarction and the alien hand sign. Archives of Neurology 38, 683–686.
Goldstone, S., 1968. Reaction time to onset and termination of lights and sounds. Perceptual and Motor Skills 27, 1023–1029.
Goltz, F. (Ed.), 1869. Beitrage zur Lehre von den Functionen der Nervencentren des Frosches. Hirschwald, A., Berlin.
Grafton, S.T., Mazziotta, J.C., Presty, S., Friston, K.J., Frackowiak, R.S., Phelps, M.E., 1992. Functional anatomy of human procedural learning determined with regional cerebral blood flow and PET. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 12, 2542–2548.
Granon, S., Passetti, F., Thomas, K.L., Dalley, J.W., Everitt, B.J., Robbins, T.W., 2000. Enhanced and impaired attentional performance after infusion of D1 dopaminergic receptor agents into rat prefrontal cortex. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 20, 1208–1215.
Gray, J.A. (Ed.), 1972. The Psychophysiological Basis of Introversion-Extraversion: a Modification of Eysenck's Theory. Academic Press, New York.
Green, L., Myerson, J., 2004. A discounting framework for choice with delayed and probabilistic rewards. Psychological Bulletin 130, 769–792.
Green, L., Myerson, J., 2010. Experimental and correlational analyses of delay and probability discounting. In: Madden, G.J., Warren, K.B. (Eds.), Impulsivity: The Behavioral and Neurological Science of Discounting. American Psychological Association, Washington, DC.
Green, L., Myerson, J., Shah, A.K., Estle, S.J., Holt, D.D., 2007. Do adjusting-amount and adjusting-delay procedures produce equivalent estimates of subjective value in pigeons? Journal of the Experimental Analysis of Behavior 87, 337–347.
Q20 Greenhouse, I., Oldenkamp, C.L., Aron, A.R., 2011a. Stopping a response has global or non-global effects on the motor system depending on preparation. Journal of Neurophysiology.
Greenhouse, I., Swann, N., Aron, A.R., 2011b. Fronto-basal-ganglia circuits for stopping action. In: Mars, R.B., Sallet, J., Rushworth, M.F.S. (Eds.), Neural Basis of Motivational and Cognitive Control. The MIT Press, Cambridge, MA.
Groman, S.M., Lee, B., London, E.D., Mandelkern, M.A., James, A.S., Feiler, K., Rivera, R., Dahlbom, M., Sossi, V., Vandervoort, E., Jentsch, J.D., 2011. Dorsal striatal D2-like receptor availability covaries with sensitivity to positive reinforcement during discrimination learning. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 31, 7291–7299.
Guillem, K., Bloem, B., Poorthuis, R.B., Loos, M., Smit, A.B., Maskos, U., Spijker, S., Mansvelder, H.D., 2011. Nicotinic acetylcholine receptor beta2 subunits in the medial prefrontal cortex control attention. Science 333, 888–891.
Gut-Fayand, A., Dervaux, A., Olie, J.P., Loo, H., Poirier, M.F., Krebs, M.O., 2001. Substance abuse and suicidality in schizophrenia: a common risk factor linked to impulsivity. Psychiatry Research 102, 65–72.
Hamidovic, A., Dlugos, A., Palmer, A.A., de Wit, H., 2010a. Catechol-O-methyltransferase val158met genotype modulates sustained attention in both the drug-free state and in response to amphetamine. Psychiatric Genetics 20, 85–92.
Hamidovic, A., Dlugos, A., Palmer, A.A., de Wit, H., 2010b. Polymorphisms in dopamine transporter (SLC6A3) are associated with stimulant effects of D-amphetamine: an exploratory pharmacogenetic study using healthy volunteers. Behavior Genetics 40, 255–261.
Hamidovic, A., Dlugos, A., Skol, A., Palmer, A.A., de Wit, H., 2009. Evaluation of genetic variability in the dopamine receptor D2 in relation to behavioral inhibition and impulsivity/sensation seeking: an exploratory study with d-amphetamine in healthy participants. Experimental and Clinical Psychopharmacology 17, 374–383.
Hampshire, A., Chamberlain, S.R., Monti, M.M., Duncan, J., Owen, A.M., 2010. The role of the right inferior frontal gyrus: inhibition and attentional control. NeuroImage 50, 1313–1319.
Hampshire, A., Thompson, R., Duncan, J., Owen, A.M., 2008. The target selective neural response – similarity, ambiguity, and learning effects. PLoS One 3, e2520.
Hampshire, A., Thompson, R., Duncan, J., Owen, A.M., 2009. Selective tuning of the right inferior frontal gyrus during target detection. Cognitive, Affective, & Behavioral Neuroscience 9, 103–112.
Hanes, D.P., Patterson 2nd, W.F., Schall, J.D., 1998. Role of frontal eye fields in countermanding saccades: visual, movement, and fixation activity. Journal of Neurophysiology 79, 817–834.
Hanes, D.P., Schall, J.D., 1996. Neural control of voluntary movement initiation. Science (New York, N.Y.) 274, 427–430.
Harati, H., Barbelivien, A., Cosquer, B., Majchrzak, M., Cassel, J.C., 2008. Selective cholinergic lesions in the rat nucleus basalis magnocellularis with limited damage in the medial septum specifically alter attention performance in the five-choice serial reaction time task. Neuroscience 153, 72–83.
Hare, T.A., Camerer, C.F., Rangel, A., 2009. Self-control in decision-making involves modulation of the vmPFC valuation system. Science 324, 646–648.
Hare, W.K., Magoun, H.W., Ranson, S.W., 1936. Electrical stimulatiuon of the interior of the cerebellum in the decerebrated cat. American Journal of Physiology 117, 261–266.
Harlow, H.F., Hicks, L.H., 1957. Discrimination learning theory: uniprocess vs duoprocess. Psychological Review 64, 104–109.
Harnishfeger, K., 1995. Development of cognitive inhibition. In: Dempster, F., Brainerd, C. (Eds.), Interference and Inhibition in Cognition. Academic Press, New York.
Harnishfeger, K.K., Bjorklund, D.F., 1944. A developmental perpective on individual differences in inhibition. Learning and Individual Differences 6, 331–355.
Head, H., Holmes, G., 1911. Sensory disturbances from cerebral lesions. Brain 34, 103–254.
Heinen, S.J., Rowland, J., Lee, B.T., Wade, A.R., 2006. An oculomotor decision process revealed by functional magnetic resonance imaging. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 26, 13515–13522.
Heinz, A.J., Beck, A., Meyer-Lindenberg, A., Sterzer, P., Heinz, A., 2011. Cognitive and neurobiological mechanisms of alcohol-related aggression. Nature Reviews. Neuroscience 12, 400–413.
Helson, H., Steger, J.A., 1962. On the inhibitory effects of a second stimulus following the primary stimulus to react. Journal of Experimental Psychology 64, 201–205.
Henry, F.M., Harrison, J.S., 1961. Refractoriness of a fast movement. Perceptual and Motor Skills 13, 351–354.
Herd, S.A., Banich, M.T., O'Reilly, R.C., 2006. Neural mechanisms of cognitive control: an integrative model of stroop task performance and FMRI data. Journal of Cognitive Neuroscience 18, 22–32.
Hermans, E.J., van Marle, H.J., Ossewaarde, L., Henckens, M.J., Qin, S., van Kesteren, M.T., Schoots, V.C., Cousijn, H., Rijpkema, M., Oostenveld, R., Fernandez, G., 2011. Stress-related noradrenergic activity prompts large-scale neural network reconfiguration. Science 334, 1151–1153.
Hester, R.L., Murphy, K., Foxe, J.J., Foxe, D.M., Javitt, D.C., Garavan, H., 2004. Predicting success: patterns of cortical activation and deactivation prior to response inhibition. Journal of Cognitive Neuroscience 16, 776–785.
Hikosaka, O., Isoda, M., 2010. Switching from automatic to controlled behavior: cortico-basal ganglia mechanisms. Trends in Cognitive Sciences 14, 154–161.
Hilgard, E.R., 1953. Introduction to Psychology. Harcourt, Brace & Co., New York.
Hodgson, T., Chamberlain, M., Parris, B., James, M., Gutowski, N., Husain, M., Kennard, C., 2007. The role of the ventrolateral frontal cortex in inhibitory oculomotor control. Brain 130, 1525–1537.
Hofmann, W., Friese, M., Strack, F., 2009. Impulse and self-control from a dual-systems perspective. Perpectives on Psychological Science 4, 162–176.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Hofmann, W., Schmeichel, B.J., Baddeley, A.D., 2012. Executive functions and self-regulation. Trends in Cognitive Sciences 16, 174–180.
Holroyd, C.B., Coles, M.G., 2002. The neural basis of human error processing: reinforcement learning, dopamine, and the error-related negativity. Psychological Review 109, 679–709.
Homberg, J.R., 2012. Serotonin and decision making processes. Neuroscience and Biobehavioral Reviews 36, 218–236.
Hon, N., Epstein, R.A., Owen, A.M., Duncan, J., 2006. Frontoparietal activity with minimal decision and control. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 26, 9805–9809.
Horak, F.B., Anderson, M.E., 1984. Influence of globus pallidus on arm movements in monkeys II. Effects of stimulation. Journal of Neurophysiology 52, 305–322.
Horn, N.R., Dolan, M., Elliott, R., Deakin, J.F., Woodruff, P.W., 2003. Response inhibition and impulsivity: an fMRI study. Neuropsychologia 41, 1959–1966.
Hornak, J., O'Doherty, J., Bramham, J., Rolls, E.T., Morris, R.G., Bullock, P.R., Polkey, C.E., 2004. Reward-related reversal learning after surgical excisions in orbitofrontal or dorsolateral prefrontal cortex in humans. Journal of Cognitive Neuroscience 16, 463–478.
Horner, W.E., Johnson, D.E., Schmidt, A.W., Rollema, H., 2007. Methylphenidate and atomoxetine increase histamine release in rat prefrontal cortex. European Journal of Pharmacology 558, 96–97.
Horstmann, G., 2003. The psychological refractory period of stopping. Journal of Experimental Psychology. Human Perception and Performance 29, 965–981.
Hull, C. (Ed.), 1943. Principles of Behavior. Appleton-Century-Crofts, New York.
Humberstone, M., Sawle, G.V., Clare, S., Hykin, J., Coxon, R., Bowtell, R., Macdonald, I.A., Morris, P.G., 1997. Functional magnetic resonance imaging of single motor events reveals human presupplementary motor area. Annals of Neurology 42, 632–637.
Hunter, J., Jasper, H.H., 1949. Effects of thalamic stimulation in unanaesthetised animals; the arrest reaction and petit mal-like seizures, activation patterns and generalized convulsions. Electroencephalography and Clinical Neurophysiology 1, 305–324.
Huster, R.J., Westerhausen, R., Pantev, C., Konrad, C., 2010. The role of the cingulate cortex as neural generator of the N200 and P300 in a tactile response inhibition task. Human Brain Mapping 31, 1260–1271.
Hutton, S.B., Ettinger, U., 2006. The antisaccade task as a research tool in psychopathology: a critical review. Psychophysiology 43, 302–313.
Inase, M., Tokuno, H., Nambu, A., Akazawa, T., Takada, M., 1999. Corticostriatal and corticosubthalamic input zones from the presupplementary motor area in the macaque monkey: comparison with the input zones from the supplementary motor area. Brain Research 833, 191–201.
Ineichen, C., Sigrist, H., Spinelli, S., Lesch, K.P., Sautter, E., Seifritz, E., Pryce, C.R., 2012. Establishing a probabilistic reversal learning test in mice: evidence for the processes mediating reward-stay and punishment-shift behaviour and for their modulation by serotonin. Neuropharmacology 63, 1012–1021.
Isles, A.R., Humby, T., Walters, E., Wilkinson, L.S., 2004. Common genetic effects on variation in impulsivity and activity in mice. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 24, 6733–6740.
Isoda, M., Hikosaka, O., 2007. Switching from automatic to controlled action by monkey medial frontal cortex. Nature Neuroscience 10, 240–248.
Isoda, M., Hikosaka, O., 2008. Role for subthalamic nucleus neurons in switching from automatic to controlled eye movement. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 28, 7209–7218.
Itami, S., Uno, H., 2002. Orbitofrontal cortex dysfunction in attention-deficit hyperactivity disorder revealed by reversal and extinction tasks. Neuroreport 13, 2453–2457.
Izquierdo, A., Belcher, A.M., Scott, L., Cazares, V.A., Chen, J., O'Dell, S.J., Malvaez, M., Wu, T., Marshall, J.F., 2010. Reversal-specific learning impairments after a binge regimen of methamphetamine in rats: possible involvement of striatal dopamine. Neuropsychopharmacology 35, 505–514.
Izquierdo, A., Jentsch, J.D., 2012. Reversal learning as a measure of impulsive and compulsive behavior in addictions. Psychopharmacology 219, 607–620.
Jackson, J.H., 1931a. Selected writings of John Hughlings Jackson. Volume 1: On Epilepsy and Epileptiform Convulsions, Hodder and Stoughton, London.
Jackson, J.H., 1931b. Selected writings of John Hughlings Jackson. Volume 2: Evolution and Dissolution of the Nervous System; Speech; Various Papers, Addresses and Lectures, Hodder and Stoughton, London.
Jacobsen, C.F., 1936. Studies of cerebral functions in primates: I the function of the frontal association area in monkeys. Comp. Psychol. Monographs 13, 3–60.
Jahfari, S., Stinear, C.M., Claffey, M., Verbruggen, F., Aron, A.R., 2009. Responding with restraint: what are the neurocognitive mechanisms? Journal of Cognitive Neuroscience 22, 1479–1492.
Jahfari, S., Waldorp, L., van den Wildenberg, W.P., Scholte, H.S., Ridderinkhof, K.R., Forstmann, B.U., 2011. Effective connectivity reveals important roles for both the hyperdirect (fronto-subthalamic) and the indirect (fronto-striatal-pallidal) fronto-basal ganglia pathways during response inhibition. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 31, 6891–6899.
James, W., 1890. The Principles of Psychology. Henry Holt, New York.
Jarrott, B., Louis, W.J., Summers, R.J., 1982. [3H]-guanfacine: a radioligand that selectively labels high affinity alpha2-adrenoceptor sites in homogenates of rat brain. British Journal of Pharmacology 75, 401–408.
Jentsch, J.D., Olausson, P., De La Garza 2nd, R., Taylor, J.R., 2002. Impairments of reversal learning and response perseveration after repeated, intermittent cocaine administrations to monkeys. Neuropsychopharmacology 26, 183–190.
Jentsch, J.D., Taylor, J.R., 1999. Impulsivity resulting from frontostriatal dysfunction in drug abuse: implications for the control of behavior by reward-related stimuli. Psychopharmacology 146, 373–390.
Jodo, E., Kayama, Y., 1992. Relation of a negative ERP component to response inhibition in a Go/No-go task. Electroencephalography and Clinical Neurophysiology 82, 477–482.
John, O.P., Caspi, A., Robins, R.W., Moffitt, T.E., Stouthamer-Loeber, R., 1994. The little five: exploring the nomological network of the five-factor model of personality in adolescent boys. Child Development 65 .
Johnstone, S.J., Barry, R.J., Clarke, A.R., 2007. Behavioural and ERP indices of response inhibition during a Stop-signal task in children with two subtypes of Attention-Deficit Hyperactivity Disorder. International Journal of Psychophysiology: Official Journal of the International Organization of Psychophysiology 66, 37–47.
Jones, B., Mishkin, M., 1972. Limbic lesions and the problem of stimulus–reinforcement associations. Experimental Neurology 36, 362–377.
Jonides, J., Smith, E.E., Marshuetz, C., Koeppe, R.A., Reuter-Lorenz, P.A., 1998. Inhibition in verbal working memory revealed by brain activation. Proceedings of the National Academy of Sciences of the United States of America 95, 8410–8413.
Jung, R., Hassler, R., 1960. The extrapyramidal motor system. In: Field, J., Magoun, H.W., Hall, V.E. (Eds.), Handbook of Physiology, Section 1, Vol. 2. American Physiological Society, Washington, D.C., pp. 863–927.
Kaada, B.R., 1951. Somato-motor, autonomic and electrocorticographic responses to electrical stimulation of rhinencephalic and other structures in primates, cat, and dog; a study of responses from the limbic, subcallosal, orbito-insular, piriform and temporal cortex, hippocampus-fornix and amygdala. Acta Physiologica Scandinavica Supplement 24, 1–262.
Kable, J.W., Glimcher, P.W., 2007. The neural correlates of subjective value during intertemporal choice. Nature Neuroscience 10, 1625–1633.
Kawashima, R., Satoh, K., Itoh, H., Ono, S., Furumoto, S., Gotoh, R., Koyama, M., Yoshioka, S., Takahashi, T., Takahashi, K., Yanagisawa, T., Fukuda, H., 1996. Functional anatomy of GO/NO-GO discrimination and response selection – a PET study in man. Brain Research 728, 79–89.
Kehagia, A.A., Murray, G.K., Robbins, T.W., 2010. Learning and cognitive flexibility: frontostriatal function and monoaminergic modulation. Current Opinion in Neurobiology 20, 199–204.
Kelly, A.M., Hester, R., Murphy, K., Javitt, D.C., Foxe, J.J., Garavan, H., 2004. Prefrontal-subcortical dissociations underlying inhibitory control revealed by event-related fMRI. The European Journal of Neuroscience 19, 3105–3112.
Kendall, P.C., Wilcox, L.E., 1979. Self-control in children: development of a rating scale. Journal of Consulting and Clinical Psychology 47, 1020–1029.
Kiehl, K.A., Liddle, P.F., Hopfinger, J.B., 2000. Error processing and the rostral anterior cingulate: an event-related fMRI study. Psychophysiology 37, 216–223.
Kimberg, D.Y., Farah, M.J., 1993. A unified account of cognitive impairments following frontal lobe damage: the role of working memory in complex, organized behavior. Journal of Experimental Psychology. General 122, 411–428.
Kimble, D.P., 1968. Hippocampus and internal inhibition. Psychological Bulletin 70, 285–295.
Kipp, K., 2005. A developmental perspective on the measurement of cognitive deficits in attention-deficit/hyperactivity disorder. Biological Psychiatry 57, 1256–1260.
Kirby, K.N., 2009. One-year temporal stability of delay-discount rates. Psychonomic Bulletin & Review 16, 457–462.
Kirby, K.N., Herrnstein, R.J., 1995. Preference reversals due to myopic discounting of delayed reward. Psychological Science: A Journal of the American Psychological Society 6, 83–89.
Kirby, K.N., Petry, N.M., Bickel, W.K., 1999. Heroin addicts have higher discount rates for delayed rewards than non-drug-using controls. Journal of Experimental Psychology. General 128, 78–87.
Klein, R.M., Taylor, T.L., 1994. Categories of cognitive inhibition with reference to attention. In: Dagenbach, D., Carr, T.H. (Eds.), Inhibitory Processes in Attention, Memory and Language. Academic Press, San Diego, CA, pp. 189–236.
Kluver, H. (Ed.), 1933. Behavior Mechanisms in Monkeys. University of Chicago Press, Chicago.
Koffarnus, M.N., Newman, A.H., Grundt, P., Rice, K.C., Woods, J.H., 2011. Effects of selective dopaminergic compounds on a delay-discounting task. Behavioural Pharmacology 22, 300–311.
Kok, A., 1999. Varieties of inhibition: manifestations in cognition, event-related potentials and aging. Acta Psychologica 101, 129–158.
Konishi, S., Nakajima, K., Uchida, I., Sekihara, K., Miyashita, Y., 1998. No-go dominant brain activity in human inferior prefrontal cortex revealed by functional magnetic resonance imaging. The European Journal of Neuroscience 10, 1209–1213.
Konorski, J., 1957. On the hyperactivity in animals following lesions of the frontal lobes. Prob. Fiziol. Tsentr. Nervnoy Sistemy, Akad. Nauk SSSR, Inst. Fiziol. Sb. (Russian).
Konorski, J., 1961. Disinhibition of inhibitory CRs after prefrontal lesionsin dogs. In: Delafresnaye, J.F. (Ed.), Brain Mechanisms and Learning. Blackwell Scientific Publications, Ltd., Oxford, pp. 567–573.
Konorski, J., 1967. Integrative Activity of the Brain. An Interdiciplinary Approach. University of Chicago Press, Chicago.
Konorski, J., Lawicka, W., 1964. Analysis of errors by prefrontal animals on the delayed-response test. In: Warren, J.M., Akert, K. (Eds.), The Frontal Granular Cortex and Behavior. McGraw-Hill Book Co., New York, pp. 271–294.
Koob, G.F., Bloom, F.E., 1988. Cellular and molecular mechanisms of drug dependence. Science 242, 715–723.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Kringelbach, M.L., Rolls, E.T., 2004. The functional neuroanatomy of the human orbitofrontal cortex: evidence from neuroimaging and neuropsychology. Progress in Neurobiology 72, 341–372.
Kuczenski, R., Segal, D.S., 1997. Effects of methylphenidate on extracellular dopamine, serotonin, and norepinephrine: comparison with amphetamine. Journal of Neurochemistry 68, 2032–2037.
Kunishio, K., Haber, S.N., 1994. Primate cingulostriatal projection: limbic striatal versus sensorimotor striatal input. The Journal of Comparative Neurology 350, 337–356.
Ladefoged, P., Silverstein, R., Papcun, G., 1973. Letter: interruptibility of speech. The Journal of the Acoustical Society of America 54, 1105–1108.
Lange, K.W., Robbins, T.W., Marsden, C.D., James, M., Owen, A.M., Paul, G.M., 1992. L-dopa withdrawal in Parkinson's disease selectively impairs cognitive performance in tests sensitive to frontal lobe dysfunction. Psychopharmacology 107, 394–404.
Lapiz-Bluhm, M.D., Soto-Pina, A.E., Hensler, J.G., Morilak, D.A., 2009. Chronic intermittent cold stress and serotonin depletion induce deficits of reversal learning in an attentional set-shifting test in rats. Psychopharmacology 202, 329–341.
Lapiz, M.D., Bondi, C.O., Morilak, D.A., 2007. Chronic treatment with desipramine improves cognitive performance of rats in an attentional set-shifting test. Neuropsychopharmacology 32, 1000–1010.
Lapiz, M.D., Morilak, D.A., 2006. Noradrenergic modulation of cognitive function in rat medial prefrontal cortex as measured by attentional set shifting capability. Neuroscience 137, 1039–1049.
Lappin, J., Eriksen, C., 1966. Use of delayed signal to stop a visual reaction-time response. Journal of Experimental Psychology 72, 805–811.
Lawrence, A., Clark, L., Labuzetta, J.N., Sahakian, B., Vyakarnum, S., 2008. The innovative brain. Nature 456, 168–169.
Ledgerwood, D.M., Alessi, S.M., Phoenix, N., Petry, N.M., 2009. Behavioral assessment of impulsivity in pathological gamblers with and without substance use disorder histories versus healthy controls. Drug and Alcohol Dependence 105, 89–96.
Leimkuhler, M.E., Mesulam, M.M., 1985. Reversible go-no go deficits in a case of frontal lobe tumor. Annals of Neurology 18, 617–619.
Leung, H.C., Cai, W., 2007. Common and differential ventrolateral prefrontal activity during inhibition of hand and eye movements. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 27, 9893–9900.
Levelt, W.J., 1983. Monitoring and self-repair in speech. Cognition 14, 41–104.
Levy, B.J., Anderson, M.C., 2002. Inhibitory processes and the control of memory retrieval. Trends in Cognitive Sciences 6, 299–305.
Levy, B.J., Wagner, A.D., 2011. Cognitive control and right ventrolateral prefrontal cortex: reflexive reorienting, motor inhibition, and action updating. Annals of the New York Academy of Sciences 1224, 40–62.
Levy, F., 2008. Pharmacological and therapeutic directions in ADHD: Specificity in the PFC. Behavioral and Brain Functions 4, 12.
Levy, R., Goldman-Rakic, P.S., 2000. Segregation of working memory functions within the dorsolateral prefrontal cortex. Experimental Brain Research 133, 23–32.
Li, C.S., Huang, C., Constable, R.T., Sinha, R., 2006. Imaging response inhibition in a stop-signal task: neural correlates independent of signal monitoring and post-response processing. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 26, 186–192.
Li, C.S., Yan, P., Sinha, R., Lee, T.W., 2008. Subcortical processes of motor response inhibition during a stop signal task. NeuroImage 41, 1352–1363.
Linden, D.E., Prvulovic, D., Formisano, E., Vollinger, M., Zanella, F.E., Goebel, R., Dierks, T., 1999. The functional neuroanatomy of target detection: an fMRI study of visual and auditory oddball tasks. Cerebral Cortex 9, 815–823.
Lisberger, S.G., Fuchs, A.F., King, W.M., Evinger, L.C., 1975. Effect of mean reaction time on saccadic responses to two-step stimuli with horizontal and vertical components. Vision Research 15, 1021–1025.
Lister, J., 1858. Preliminary account of an inquiry into the functions of the visceral nerves, with special reference to the so-called 'inhibitory system'. Proceedings of the Royal Society of London 9, 367–380.
Loeber, S., Duka, T., 2009. Acute alcohol impairs conditioning of a behavioural reward-seeking response and inhibitory control processes–implications for addictive disorders. Addiction 104, 2013–2022.
Logan, G.D., 1982. On the ability to inhibit complex movements: A stop signal study of typewriting. Journal of Experimental Psychology: Human Perception and Performance 8, 778–792.
Logan, G.D., 1983. On the ability to inhibit simple thoughts and actions: 1. Stop signal studies of decision and memory. JOurnal of Experimental Psychology: Learning, Memory and Cognition 9, 585–606.
Logan, G.D., 1994. On the ability to inhibit thought and action. A users' guide to the stop signal paradigm. In: Dagenbach, D., Carr, T.H. (Eds.), Inhibitory Processes in Attention, Memory and Language. Academic Press, San Diego, CA, pp. 189–236.
Logan, G.D., Cowan, W.B., 1984. On the ability to inhibit thought and action – a theory of an act of control. Psychological Review 91, 295–327.
Logan, G.D., Cowan, W.B., Davis, K.A., 1984. On the ability to inhibit simple and choice reaction time responses: a model and a method. Journal of Experimental Psychology 10, 276–291.
Logan, G.D., Irwin, D.E., 2000. Don't look! Don't touch! Inhibitory control of eye and hand movements Psychonomic Bulletin & Review 7, 107–112.
Long, J., 1976. Visual feedback and skilled keying: differential effects of masking the printed copy and the keyboard. Ergonomics 19, 93–110.
Lubow, R.E., Moore, A.U., 1959. Latent inhibition: the effect of nonreinforced pre-exposure to the conditional stimulus. Journal of Comparative Physiology & Psychology 52, 415–419.
Luders, H., Lesser, R.P., Dinner, D.S., Morris, H.H., Wyllie, E., Godoy, J., 1988. Localization of cortical function: new information from extraoperative monitoring of patients with epilepsy. Epilepsia 29 (Suppl. 2) S56–S65.
Luengo, M.A., Carrillo-de-la-Pena, M.T., Otero, J.M., Romero, E., 1994. A short-term longitudinal study of impulsivity and antisocial behavior. Journal of Personality and Social Psychology 66, 542–548.
Luria, A.R. (Ed.), 1966. Higher Cortical Functions in Man. Basic Books, New York.
Luria, A.R., 1973. The Working Brain: An Introduction to Neuropsychology. Basic, New York.
Lynn, R., 1966. Attention, Arousal and the Orienting Reaction. Pergamon Press, Oxford.
MacLeod, C.M., 2007. The concept of inhibition in cognition. In: MacLeod, David S., Gorfein, Colin M. (Eds.), Inhibition in Cognition. American Psychological Association.
MacLeod, C.M., Dodd, M.D., Sheard, E.D., Wilson, D.E., Bibi, U., 2003. In opposition to inhibition. Psychology of Learning and Motivation 43, 163–214.
Macmillan, M., 1992. Inhibition and the control of behavior. From Gall to Freud via Phineas Gage and the frontal lobes. Brain and Cognition 19, 72–104.
Macmillan, M., 1996. The concept of inhibition in some nineteenth century theories of thinking. Brain and Cognition 30, 4–19.
Madden, G.J., Bickel, W.K., 2009. Impulsivity: the Behavioral and Neurological Science of Discounting. American Psychological Association, Washington DC.
Madden, G.J., Petry, N.M., Badger, G.J., Bickel, W.K., 1997. Impulsive and self-control choices in opioid-dependent patients and non-drug-using control participants: drug and monetary rewards. Experimental and Clinical Psychopharmacology 5, 256–262.
Madden, G.J., Smith, N.G., Brewer, A.T., Pinkston, J.W., Johnson, P.S., 2008. Steady-state assessment of impulsive choice in Lewis and Fischer 344 rats: between-condition delay manipulations. Journal of the Experimental Analysis of Behavior 90, 333–344.
Magoun, H.W., Rhines, R., 1946. An inhibitory mechanism in the bulbar reticular formation. Journal of Neurophysiology 9, 165–171.
Majid, D.S., Cai, W., George, J.S., Verbruggen, F., Aron, A.R., 2012. Transcranial magnetic stimulation reveals dissociable mechanisms for global versus selective corticomotor suppression underlying the stopping of action. Cerebral Cortex 22, 363–371.
Mar, A.C., Walker, A.L., Theobald, D.E., Eagle, D.M., Robbins, T.W., 2011. Dissociable effects of lesions to orbitofrontal cortex subregions on impulsive choice in the rat. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 31, 6398–6404.
Mars, R.B., Piekema, C., Coles, M.G., Hulstijn, W., Toni, I., 2007. On the programming and reprogramming of actions. Cerebral Cortex 17, 2972–2979.
Masaki, D., Yokoyama, C., Kinoshita, S., Tsuchida, H., Nakatomi, Y., Yoshimoto, K., Fukui, K., 2006. Relationship between limbic and cortical 5-HT neurotransmission and acquisition and reversal learning in a go/no-go task in rats. Psychopharmacology 189, 249–258.
Mattay, V.S., Goldberg, T.E., Fera, F., Hariri, A.R., Tessitore, A., Egan, M.F., Kolachana, B., Callicott, J.H., Weinberger, D.R., 2003. Catechol O-methyltransferase val158-met genotype and individual variation in the brain response to amphetamine. Proceedings of the National Academy of Sciences of the United States of America 100, 6186–6191.
Mazur, J.E., 1987. An adjusting procedure for studying delayed reinforcement. In: Commons, M.L., Mazur, J.E., Nevin, J.A., Rachlin, H. (Eds.), Quantitative Analysis of Behavior. Erlbaum, Hillsdale, NJ, pp. 55–73.
McClure, S.M., Laibson, D.I., Loewenstein, G., Cohen, J.D., 2004. Separate neural systems value immediate and delayed monetary rewards. Science 306, 503–507.
McCulloch, W.S., Graf, C., Magoun, H.W., 1946. A cortico-bulbo-reticular pathway from area 4-S. Journal of Neurophysiology 9, 127–132.
McDonald, J., Schleifer, L., Richards, J.B., de Wit, H., 2003. Effects of THC on behavioral measures of impulsivity in humans. Neuropsychopharmacology 28, 1356–1365.
McGaughy, J., Ross, R.S., Eichenbaum, H., 2008. Noradrenergic, but not cholinergic, deafferentation of prefrontal cortex impairs attentional set-shifting. Neuroscience 153, 63–71.
McKerchar, T.L., Green, L., Myerson, J., Pickford, T.S., Hill, J.C., Stout, S.C., 2009. A comparison of four models of delay discounting in humans. Behavioural Processes 81, 256–259.
McNab, F., Leroux, G., Strand, F., Thorell, L., Bergman, S., Klingberg, T., 2008. Common and unique components of inhibition and working memory: an fMRI, within-subjects investigation. Neuropsychologia 46, 2668–2682.
Meltzer, S.J., 1899. Inhibition. New York Medical Journal 69 (i) . Q23
Menon, V., Adleman, N.E., White, C.D., Glover, G.H., Reiss, A.L., 2001. Error-related brain activation during a Go/NoGo response inhibition task. Human Brain Mapping 12, 131–143.
Metcalfe, J., Mischel, W., 1999. A hot/cool-system analysis of delay of gratification: dynamics of willpower. Psychological Review 106, 3–19.
Mettler, F.A., Mettler, C.C., 1942. The effects of striatal injury. Brain 65, 242–255.
Michael, G.A., Garcia, S., Fernandez, D., Sellal, F., Boucart, M., 2006. The ventral premotor cortex (vPM) and resistance to interference. Behavioral Neuroscience 120, 447–462.
Michel, F., Anderson, M., 2009. Using the antisaccade task to investigate the relationship between the development of inhibition and the development of intelligence. Developmental Science 12, 272–288.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Miller, E.K., Cohen, J.D., 2001. An integrative theory of prefrontal cortex function. Annual Review of Neuroscience 24, 167–202.
Minzenberg, M.J., Carter, C.S., 2007. Modafinil: a review of neurochemical actions and effects on cognition. Neuropsychopharmacology.
Minzenberg, M.J., Watrous, A.J., Yoon, J.H., Ursu, S., Carter, C.S., 2008. Modafinil shifts human locus coeruleus to low-tonic, high-phasic activity during functional MRI. Science 322, 1700–1702.
Mirabella, G., Iaconelli, S., Romanelli, P., Modugno, N., Lena, F., Manfredi, M., Cantore, G., 2012. Deep brain stimulation of subthalamic nuclei affects arm response inhibition in Parkinson's patients. Cerebral Cortex 22, 1124–1132.
Mishkin, M., 1964. Perseveration of central sets after frontal lesions in monkeys. In: Warren, J.M., Akert, K. (Eds.), The Frontal Granular Cortex and Behavior. McGraw-Hill Book Co., New York, pp. 219–241.
Mishkin, M., Prockop, E.S., Rosvold, H.E., 1962. One-trial objectdiscrimination learning in monkeys with frontal lesions. Journal of Comparative Physiology & Psychology 55, 178–181.
Mitchell, S.H., 2004. Measuring impulsivity and modeling its association with cigarette smoking. Behavioral and Cognitive Neuroscience Reviews 3, 261–275.
Miyake, A., Friedman, N.P., Emerson, M.J., Witzki, A.H., Howerter, A., Wager, T.D., 2000. The unity and diversity of executive functions and their contributions to complex Frontal Lobe tasks: a latent variable analysis. Cognitive Psychology 41, 49–100.
Miyazaki, K., Miyazaki, K.W., Doya, K., 2011a. Activation of dorsal raphe serotonin neurons underlies waiting for delayed rewards. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 31, 469–479.
Miyazaki, K., Miyazaki, K.W., Doya, K., 2012. The role of serotonin in the regulation of patience and impulsivity. Molecular Neurobiology 45, 213–224.
Miyazaki, K.W., Miyazaki, K., Doya, K., 2011b. Activation of the central serotonergic system in response to delayed but not omitted rewards. The European Journal of Neuroscience 33, 153–160.
Mobini, S., Body, S., Ho, M.Y., Bradshaw, C.M., Szabadi, E., Deakin, J.F., Anderson, I.M., 2002. Effects of lesions of the orbitofrontal cortex on sensitivity to delayed and probabilistic reinforcement. Psychopharmacology 160, 290–298.
Mobini, S., Chiang, T.J., Al-Ruwaitea, A.S., Ho, M.Y., Bradshaw, C.M., Szabadi, E., 2000. Effect of central 5-hydroxytryptamine depletion on inter-temporal choice: a quantitative analysis. Psychopharmacology 149, 313–318.
Moeller, F.G., Barratt, E.S., Dougherty, D.M., Schmitz, J.M., Swann, A.C., 2001. Psychiatric aspects of impulsivity. The American Journal of Psychiatry 158, 1783–1793.
Moffitt, T.E., 1993. Adolescence-limited and life-course-persistent antisocial behavior: a developmental taxonomy. Psychological Review 100, 674–701.
Monterosso, J.R., Ainslie, G., Xu, J., Cordova, X., Domier, C.P., London, E.D., 2007. Frontoparietal cortical activity of methamphetamine-dependent and comparison subjects performing a delay discounting task. Human Brain Mapping 28, 383–393.
Moran, J., Desimone, R., 1985. Selective attention gates visual processing in the extrastriate cortex. Science (New York, N.Y.) 229, 782–784.
Morein-Zamir, S., Fineberg, N.A., Robbins, T.W., Sahakian, B.J., 2010. Inhibition of thoughts and actions in obsessive-compulsive disorder: extending the endophenotype? Psychological Medicine 40, 263–272.
Morein-Zamir, S., Kingstone, A., 2006. Fixation offset and stop signal intensity effects on saccadic countermanding: a crossmodal investigation. Experimental Brain Research 175, 453–462.
Morein-Zamir, S., Nagelkerke, P., Chua, R., Franks, I., Kingstone, A., 2004. Inhibiting prepared and ongoing responses: is there more than one kind of stopping? Psychonomic Bulletin Review 11, 1034–1040.
Morgan, C.L., 1891. Animal Life and Intelligence. Ginn & Company, Boston.
Moruzzi, G., 1950. Problems in Cerebellar Physiology. Thomas, Springfield, Ill.
Mostofsky, S.H., Schafer, J.G., Abrams, M.T., Goldberg, M.C., Flower, A.A., Boyce, A., Courtney, S.M., Calhoun, V.D., Kraut, M.A., Denckla, M.B., Pekar, J.J., 2003. fMRI evidence that the neural basis of response inhibition is task-dependent. Brain Research. Cognitive Brain Research 17, 419–430.
Mostofsky, S.H., Simmonds, D.J., 2008. Response inhibition and response selection: two sides of the same coin. Journal of Cognitive Neuroscience 20, 751–761.
Muir, J.L., Everitt, B.J., Robbins, T.W., 1996. The cerebral cortex of the rat and visual attentional function: dissociable effects of mediofrontal, cingulate, anterior dorsolateral, and parietal cortex lesions on a five-choice serial reaction time task. Cerebral Cortex 6, 470–481.
Muller-Preuss, P., Jurgens, U., 1976. Projections from the 'cingular' vocalization area in the squirrel monkey. Brain Research 103, 29–43.
Muller, U., Clark, L., Lam, M.L., Moore, R.M., Murphy, C.L., Richmond, N.K., Sandhu, R.S., Wilkins, I.A., Menon, D.K., Sahakian, B.J., Robbins, T.W., 2005. Lack of effects of guanfacine on executive and memory functions in healthy male volunteers. Psychopharmacology 182, 205–213.
Mulvihill, L.E., Skilling, T.A., Vogel-Sprott, M., 1997. Alcohol and the ability to inhibit behavior in men and women. Journal of Studies Alcohol 58, 600–605.
Munakata, Y., Herd, S.A., Chatham, C.H., Depue, B.E., Banich, M.T., O'Reilly, R.C., 2011. A unified framework for inhibitory control. Trends in Cognitive Sciences 15, 453–459.
Munoz, D.P., Wurtz, R.H., 1993a. Fixation cells in monkey superior colliculus I. Characteristics of cell discharge. Journal of Neurophysiology 70, 559–575.
Munoz, D.P., Wurtz, R.H., 1993b. Fixation cells in monkey superior colliculus II. Reversible activation and deactivation. Journal of Neurophysiology 70, 576–589.
Muraven, M., Shmueli, D., Burkley, E., 2006. Conserving self-control strength. Journal of Personality and Social Psychology 91, 524–537.
Murphy, F.C., Michael, A., Robbins, T.W., Sahakian, B.J., 2003. Neuropsychological impairment in patients with major depressive disorder: the effects of feedback on task performance. Psychological Medicine 33, 455–467.
Murtha, S., Chertkow, H., Beauregard, M., Dixon, R., Evans, A., 1996. Anticipation causes increased blood flow to the anterior cingulate cortex. Human Brain Mapping 4, 103–112.
Nachev, P., Rees, G., Parton, A., Kennard, C., Husain, M., 2005. Volition and conflict in human medial frontal cortex. Current Biology: CB 15, 122–128.
Nachev, P., Wydell, H., O'Neill, K., Husain, M., Kennard, C., 2007. The role of the pre-supplementary motor area in the control of action. NeuroImage 36 (Suppl. 2) T155–T163.
Nakamura, H., Kitagawa, H., Kawaguchi, Y., Tsuji, H., 1997. Intracortical facilitation and inhibition after transcranial magnetic stimulation in conscious humans. The Journal of Physiology 498 (Pt 3) 817–823.
Nakamura, K., Kawashima, R., Ito, K., Sugiura, M., Kato, T., Nakamura, A., Hatano, K., Nagumo, S., Kubota, K., Fukuda, H., Kojima, S., 1999. Activation of the right inferior frontal cortex during assessment of facial emotion. Journal of Neurophysiology 82, 1610–1614.
Nakata, H., Sakamoto, K., Ferretti, A., Gianni Perrucci, M., Del Gratta, C., Kakigi, R., Luca Romani, G., 2008. Somato-motor inhibitory processing in humans: an event-related functional MRI study. NeuroImage 39, 1858–1866.
Nakata, H., Sakamoto, K., Ferretti, A., Gianni Perrucci, M., Del Gratta, C., Kakigi, R., Luca Romani, G., 2009. Negative BOLD effect on somato-motor inhibitory processing: an fMRI study. Neuroscience Letters 462, 101–104.
Nambu, A., Tokuno, H., Takada, M., 2002. Functional significance of the cortico-subthalamo-pallidal 'hyperdirect' pathway. Neuroscience Research 43, 111–117.
Nandam, L.S., Hester, R., Wagner, J., Cummins, T.D., Garner, K., Dean, A.J., Kim, B.N., Nathan, P.J., Mattingley, J.B., Bellgrove, M.A., 2011. Methylphenidate but not atomoxetine or citalopram modulates inhibitory control and response time variability. Biological Psychiatry 69, 902–904.
Nandam, L.S., Hester, R., Wagner, J., Dean, A.J., Messer, C., Honeysett, A., Nathan, P.J., Bellgrove, M.A., 2013. Dopamine D(2) receptor modulation of human response inhibition and error awareness. Journal of Cognitive Neuroscience 25, 649–656.
Narayanan, N.S., Horst, N.K., Laubach, M., 2006. Reversible inactivations of rat medial prefrontal cortex impair the ability to wait for a stimulus. Neuroscience 139, 865–876.
Neill, W.T., 1977. Inhibitory and facilitatory processes in attention. Journal of Experimental Psychology: Human Perception and Performance 3, 440–450.
Nestler, E.J., Carlezon Jr., W.A., 2006. The mesolimbic dopamine reward circuit in depression. Biological Psychiatry 59, 1151–1159.
Newman, J.P., Widom, C.S., Nathan, S., 1985. Passive avoidance in syndromes of disinhibition: psychopathy and extraversion. Journal of Personality and Social Psychology 48, 1316–1327.
Newman, L.A., Darling, J., McGaughy, J., 2008. Atomoxetine reverses attentional deficits produced by noradrenergic deafferentation of medial prefrontal cortex. Psychopharmacology 200, 39–50.
Nieuwenhuis, S., 2010. Learning, the P3, and the locus coeruleus-norepinephrine system. In: Mars, R.B., Sallet, J., Rushworth, M.F., Yeung, N. (Eds.), Neural Basis of Motivational and Cognitive Control. The MIT Press, Cambridge, MA.
Nieuwenhuis, S., Aston-Jones, G., Cohen, J.D., 2005. Decision making, the P3, and the locus coeruleus-norepinephrine system. Psychological Bulletin 131, 510–532.
Nieuwenhuis, S., De Geus, E.J., Aston-Jones, G., 2010. The anatomical and functional relationship between the P3 and autonomic components of the orienting response. Psychophysiology.
Nigg, J.T., 2000. On inhibition/disinhibition in developmental psychopathology: views from cognitive and personality psychology and a working inhibition taxonomy. Psychological Bulletin 126, 220–246.
Nigg, J.T., 2001. Is ADHD a disinhibitory disorder? Psychological Bulletin 127, 571–598.
Nigg, J.T., 2005. Neuropsychologic theory and findings in attention-deficit/hyperactivity disorder: the state of the field and salient challenges for the coming decade. Biological Psychiatry 57, 1424–1435.
Nigg, J.T., Casey, B.J., 2005. An integrative theory of attention-deficit/hyperactivity disorder based on the cognitive and affective neurosciences. Development and Psychopathology 17, 785–806.
Nigg, J.T., Wong, M.M., Martel, M.M., Jester, J.M., Puttler, L.I., Glass, J.M., Adams, K.M., Fitzgerald, H.E., Zucker, R.A., 2006. Poor response inhibition as a predictor of problem drinking and illicit drug use in adolescents at risk for alcoholism and other substance use disorders. Journal of the American Academy of Child and Adolescent Psychiatry 45, 468–475.
Nomura, M., Iidaka, T., Kakehi, K., Tsukiura, T., Hasegawa, T., Maeda, Y., Matsue, Y., 2003. Frontal lobe networks for effective processing of ambiguously expressed emotions in humans. Neuroscience Letters 348, 113–116.
Norbury, R., Taylor, M.J., Selvaraj, S., Murphy, S.E., Harmer, C.J., Cowen, P.J., 2009. Short-term antidepressant treatment modulates amygdala response to happy faces. Psychopharmacology 206, 197–204.
Norman, D., Shallice, T., 1986. Attention to action: willed and automatic control of behavior. In: Davidson, R., Schwartz, R., Shapiro, D. (Eds.), Consciousness and Self Regulation: Advances in Research and Theory IV. Plenum Press, New York.
Novick, J.M., Trueswell, J.C., Thompson-Schill, S.L., 2005. Cognitive control and parsing: reexamining the role of Broca's area in sentence comprehension. Cognitive, Affective, & Behavioral Neuroscience 5, 263–281.
O'Brien, C.P., Volkow, N., Li, T.K., 2006. What's in a word? Addiction versus dependence in DSM-V. The American Journal of Psychiatry 163, 764–765.

O'Doherty, J., Kringelbach, M.L., Rolls, E.T., Hornak, J., Andrews, C., 2001. Abstract reward and punishment representations in the human orbitofrontal cortex. Nature Neuroscience 4, 95–102.
O'Keefe, E.J., 1975. Porteus Maze Q score as a measure of impulsivity. Perceptual and Motor Skills 41, 675–678.
Obeso, I., Wilkinson, L., Casabona, E., Bringas, M.L., Alvarez, M., Alvarez, L., Pavon, N., Rodriguez-Oroz, M.C., Macias, R., Obeso, J.A., Jahanshahi, M., 2011. Deficits in inhibitory control and conflict resolution on cognitive and motor tasks in Parkinson's disease. Experimental Brain Research 212, 371–384.
Ohmura, Y., Takahashi, T., Kitamura, N., Wehr, P., 2006. Three-month stability of delay and probability discounting measures. Experimental and Clinical Psychopharmacology 14, 318–328.
Olmstead, M.C., 2006. Animal models of drug addiction: where do we go from here? Quarterly Journal of Experimental Psychology 59, 625–653.
Overtoom, C.C., Bekker, E.M., van der Molen, M.W., Verbaten, M.N., Kooij, J.J., Buitelaar, J.K., Kenemans, J.L., 2009. Methylphenidate restores link between stop-signal sensory impact and successful stopping in adults with attention-deficit/hyperactivity disorder. Biological Psychiatry 65, 614–619.
Overtoom, C.C., Kenemans, J.L., Verbaten, M.N., Kemner, C., van der Molen, M.W., van Engeland, H., Buitelaar, J.K., Koelega, H.S., 2002. Inhibition in children with attention-deficit/hyperactivity disorder: a psychophysiological study of the stop task. Biological Psychiatry 51, 668–676.
Overtoom, C.C., Verbaten, M.N., Kemner, C., Kenemans, J.L., van Engeland, H., Buitelaar, J.K., van der Molen, M.W., van der Gugten, J., Westenberg, H., Maes, R.A., Koelega, H.S., 2003. Effects of methylphenidate, desipramine, and L-dopa on attention and inhibition in children with Attention Deficit Hyperactivity Disorder. Behavioural Brain Research 145, 7–15.
Padoa-Schioppa, C., Cai, X., 2011. The orbitofrontal cortex and the computation of subjective value: consolidated concepts and new perspectives. Annals of the New York Academy of Sciences 1239, 130–137.
Paine, T.A., Slipp, L.E., Carlezon Jr., W.A., 2011. Schizophrenia-like attentional deficits following blockade of prefrontal cortex GABAA receptors. Neuropsychopharmacology 36, 1703–1713.
Paloyelis, Y., Stahl, D.R., Mehta, M., 2010. Are steeper discounting rates in attention-deficit/hyperactivity disorder specifically associated with hyperactivity-impulsivity symptoms or is this a statistical artifact? Biological Psychiatry 68, e15–e16.
Pandya, D.N., Van Hoesen, G.W., Mesulam, M.M., 1981. Efferent connections of the cingulate gyrus in the rhesus monkey. Experimental Brain Research 42, 319–330.
Parent, A., Hazrati, L.N., 1995. Functional anatomy of the basal ganglia II. The place of subthalamic nucleus and external pallidum in basal ganglia circuitry. Brain Research. Brain Research Reviews 20, 128–154.
Pashler, H., 1994. Dual-task interference in simple tasks: data and theory. Psychological Bulletin 116, 220–244.
Passetti, F., Chudasama, Y., Robbins, T.W., 2002. The frontal cortex of the rat and visual attentional performance: dissociable functions of distinct medial prefrontal subregions. Cerebral Cortex 12, 1254–1268.
Passingham, R.E., Toni, I., Rushworth, M.F., 2000. Specialisation within the prefrontal cortex: the ventral prefrontal cortex and associative learning. Experimental Brain Research 133, 103–113.
Pattij, T., Janssen, M.C., Schepers, I., Gonzalez-Cuevas, G., de Vries, T.J., Schoffelmeer, A.N., 2007. Effects of the cannabinoid CB1 receptor antagonist rimonabant on distinct measures of impulsive behavior in rats. Psychopharmacology 193, 85–96.
Pattij, T., Schetters, D., Janssen, M.C., Wiskerke, J., Schoffelmeer, A.N., 2009. Acute effects of morphine on distinct forms of impulsive behavior in rats. Psychopharmacology 205, 489–502.
Pattij, T., Vanderschuren, L.J., 2008. The neuropharmacology of impulsive behaviour. Trends in Pharmacological Sciences 29, 192–199.
Patton, J.H., Stanford, M.S., Barratt, E.S., 1995. Factor structure of the Barratt impulsiveness scale. Journal of Clinical Psychology 51, 768–774.
Paus, T., 2001. Primate anterior cingulate cortex: where motor control, drive and cognition interface. Nature Reviews. Neuroscience 2, 417–424.
Paus, T., Kalina, M., Patockova, L., Angerova, Y., Cerny, R., Mecir, P., Bauer, J., Krabec, P., 1991. Medial vs lateral frontal lobe lesions and differential impairment of central-gaze fixation maintenance in man. Brain 114 (Pt 5) 2051–2067.
Paus, T., Petrides, M., Evans, A.C., Meyer, E., 1993. Role of the human anterior cingulate cortex in the control of oculomotor, manual, and speech responses: a positron emission tomography study. Journal of Neurophysiology 70, 453–469.
Pavlov, I.P. (Ed.), 1927. Conditional Reflexes: An Investigation of the Physiological Activity of the Cerebral Cortex. Oxford University Press, London.
Pavlov, K.A., Chistiakov, D.A., Chekhonin, V.P., 2012. Genetic determinants of aggression and impulsivity in humans. Journal of Applied Genetics 53, 61–82.
Perry, J.L., Carroll, M.E., 2008. The role of impulsive behavior in drug abuse. Psychopharmacology 200, 1–26.
Perry, J.L., Larson, E.B., German, J.P., Madden, G.J., Carroll, M.E., 2005. Impulsivity (delay discounting) as a predictor of acquisition of IV cocaine self-administration in female rats. Psychopharmacology 178, 193–201.
Perry, J.L., Nelson, S.E., Carroll, M.E., 2008. Impulsive choice as a predictor of acquisition of IV cocaine self- administration and reinstatement of cocaine-seeking behavior in male and female rats. Experimental and Clinical Psychopharmacology 16, 165–177.
Peters, J., Buchel, C., 2011. The neural mechanisms of inter-temporal decision-making: understanding variability. Trends in Cognitive Sciences 15, 227–239.
Petit, L., Courtney, S.M., Ungerleider, L.G., Haxby, J.V., 1998. Sustained activity in the medial wall during working memory delays. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 18, 9429–9437.
Petrides, M., 2000. The role of the mid-dorsolateral prefrontal cortex in working memory. Experimental Brain Research 133, 44–54.
Petrides, M., Pandya, D.N., 2002. Comparative cytoarchitectonic analysis of the human and the macaque ventrolateral prefrontal cortex and corticocortical connection patterns in the monkey. The European Journal of Neuroscience 16, 291–310.
Petry, N.M., 2001a. Delay discounting of money and alcohol in actively using alcoholics, currently abstinent alcoholics, and controls. Psychopharmacology 154, 243–250.
Petry, N.M., 2001b. Pathological gamblers, with and without substance use disorders, discount delayed rewards at high rates. Journal of Abnormal Psychology 110, 482–487.
Pezze, M.A., Dalley, J.W., Robbins, T.W., 2009. Remediation of attentional dysfunction in rats with lesions of the medial prefrontal cortex by intra-accumbens administration of the dopamine D(2/3) receptor antagonist sulpiride. Psychopharmacology 202, 307–313.
Pfefferbaum, A., Ford, J.M., Weller, B.J., Kopell, B.S., 1985. ERPs to response production and inhibition. Electroencephalography and Clinical Neurophysiology 60, 423–434.
Picton, T.W., Stuss, D.T., Alexander, M.P., Shallice, T., Binns, M.A., Gillingham, S., 2007. Effects of focal frontal lesions on response inhibition. Cerebral Cortex 17, 826–838.
Pilkington, G.W., McKellar, P., 1960. Inhibition as a concept in psychology. British Journal of Psychology 51, 194.
Plichta, M.M., Vasic, N., Wolf, R.C., Lesch, K.P., Brummer, D., Jacob, C., Fallgatter, A.J., Gron, G., 2009. Neural hyporesponsiveness and hyperresponsiveness during immediate and delayed reward processing in adult attention-deficit/hyperactivity disorder. Biological Psychiatry 65, 7–14.
Poldrack, R.A., Wagner, A.D., Prull, M.W., Desmond, J.E., Glover, G.H., Gabrieli, J.D., 1999. Functional specialization for semantic and phonological processing in the left inferior prefrontal cortex. NeuroImage 10, 15–35.
Posner, M.I., Cohen, Y.P.C., 1984. Components of visual orienting. In: Bouma, H., Bouwhuis, D. (Eds.), Attention and Performance X. Lawrence Erlbaum, London, pp. 531–556.
Posner, M.I., Nissen, M.J., Klein, R.M., 1976. Visual dominance: an information-processing account of its origins and significance. Psychological Review 83, 157–171.
Posner, M.I., Petersen, S.E., Fox, P.T., Raichle, M.E., 1988. Localization of cognitive operations in the human brain. Science (New York, N.Y.) 240, 1627–1631.
Potter, A.S., Bucci, D.J., Newhouse, P.A., 2012. Manipulation of nicotinic acetylcholine receptors differentially affects behavioral inhibition in human subjects with and without disordered baseline impulsivity. Psychopharmacology 220, 331–340.
Potter, A.S., Newhouse, P.A., 2008. Acute nicotine improves cognitive deficits in young adults with attention-deficit/hyperactivity disorder. Pharmacology, Biochemistry, and Behavior 88, 407–417.
Preuss, T.M., 1995. Do rats have prefrontal cortex? The Rose-Woolsey-Akert program reconsidered. Journal of Cognitive Neuroscience 7, 1–24.
Pribram, K.H., 1961. Limbic system. In: Sheer, D.E. (Ed.), Electrical Stimulation of the Brain, an Interdisciplinary Survey of Behavioral Integrative Systems. University of Texas Press, Austin.
Pribram, K.H., Mishkin, M., Rosvold, H.E., Kaplan, S.J., 1952. Effects on delayed-response performance of lesions of dorsolateral and ventromedial frontal cortex of baboons. Journal of Comparative Physiology & Psychology 45, 565–575.
Quay, H.C., 1988. Theories of ADDH. Journal of the American Academy of Child and Adolescent Psychiatry 27, 262–263.
Rabbitt, P., 1997. Introduction: methodologies and models in the study of executive function. In: Rabbitt, P. (Ed.), Methodology of Frontal and Executive Function. Psychology Press, Hove, UK, pp. 1–38.
Rabbitt, P.M.A., 1978. Detection of errors by skilled typists. Ergonomics 21, 945–958.
Rachlin, H., 2000. The Science of Self-Control. Harvard University Press, Cambridge, MA.
Rachlin, H., Green, L., 1972. Commitment, choice and self-control. Journal of the Experimental Analysis of Behavior 17, 15–22.
Rafal, R., Henik, A., 1994. The neurology of inhibition: integrating controlled and automatica processes. In: Dagenbach, D., Carr, T.H. (Eds.), Inhibitory Processes in Attention, Memory and Language. Academic Press, Inc., San Diego, CA, pp. 1–44.
Rajkowski, J., Majczynski, H., Clayton, E., Aston-Jones, G., 2004. Activation of monkey locus coeruleus neurons varies with difficulty and performance in a target detection task. Journal of Neurophysiology 92, 361–371.
Ramaekers, J.G., Kauert, G., Theunissen, E.L., Toennes, S.W., Moeller, M.R., 2009. Neurocognitive performance during acute THC intoxication in heavy and occasional cannabis users. Journal of Psychopharmacology 23, 266–277.
Ramaekers, J.G., Kauert, G., van Ruitenbeek, P., Theunissen, E.L., Schneider, E., Moeller, M.R., 2006. High-potency marijuana impairs executive function and inhibitory motor control. Neuropsychopharmacology 31, 2296–2303.
Ramaekers, J.G., Kuypers, K.P., 2006. Acute effects of 3,4-methylenedioxymethamphetamine (MDMA) on behavioral measures of impulsivity: alone and in combination with alcohol. Neuropsychopharmacology 31, 1048–1055.
Ramautar, J.R., Kok, A., Ridderinkhof, K.R., 2004. Effects of stop-signal probability in the stop-signal paradigm: the N2/P3 complex further validated. Brain and Cognition 56, 234–252.
Ramautar, J.R., Kok, A., Ridderinkhof, K.R., 2006a. Effects of stop-signal modality on the N2/P3 complex elicited in the stop-signal paradigm. Biological Psychology 72, 96–109.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Ramautar, J.R., Slagter, H.A., Kok, A., Ridderinkhof, K.R., 2006b. Probability effects in the stop-signal paradigm: the insula and the significance of failed inhibition. Brain Research 1105, 143–154.

Ray, N.J., Brittain, J.S., Holland, P., Joundi, R.A., Stein, J.F., Aziz, T.Z., Jenkinson, N., 2012. The role of the subthalamic nucleus in response inhibition: evidence from local field potential recordings in the human subthalamic nucleus. NeuroImage 60, 271–278.

Reid, R.L., 1960. Inhibition – Pavlov, Hull, Eysenck. British Journal of Psychology 51, 226–236.

Remijnse, P.L., Nielen, M.M., van Balkom, A.J., Cath, D.C., van Oppen, P., Uylings, H.B., Veltman, D.J., 2006. Reduced orbitofrontal-striatal activity on a reversal learning task in obsessive-compulsive disorder. Archives of General Psychiatry 63, 1225–1236.

Q27 Rescorla, R.A., 1969. Pavlovian conditioned inhibition. Psychological Bulletin 72 .

Revelle, W., 1997. Extraversion and impulsivity. In: Nyborg, H. (Ed.), The Scientific Study of Human Nature: Tribute to Hans J Eysenck at Eighty. Elsevier Science Press, London.

Reynolds, B., 2006. A review of delay-discounting research with humans: relations to drug use and gambling. Behavioural Pharmacology 17, 651–667.

Reynolds, B., Ortengren, A., Richards, J.B., De Wit, H., 2006. Dimensions of impulsive behavior: personality and behavioral measures. Personality and Individual Differences 40, 305–315.

Reynolds, B., Richards, J.B., Dassinger, M., de Wit, H., 2004. Therapeutic doses of diazepam do not alter impulsive behavior in humans. Pharmacology, Biochemistry, and Behavior 79, 17–24.

Reynolds, B., Schiffbauer, R., 2004. Measuring state changes in human delay discounting: an experiential discounting task. Behavioural Processes 67, 343–356.

Riba, J., Rodriguez-Fornells, A., Morte, A., Munte, T.F., Barbanoj, M.J., 2005. Noradrenergic stimulation enhances human action monitoring. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 25, 4370–4374.

Richards, J.B., Mitchell, S.H., de Wit, H., Seiden, L.S., 1997. Determination of discount functions in rats with an adjusting-amount procedure. Journal of the Experimental Analysis of Behavior 67, 353–366.

Ridderinkhof, K.R., Ullsperger, M., Crone, E.A., Nieuwenhuis, S., 2004. The role of the medial frontal cortex in cognitive control. Science (New York, N.Y.) 306, 443–447.

Rizzo, V., Siebner, H.R., Modugno, N., Pesenti, A., Munchau, A., Gerschlager, W., Webb, R.M., Rothwell, J.C., 2004. Shaping the excitability of human motor cortex with premotor rTMS. The Journal of Physiology 554, 483–495.

Robbins, T.W., 1996. Dissociating executive functions of the prefrontal cortex. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences 351, 1463–1470, discussion 1470-1461.

Robbins, T.W., 1998. Homology in behavioural pharmacology: an approach to animal models of human cognition. Behavioural Pharmacology 9, 509–519.

Robbins, T.W., 2002. The 5-choice serial reaction time task: behavioural pharmacology and functional neurochemistry. Psychopharmacology 163, 362–380.

Robbins, T.W., 2007. Shifting and stopping: fronto-striatal substrates, neurochemical modulation and clinical implications. Philosophical Transactions of the Royal Society of London 362, 917–932.

Robbins, T.W., Arnsten, A.F., 2009. The neuropsychopharmacology of fronto-executive function: monoaminergic modulation. Annual Review of Neuroscience 32, 267–287.

Robbins, T.W., Everitt, B.J., 1982. Functional studies of the central catecholamines. International Review of Neurobiology 23, 303–365.

Robbins, T.W., Gillan, C.M., Smith, D.G., de Wit, S., Ersche, K.D., 2012. Neurocognitive endophenotypes of impulsivity and compulsivity: towards dimensional psychiatry. Trends in Cognitive Sciences 16, 81–91.

Robinson, E.S., Eagle, D.M., Economidou, D., Theobald, D.E., Mar, A.C., Murphy, E.R., Robbins, T.W., Dalley, J.W., 2009. Behavioural characterisation of high impulsivity on the 5-choice serial reaction time task: specific deficits in 'waiting' versus 'stopping'. Behavioural Brain Research 196, 310–316.

Robinson, E.S., Eagle, D.M., Mar, A.C., Bari, A., Banerjee, G., Jiang, X., Dalley, J.W., Robbins, T.W., 2008. Similar effects of the selective noradrenaline reuptake inhibitor atomoxetine on three distinct forms of impulsivity in the rat. Neuropsychopharmacology 33, 1028–1037.

Roesch, M.R., Olson, C.R., 2005. Neuronal activity in primate orbitofrontal cortex reflects the value of time. Journal of Neurophysiology 94, 2457–2471.

Rogers, R.D., Moeller, F.G., Swann, A.C., Clark, L., 2010. Recent research on impulsivity in individuals with drug use and mental health disorders: implications for alcoholism. Alcoholism, Clinical and Experimental Research 34, 1319–1333.

Roiser, J.P., Cannon, D.M., Gandhi, S.K., Taylor Tavares, J., Erickson, K., Wood, S., Klaver, J.M., Clark, L., Zarate Jr., C.A., Sahakian, B.J., Drevets, W.C., 2009. Hot and cold cognition in unmedicated depressed subjects with bipolar disorder. Bipolar Disorders 11, 178–189.

Rolls, E.T., Hornak, J., Wade, D., McGrath, J., 1994. Emotion-related learning in patients with social and emotional changes associated with frontal lobe damage. Journal of Neurology, Neurosurgery, and Psychiatry 57, 1518–1524.

Romer, D., Betancourt, L., Giannetta, J.M., Brodsky, N.L., Farah, M., Hurt, H., 2009. Executive cognitive functions and impulsivity as correlates of risk taking and problem behavior in preadolescents. Neuropsychologia 47, 2916–2926.

Rosvold, H.E., Mishkin, M., 1961. Non-sensory effects of frontal lesions on discrimination learning and performance. In: Delafresnaye, J.F. (Ed.), Brain Mechanisms and Learning. Blackwell Scientific Publications, Ltd, Oxford, pp. 555–576.

Rowe, J.B., Hughes, L., Nimmo-Smith, I., 2010. Action selection: a race model for selected and non-selected actions distinguishes the contribution of premotor and prefrontal areas. NeuroImage 51, 888–896.

Rubia, K., Halari, R., Christakou, A., Taylor, E., 2009. Impulsiveness as a timing disturbance: neurocognitive abnormalities in attention-deficit hyperactivity disorder during temporal processes and normalization with methylphenidate. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences 364, 1919–1931.

Rubia, K., Halari, R., Cubillo, A., Mohammad, A.M., Scott, S., Brammer, M., 2010. Disorder-specific inferior prefrontal hypofunction in boys with pure attention- Q28 deficit/hyperactivity disorder compared to boys with pure conduct disorder during cognitive flexibility. Human Brain Mapping.

Rubia, K., Lee, F., Cleare, A.J., Tunstall, N., Fu, C.H., Brammer, M., McGuire, P., 2005. Tryptophan depletion reduces right inferior prefrontal activation during response inhibition in fast, event-related fMRI. Psychopharmacology 179, 791–803.

Rubia, K., Russell, T., Overmeyer, S., Brammer, M.J., Bullmore, E.T., Sharma, T., Simmons, A., Williams, S.C., Giampietro, V., Andrew, C.M., Taylor, E., 2001. Mapping motor inhibition: conjunctive brain activations across different versions of go/no-go and stop tasks. NeuroImage 13, 250–261.

Rubia, K., Smith, A.B., Brammer, M.J., Taylor, E., 2003. Right inferior prefrontal cortex mediates response inhibition while mesial prefrontal cortex is responsible for error detection. NeuroImage 20, 351–358.

Rubio, G., Jimenez, M., Rodriguez-Jimenez, R., Martinez, I., Avila, C., Ferre, F., Jimenez-Arriero, M.A., Ponce, G., Palomo, T., 2008. The role of behavioral impulsivity in the development of alcohol dependence: a 4-year follow-up study. Alcoholism, Clinical and Experimental Research 32, 1681–1687.

Rudebeck, P.H., Behrens, T.E., Kennerley, S.W., Baxter, M.G., Buckley, M.J., Walton, M.E., Rushworth, M.F., 2008. Frontal cortex subregions play distinct roles in choices between actions and stimuli. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 28, 13775–13785.

Rudebeck, P.H., Murray, E.A., 2008. Amygdala and orbitofrontal cortex lesions differentially influence choices during object reversal learning. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 28, 8338–8343.

Rudebeck, P.H., Murray, E.A., 2011. Balkanizing the primate orbitofrontal cortex: distinct subregions for comparing and contrasting values. Annals of the New York Academy of Sciences 1239, 1–13.

Rushworth, M.F., Walton, M.E., Kennerley, S.W., Bannerman, D.M., 2004. Action sets and decisions in the medial frontal cortex. Trends in Cognitive Sciences 8, 410–417.

Sagvolden, T., Johansen, E.B., Aase, H., Russell, V.A., 2005. A dynamic developmental theory of attention-deficit/hyperactivity disorder (ADHD) predominantly hyperactive/impulsive and combined subtypes. The Behavioral and Brain Sciences 28, 397–419, discussion 419-368.

Salamone, J.D., Correa, M., Nunes, E.J., Randall, P.A., Pardo, M., 2012. The behavioral pharmacology of effort-related choice behavior: dopamine, adenosine and beyond. Journal of the Experimental Analysis of Behavior 97, 125–146.

Sanders, A.F., 1998. Elements of Human Performance: Reaction Processes and Attention in Human Skill. Lawrence Erlbaum, Mahwah, NJ.

Sara, S.J., 2009. The locus coeruleus and noradrenergic modulation of cognition. Nature Reviews. Neuroscience 10, 211–223.

Sara, S.J., Bouret, S., 2012. Orienting and reorienting: the locus coeruleus mediates cognition through arousal. Neuron 76, 130–141.

Sarter, M., Paolone, G., 2011. Deficits in attentional control: cholinergic mechanisms and circuitry-based treatment approaches. Behavioral Neuroscience 125, 825–835.

Sasaki, K., Gemba, H., Nambu, A., Matsuzaki, R., 1993. No-go activity in the frontal association cortex of human subjects. Neuroscience Research 18, 249–252.

Sasaki, K., Gemba, H., Tsujimoto, T., 1989. Suppression of visually initiated hand movement by stimulation of the prefrontal cortex in the monkey. Brain Research 495, 100–107.

Schachar, R., Logan, G.D., 1990. Impulsivity and inhibitory control in normal development and childhood psychopathology. Developmental Psychology 26, 710–720.

Schachar, R., Logan, G.D., Robaey, P., Chen, S., Ickowicz, A., Barr, C., 2007. Restraint and cancellation: multiple inhibition deficits in attention deficit hyperactivity disorder. Journal of Abnormal Child Psychology 35, 229–238.

Schachar, R., Tannock, R., Marriott, M., Logan, G., 1995. Deficient inhibitory control in attention deficit hyperactivity disorder. Journal of Abnormal Child Psychology 23, 411–437.

Schall, J.D., Boucher, L., 2007. Executive control of gaze by the frontal lobes. Cognitive, Affective, & Behavioral Neuroscience 7, 396–412.

Schall, J.D., Thompson, K.G., 1999. Neural selection and control of visually guided eye movements. Annual Review of Neuroscience 22, 241–259.

Schoenbaum, G., Saddoris, M.P., Ramus, S.J., Shaham, Y., Setlow, B., 2004. Cocaine-experienced rats exhibit learning deficits in a task sensitive to orbitofrontal cortex lesions. The European Journal of Neuroscience 19, 1997–2002.

Schoenbaum, G., Takahashi, Y., Liu, T.L., McDannald, M.A., 2011. Does the orbitofrontal cortex signal value? Annals of the New York Academy of Sciences 1239, 87–99.

Schweighofer, N., Bertin, M., Shishida, K., Okamoto, Y., Tanaka, S.C., Yamawaki, S., Doya, K., 2008. Low-serotonin levels increase delayed reward discounting in humans. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 28, 4528–4532.

Scoriels, L., Jones, P.B., Sahakian, B.J., 2013. Modafinil effects on cognition and emotion in schizophrenia and its neurochemical modulation in the brain. Neuropharmacology 64, 168–184.

Sechenov, I., 1863. Etudes physiologiques sur les centres modérateurs des mouvements reflexes dans le cerveau de la grénouille. Annales des sciences naturelles (Ser. 4) 19, 109–134 [as cited in MacLeod et al., 2003].

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

Setlow, B., Mendez, I.A., Mitchell, M.R., Simon, N.W., 2009. Effects of chronic administration of drugs of abuse on impulsive choice (delay discounting) in animal models. Behavioural Pharmacology 20, 380–389.
Seu, E., Lang, A., Rivera, R.J., Jentsch, J.D., 2009. Inhibition of the norepinephrine transporter improves behavioral flexibility in rats and monkeys. Psychopharmacology 202, 505–519.
Sharp, D.J., Bonnelle, V., De Boissezon, X., Beckmann, C.F., James, S.G., Patel, M.C., Mehta, M.A., 2013. Distinct frontal systems for response inhibition, attentional capture, and error processing. Proceedings of the National Academy of Sciences of the United States of America 107, 6106–6111, in press.
Sharp, D.J., Bonnelle, V., De Boissezon, X., Beckmann, C.F., James, S.G., Patel, M.C., Mehta, M.A., 2010. Distinct frontal systems for response inhibition, attentional capture, and error processing. Proceedings of the National Academy of Sciences of the United States of America 107, 6106–6111.
Sherrington, C.S., 1906. The Integrative Action of the Nervous System. Yale University Press, Cambridge.
Simmonds, D.J., Pekar, J.J., Mostofsky, S.H., 2008. Meta-analysis of Go/No-go tasks demonstrating that fMRI activation associated with response inhibition is task-dependent. Neuropsychologia 46, 224–232.
Skaggs, E.B., 1929. The major descriptive categories of inhibition in psychology. Journal of Abnormal and Social Psychology 24, 310–317.
Skinner, B.F., 1953. Science and Human Behavior. Macmillan, New York.
Skinner, J.E., Yingling, C.D. (Eds.), 1977. Central Gating Mechanisms that Regulate Event-related Potentials and Behavior. Karger, Basel.
Slaats-Willemse, D., Swaab-Barneveld, H., de Sonneville, L., van der Meulen, E., Buitelaar, J., 2003. Deficient response inhibition as a cognitive endophenotype of ADHD. Journal of the American Academy of Child and Adolescent Psychiatry 42, 1242–1248.
Slemmer, J.E., Martin, B.R., Damaj, M.I., 2000. Bupropion is a nicotinic antagonist. Journal of Pharmacology and Experimental Therapeutics 295, 321–327.
Smith, J.L., Jamadar, S., Provost, A.L., Michie, P.T., 2012. Motor and non-motor inhibition in the Go/NoGo task: an ERP and fMRI study. International Journal of Psychophysiology: Official Journal of the International Organization of Psychophysiology.
Smith, R., 1992. Inhibition: History and Meaning in the Sciences of Mind and Brain. University of California Press, Berkeley, CA.
Solanto, M.V., 1998. Neuropsychopharmacological mechanisms of stimulant drug action in attention-deficit hyperactivity disorder: a review and integration. Behavioural Brain Research 94, 127–152.
Solanto, M.V., Abikoff, H., Sonuga-Barke, E., Schachar, R., Logan, G.D., Wigal, T., Hechtman, L., Hinshaw, S., Turkel, E., 2001. The ecological validity of delay aversion and response inhibition as measures of impulsivity in AD/HD: a supplement to the NIMH multimodal treatment study of AD/HD. Journal of Abnormal Child Psychology 29, 215–228.
Sonuga-Barke, E.J., 2002. Psychological heterogeneity in AD/HD – a dual pathway model of behaviour and cognition. Behavioural Brain Research 130, 29–36.
Soubrié, P., 1986. Reconciling the role of central serotonin neurons in human and animal behavior. The Behavioral and Brain Sciences 9, 319–335.
Sowell, E.R., Thompson, P.M., Welcome, S.E., Henkenius, A.L., Toga, A.W., Peterson, B.S., 2003. Cortical abnormalities in children and adolescents with attention-deficit hyperactivity disorder. Lancet 362, 1699–1707.
Spencer, T., Biederman, J., Wilens, T., Faraone, S., Prince, J., Gerard, K., Doyle, R., Parekh, A., Kagan, J., Bearman, S.K., 2001. Efficacy of a mixed amphetamine salts compound in adults with attention-deficit/hyperactivity disorder. Archives of General Psychiatry 58, 775–782.
Stanford, M.S., Barratt, E.S., 1996. Verbal skills, finger tapping, and cognitive tempo define a second-order factor of temporal information processing. Brain and Cognition 31, 35–45.
Stanley, W.C., Jaynes, J., 1949. The function of the frontal cortex. Psychological Review 56, 18–32.
Steffens, D.C., Wagner, H.R., Levy, R.M., Horn, K.A., Krishnan, K.R., 2001. Performance feedback deficit in geriatric depression. Biological Psychiatry 50, 358–363.
Still, G.F., 1902. Some abnormal physical conditions in children. Lancet 1 .
Strack, F., Deutsch, R., 2004. Reflective and impulsive determinants of social behavior. Personality and Social Psychology Review: An Official Journal of the Society for Personality and Social Psychology, Inc. 8, 220–247.
Stroop, J.R., 1935. Studies of interference in serial verbal reactions. Journal of Experimental Psychology 18, 643–662.
Strotz, R.H., 1956. Myopia and inconsistency in dynamic utility maximisation. Review of Economic Studies 23, 165–180.
Stuphorn, V., Schall, J.D., 2006. Executive control of countermanding saccades by the supplementary eye field. Nature Neuroscience 9, 925–931.
Stuphorn, V., Taylor, T.L., Schall, J.D., 2000. Performance monitoring by the supplementary eye field. Nature 408, 857–860.
Stuss, D.T., 1992. Biological and psychological development of executive functions. Brain and Cognition 20, 8–23.
Stuss, D.T., Binns, M.A., Murphy, K.J., Alexander, M.P., 2002. Dissociations within the anterior attentional system: effects of task complexity and irrelevant information on reaction time speed and accuracy. Neuropsychology 16, 500–513.
Sullivan, R.M., Gratton, A., 2002. Behavioral effects of excitotoxic lesions of ventral medial prefrontal cortex in the rat are hemisphere-dependent. Brain Research 927, 69–79.
Swainson, R., Rogers, R.D., Sahakian, B.J., Summers, B.A., Polkey, C.E., Robbins, T.W., 2000. Probabilistic learning and reversal deficits in patients with Parkinson's disease or frontal or temporal lobe lesions: possible adverse effects of dopaminergic medication. Neuropsychologia 38, 596–612.
Swann, A.C., Bjork, J.M., Moeller, F.G., Dougherty, D.M., 2002. Two models of impulsivity: relationship to personality traits and psychopathology. Biological Psychiatry 51, 988–994.
Swick, D., Ashley, V., Turken, A.U., 2008. Left inferior frontal gyrus is critical for response inhibition. BMC Neuroscience 9, 102.
Swick, D., Ashley, V., Turken, U., 2011. Are the neural correlates of stopping and not going identical? Quantitative meta-analysis of two response inhibition tasks. NeuroImage 56, 1655–1665.
Tabibnia, G., Monterosso, J.R., Baicy, K., Aron, A.R., Poldrack, R.A., Chakrapani, S., Lee, B., London, E.D., 2011. Different forms of self-control share a neurocognitive substrate. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience 31, 4805–4810.
Tanaka, S.C., Doya, K., Okada, G., Ueda, K., Okamoto, Y., Yamawaki, S., 2004. Prediction of immediate and future rewards differentially recruits cortico-basal ganglia loops. Nature Neuroscience 7, 887–893.
Teasdale, J.D., Lloyd, C.A., Hutton, J.M., 1998. Depressive thinking and dysfunctional schematic mental models. The British Journal of Clinical Psychology 37 (Pt 3) 247–257.
Temel, Y., Blokland, A., Steinbusch, H.W., Visser-Vandewalle, V., 2005. The functional role of the subthalamic nucleus in cognitive and limbic circuits. Progress in Neurobiology 76, 393–413.
Theunissen, E.L., van Kroonenburgh, M.J., van Deursen, J.A., Blom-Coenjaerts, C., Ramaekers, J.G., 2006. Stimulating effects of the antihistamine fexofenadine: testing the dopamine transporter hypothesis. Psychopharmacology 187, 95–102.
Thompson-Schill, S.L., D'Esposito, M., Aguirre, G.K., Farah, M.J., 1997. Role of left inferior prefrontal cortex in retrieval of semantic knowledge: a reevaluation. Proceedings of the National Academy of Sciences of the United States of America 94, 14792–14797.
Thompson-Schill, S.L., Jonides, J., Marshuetz, C., Smith, E.E., D'Esposito, M., Kan, I.P., Knight, R.T., Swick, D., 2002. Effects of frontal lobe damage on interference effects in working memory. Cognitive, Affective, & Behavioral Neuroscience 2, 109–120.
Thurstone, L.L., 1924. The Nature of Intelligence. Routledge, London.
Tieges, Z., Snel, J., Kok, A., Richard Ridderinkhof, K., 2009. Caffeine does not modulate inhibitory control. Brain and Cognition 69, 316–327.
Tipper, S.P., 1985. The negative priming effect: inhibitory priming by ignored objects. Quaterly Journal of Experimental Psychology. A 37, 571–590.
Tipper, S.P., 1992. Selection for action: the role of inhibitory mechanisms. Current Directions in Psychological Science 1 .
Tipper, S.P., 2001. Does negative priming reflect inhibitory mechanisms? A review and integration of conflicting views. Quaterly Journal of Experimental Psychology. A 54, 321–343.
Tipper, S.P., Cranston, M., 1985. Selective attention and priming: inhibitory and facilitatory effects of ignored primes. Quaterly Journal of Experimental Psychology. A 37, 591–611.
Torregrossa, M.M., Xie, M., Taylor, J.R., 2012. Chronic corticosterone exposure during adolescence reduces impulsive action but increases impulsive choice and sensitivity to yohimbine in male Sprague-Dawley rats. Neuropsychopharmacology 37, 1656–1670.
Tower, S.S., 1936. Extrapyramidal action from cat's cerebral cortex: motor and inhibitory. Brain 59, 408–444.
Tremblay, R.E., Pihl, R.O., Vitaro, F., Dobkin, P.L., 1994. Predicting early onset of male antisocial behavior from preschool behavior. Archives of General Psychiatry 51, 732–739.
Trommer, B.L., Hoeppner, J.A., Lorber, R., Armstrong, K.J., 1988. The go-no-go paradigm in attention deficit disorder. Annals of Neurology 24, 610–614.
Turner, D.C., Clark, L., Dowson, J., Robbins, T.W., Sahakian, B.J., 2004a. Modafinil improves cognition and response inhibition in adult attention-deficit/hyperactivity disorder. Biological Psychiatry 55, 1031–1040.
Turner, D.C., Clark, L., Pomarol-Clotet, E., McKenna, P., Robbins, T.W., Sahakian, B.J., 2004b. Modafinil improves cognition and attentional set shifting in patients with chronic schizophrenia. Neuropsychopharmacology 29, 1363–1373.
Turner, D.C., Robbins, T.W., Clark, L., Aron, A.R., Dowson, J., Sahakian, B.J., 2003. Cognitive enhancing effects of modafinil in healthy volunteers. Psychopharmacology 165, 260–269.
Urcelay, G.P., Dalley, J.W., 2012. Linking ADHD, impulsivity, and drug abuse: a neuropsychological perspective. Current Topics in Behavioral Neuroscience 9, 173–197.
Ursin, H., 1976. Inhibition and the septal nuclei: breakdown of the single concept model. Acta Neurobiologiae Experimentalis 36, 91–115.
Ursin, H., 2005. Press stop to start: the role of inhibition for choice and health. Psychoneuroendocrinology 30, 1059–1065.
Uslaner, J.M., Robinson, T.E., 2006. Subthalamic nucleus lesions increase impulsive action and decrease impulsive choice – mediation by enhanced incentive motivation? The European Journal of Neuroscience 24, 2345–2354.
Uylings, H.B., Groenewegen, H.J., Kolb, B., 2003. Do rats have a prefrontal cortex? Behavioural Brain Research 146, 3–17.
van Boxtel, G.J., van der Molen, M.W., Jennings, J.R., Brunia, C.H., 2001. A psychophysiological analysis of inhibitory motor control in the stop-signal paradigm. Biological Psychology 58, 229–262.
van den Wildenberg, W.P., van Boxtel, G.J., van der Molen, M.W., Bosch, D.A., Speelman, J.D., Brunia, C.H., 2006. Stimulation of the subthalamic region facilitates the selection and inhibition of motor responses in Parkinson's disease. Journal of Cognitive Neuroscience 18, 626–636.
van den Wildenberg, W.P., van der Molen, M.W., 2004. Additive factors analysis of inhibitory processing in the stop-signal paradigm. Brain and Cognition 56, 253–266.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005

van der Schoot, M., Licht, R., Horsley, T.M., Sergeant, J.A., 2005. Effects of stop signal modality, stop signal intensity and tracking method on inhibitory performance as determined by use of the stop signal paradigm. Scandinavian Journal of Psychology 46, 331–341.
Van der Werff, J.J., Verster, J., 1987. Heymans' temperamental dimensions recomputed. Personality and Individual Differences 8 (2) 271–276.
van Gaalen, M.M., Brueggeman, R.J., Bronius, P.F., Schoffelmeer, A.N., Vanderschuren, L.J., 2006a. Behavioral disinhibition requires dopamine receptor activation. Psychopharmacology 187, 73–85.
van Gaalen, M.M., van Koten, R., Schoffelmeer, A.N., Vanderschuren, L.J., 2006b. Critical involvement of dopaminergic neurotransmission in impulsive decision making. Biological Psychiatry 60, 66–73.
Verbruggen, F., Aron, A.R., Stevens, M.A., Chambers, C.D., 2010. Theta burst stimulation dissociates attention and action updating in human inferior frontal cortex. Proceedings of the National Academy of Sciences of the United States of America 107, 13966–13971.
Verbruggen, F., Logan, G.D., 2008. Response inhibition in the stop-signal paradigm. Trends in Cognitive Sciences 12, 418–424.
Verbruggen, F., Logan, G.D., 2009. Models of response inhibition in the stop-signal and stop-change paradigms. Neuroscience and Biobehavioral Reviews 33, 647–661.
Verbruggen, F., Schneider, D.W., Logan, G.D., 2008. How to stop and change a response: the role of goal activation in multitasking. Journal of Experimental Psychology 34, 1212–1228.
Verdejo-Garcia, A., Lawrence, A.J., Clark, L., 2008. Impulsivity as a vulnerability marker for substance-use disorders: review of findings from high-risk research, problem gamblers and genetic association studies. Neuroscience and Biobehavioral Reviews 32, 777–810.
Verfaellie, M., Heilman, K.M., 1987. Response preparation and response inhibition after lesions of the medial frontal lobe. Archives of Neurology 44, 1265–1271.
Q33 Vince, M.A., 1948. The intermittency of control movements and the psychological refractory period. Br J Psychol Gen Sect 38, 149–157.
Vince, M.A., Welford, A.T., 1967. Time taken to change the speed of a response. Nature 213, 532–533.
Vink, M., Kahn, R.S., Raemaekers, M., van den Heuvel, M., Boersma, M., Ramsey, N.F., 2005. Function of striatum beyond inhibition and execution of motor responses. Human Brain Mapping 25, 336–344.
Vink, M., Ramsey, N.F., Raemaekers, M., Kahn, R.S., 2006. Striatal dysfunction in schizophrenia and unaffected relatives. Biological Psychiatry 60, 32–39.
Vogt, B.A., Finch, D.M., Olson, C.R., 1992. Functional heterogeneity in cingulate cortex: the anterior executive and posterior evaluative regions. Cerebral Cortex 2, 435–443.
Vogt, B.A., Pandya, D.N., 1987. Cingulate cortex of the rhesus monkey: II Cortical afferents. The Journal of Comparative Neurology 262, 271–289.
Volkmann, A.W., 1838a. Uber reflexbewegungen. Archives of Anatomy Physiology 15, 15–43.
Volkmann, A.W., 1838b. Von dem Baue and den Verrichtungen der Kopfnerven des Frosches. Archives of Anatomy Physiology 5, 70–89.
Q34 Volkmann, A.W., 1842. Ueber die Beweiskraft derjenigen Experimente, durch welche man einen direkten Einfluss der Centralorgane auf die Eingeweide zu erweisen suchte. Archives of Anatomy Physiology 372–377.
Volkow, N.D., Fowler, J.S., Wang, G.J., 2002. Role of dopamine in drug reinforcement and addiction in humans: results from imaging studies. Behavioural Pharmacology 13, 355–366.
Volkow, N.D., Fowler, J.S., Wang, G.J., Swanson, J.M., 2004. Dopamine in drug abuse and addiction: results from imaging studies and treatment implications. Molecular Psychiatry 9, 557–569.
Volkow, N.D., Fowler, J.S., Wang, G.J., Swanson, J.M., Telang, F., 2007. Dopamine in drug abuse and addiction: results of imaging studies and treatment implications. Archives of Neurology 64, 1575–1579.
Volkow, N.D., Wang, G.J., Fowler, J.S., Logan, J., Gatley, S.J., Gifford, A., Hitzemann, R., Ding, Y.S., Pappas, N., 1999a. Prediction of reinforcing responses to psychostimulants in humans by brain dopamine D2 receptor levels. The American Journal of Psychiatry 156, 1440–1443.
Volkow, N.D., Wang, G.J., Fowler, J.S., Logan, J., Gatley, S.J., Wong, C., Hitzemann, R., Pappas, N.R., 1999b. Reinforcing effects of psychostimulants in humans are associated with increases in brain dopamine and occupancy of D(2) receptors. Journal of Pharmacology and Experimental Therapeutics 291, 409–415.
Volkow, N.D., Wang, G.J., Kollins, S.H., Wigal, T.L., Newcorn, J.H., Telang, F., Fowler, J.S., Zhu, W., Logan, J., Ma, Y., Pradhan, K., Wong, C., Swanson, J.M., 2009. Evaluating dopamine reward pathway in ADHD: clinical implications. JAMA: the Journal of the American Medical Association 302, 1084–1091.
Vossel, S., Weidner, R., Thiel, C.M., Fink, G.R., 2009. What is odd in Posner's location-cueing paradigm? Neural responses to unexpected location and feature changes compared. Journal of Cognitive Neuroscience 21, 30–41.
Wager, T.D., Sylvester, C.Y., Lacey, S.C., Nee, D.E., Franklin, M., Jonides, J., 2005. Common and unique components of response inhibition revealed by fMRI. NeuroImage 27, 323–340.
Wallis, J.D., 2007. Orbitofrontal cortex and its contribution to decision-making. Annual Review of Neuroscience 30, 31–56.
Wallis, J.D., 2012. Cross-species studies of orbitofrontal cortex and value-based decision-making. Nature Neuroscience 15, 13–19.
Walton, M.E., Devlin, J.T., Rushworth, M.F., 2004. Interactions between decision making and performance monitoring within prefrontal cortex. Nature Neuroscience 7, 1259–1265.
Wang, Y., Tian, S., Wang, H., Cui, L., Zhang, Y., 2002. Event-related potentials in a No-go task involving response-tendency conflict. Clinical Electroencephalography 33, 82–85.
Watanabe, J., Sugiura, M., Sato, K., Sato, Y., Maeda, Y., Matsue, Y., Fukuda, H., Kawashima, R., 2002. The human prefrontal and parietal association cortices are involved in NO-GO performances: an event-related fMRI study. NeuroImage 17, 1207–1216.
Weber, E.F.W., Weber, E.H.W., 1845. Experimenta, quibus probatur nervos vagos Q35 rotatione machinae galvanomagneticae irritatos, mortum cordis retardare et adeo intercipere. Ann. Univ. Med. 20, 227–233.
Weber, E.F.W., Weber, E.H.W. (Eds.), 1966. Experiments in Which It is Proven that When Stimulated with a Rotary Electro-Magnetic Apparatus the Vagus Nerves Slow Down and, to a Considerable Extent, Interrupt the Heart Beat. Thomas, Springfield, IL, [Original work published 1845].
Weiskrantz, L., Mihailovic, L., Gross, C.G., 1960. Stimulation of frontal cortex and delayed alternation performance in the monkey. Science (New York, N.Y.) 131, 1443–1444.
Welford, A.T., 1967. Single-channel operation in the brain. Acta Psychologica 27, 5–22.
Weller, R.E., Cook 3rd, E.W., Avsar, K.B., Cox, J.E., 2008. Obese women show greater delay discounting than healthy-weight women. Appetite 51, 563–569.
Wendelken, C., Ditterich, J., Bunge, S.A., Carter, C.S., 2009. Stimulus and response conflict processing during perceptual decision making. Cognitive, Affective, & Behavioral Neuroscience 9, 434–447.
Whelan, R., Conrod, P.J., Poline, J.B., Lourdusamy, A., Banaschewski, T., Barker, G.J., Bellgrove, M.A., Buchel, C., Byrne, M., Cummins, T.D., Fauth-Buhler, M., Flor, H., Gallinat, J., Heinz, A., Ittermann, B., Mann, K., Martinot, J.L., Lalor, E.C., Lathrop, M., Loth, E., Nees, F., Paus, T., Rietschel, M., Smolka, M.N., Spanagel, R., Stephens, D.N., Struve, M., Thyreau, B., Vollstaedt-Klein, S., Robbins, T.W., Schumann, G., Garavan, H., 2012. Adolescent impulsivity phenotypes characterized by distinct brain networks. Nature Neuroscience 15, 920–925.
White, J.L., Moffitt, T.E., Caspi, A., Bartusch, D.J., Needles, D.J., Stouthamer-Loeber, M., 1994. Measuring impulsivity and examining its relationship to delinquency. Journal of Abnormal Psychology 103, 192–205.
Wickens, C.D., Kessel, C., 1980. Processing resource demands of failure detection in dynamic systems. Journal of Experimental Psychology. Human Perception and Performance 6, 564–577.
Wilhelm, C.J., Mitchell, S.H., 2009. Strain differences in delay discounting using inbred rats. Genes, Brain, and Behavior 8, 426–434.
Williams, J., Taylor, E., 2006. The evolution of hyperactivity, impulsivity and cognitive diversity. Journal of the Royal Society, Interface 3, 399–413.
Wingrove, J., Bond, A.J., 1997. Impulsivity: a state as well as trait variable. Does mood awarness explain low correlations between trait and behavioural measures of impulsivity? Personality and Individual Differences 22, 333–339.
Winstanley, C.A., Baunez, C., Theobald, D.E., Robbins, T.W., 2005. Lesions to the subthalamic nucleus decrease impulsive choice but impair autoshaping in rats: the importance of the basal ganglia in Pavlovian conditioning and impulse control. The European Journal of Neuroscience 21, 3107–3116.
Winstanley, C.A., Eagle, D.M., Robbins, T.W., 2006. Behavioral models of impulsivity in relation to ADHD: translation between clinical and preclinical studies. Clinical Psychology Review 26, 379–395.
Wogar, M.A., Bradshaw, C.M., Szabadi, E., 1993a. Does the effect of central 5-hydroxytryptamine depletion on timing depend on motivational change? Psychopharmacology 112, 86–92.
Wogar, M.A., Bradshaw, C.M., Szabadi, E., 1993b. Effect of lesions of the ascending 5-hydroxytryptaminergic pathways on choice between delayed reinforcers. Psychopharmacology 111, 239–243.
Wundt, W.M., 1904. Principles of Physiological Psychology. Macmillan, New York.
Wylie, G., Allport, A., 2000. Task switching and the measurement of switch costs. Psychological Research 63, 212–233.
Yamasaki, H., LaBar, K.S., McCarthy, G., 2002. Dissociable prefrontal brain systems for attention and emotion. Proceedings of the National Academy of Sciences of the United States of America 99, 11447–11451.
Yeterian, E.H., Van Hoesen, G.W., 1978. Cortico-striate projections in the rhesus monkey: the organization of certain cortico-caudate connections. Brain Research 139, 43–63.
Yu, A.J., Dayan, P., 2005. Uncertainty, neuromodulation, and attention. Neuron 46, 681–692.
Zack, M., Poulos, C.X., 2009. Effects of the atypical stimulant modafinil on a brief gambling episode in pathological gamblers with high vs low impulsivity. Journal of Psychopharmacology 23, 660–671.
Zacks, R.T., Hasher, L., 1994. Direct ignoring: inhibitory regultion of working memory. In: Dagenbach, D., Carr, T.H. (Eds.), Inhibitory Processes in Attention, Memory and Language. Academic Press, San Diego, CA, pp. 241–264.
Zacny, J.P., de Wit, H., 2009. The prescription opioid, oxycodone, does not alter behavioral measures of impulsivity in healthy volunteers. Pharmacology, Biochemistry, and Behavior 94, 108–113.
Zbrodoff, N.J., Logan, G.D., 1986. On the autonomy of mental processes: a case study of arithmetic. Journal of Experimental Psychology. General 115, 118–130.
Zelazo, P.D., Mueller, U., 2002. Executive function in typical and atypical development. In: Goswami, U. (Ed.), Handbook of Childhood Cognitive Development. Blackwell, pp. 445–469.
Zheng, D., Oka, T., Bokura, H., Yamaguchi, S., 2008. The key locus of common response inhibition network for no-go and stop signals. Journal of Cognitive Neuroscience 20, 1434–1442.

Please cite this article in press as: Bari, A., Robbins, T.W., Inhibition and impulsivity. Prog. Neurobiol. (2013), http://dx.doi.org/10.1016/j.pneurobio.2013.06.005