



Successful inhibitory control over an immediate reward is associated with attentional disengagement in visual processing areas

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ABSTRACT

We examined the neural basis of the capacity to resist an immediately rewarding stimulus in order to obtain a larger delayed reward. This was investigated with a Go/No-go task employing No-go targets that provided two types of reward outcomes. These were contingent on inhibitory control performance: failure to inhibit Reward No-go targets provided a small monetary reward with immediate feedback; while successful inhibitory control resulted in larger rewards with delayed feedback based on the highest number of consecutive inhibitions. We observed faster Go trial responses with maintained levels of inhibition accuracy during the Reward No-go condition compared to a neutral No-go condition. Comparisons between conditions of BOLD activity showed successful inhibitory control over rewarding No-Go targets was associated with hypoactivity in regions previously associated with regulating emotion and inhibitory control, including insula and right inferior frontal gyrus. In addition, regions previously associated with visual processing centers that are modulated as a function of visual attention, namely the left fusiform and right superior temporal gyri, were hypoactive. These findings suggest a role for attentional disengagement as an aid to withholding response over a rewarding stimulus and are consistent with the notion that gratification can be delayed by directing attention away from immediate rewards.

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Introduction

The ability to forego immediate short-term rewards in exchange for larger long-term goals is an integral component of mental and physical wellbeing. The capacity to delay gratification in childhood, as measured by the length of time that a child is able to resist the lure of an immediate reward (e.g., one marshmallow) in favor of a larger gain (e.g. more than one marshmallow), predicts a number of outcomes in later life such as academic success (Shoda et al., 1990), stress management (Mischel et al., 1988), cognitive control (Casey et al., 2011; Eigsti et al., 2006) and reduced levels of drug use (Ayduk et al., 2000). Given the lasting societal and individual costs associated with substance use disorders (Collins and Lapsley, 2008; Kamerow et al., 1986), the consequences for those individuals whose capacity to resist short-term rewards has not matured by adulthood may be particularly detrimental.

Recent studies have investigated the neural activity of individuals while attempting to regulate craving over reward-related cues. Smokers who were instructed to strategically inhibit craving feelings while

presented with images of cigarettes and food produced increased activation in regions of the right prefrontal cortex (PFC) implicated in cognitive control processes including the right inferior frontal gyrus (rIFG; Aron, 2007; Aron et al., 2004; Koechlin et al., 2003; Kober et al., 2010). Concurrent reductions in activity were reported in regions of the ventral and tegmental striatum associated with reward including the nucleus accumbens (NAcc; David et al., 2005; O'Doherty, 2004; Schultz et al., 1992) and regions of the limbic system associated with emotion including the amygdala (Adolphs et al., 1994; Due et al., 2002; Hariri et al., 2000). Similarly, when cocaine users were asked to inhibit craving in response to a cocaine-cue video, participants showed reductions in regions involved in reward and emotion including the NAcc and insula (Damasio et al., 2000; Franklin et al., 2007) compared to a neutral condition (without video) (Volkow et al., 2010). Comparisons with passive cocaine-cue viewing were associated with decreased metabolism in the orbitofrontal cortex (Schultz et al., 2000) and right NAcc, the latter of which was correlated with increasing metabolism in the rIFG. Findings of this kind support a prefrontal-subcortical balance model of self-regulation whereby resistance over an alluring stimulus can be described as a reflection of reciprocal activity between brain regions implicated in impulse and self-control (see Heatherton and Wagner, 2011 for a recent review).

The importance of attention to the regulation of resistance over immediate reward has been acknowledged since early observations

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made by Mischel and colleagues that those children most effective in sustaining delay for reward, were more likely to engage in spontaneous behaviors to avoid looking at rewards, such as covering their eyes (Mischel et al., 1989). By directing attention away from alluring immediate rewards through, for example, obscuring reward objects and distraction, children were able to delay gratification for a substantially longer time (Mischel and Ebbeson, 1970; Mischel et al., 1972). Inhibitory control performance of the same cohort as adults was examined using a Go/No-go task (Eigsti et al., 2006). Adults who, as preschoolers, were able to delay gratification for an extended time by directing attention away from the rewarding aspects of a stimulus were found to perform more efficiently. Specifically, this group was able to make faster Go trial responses while maintaining the same level of No-go accuracy as those who directed attention towards the rewarding aspects of a stimulus.

Moreover, in addition to the involvement of prefrontal–subcortical circuitry, recent craving resistance studies also suggest a potential role for attentional mechanisms. Specifically, neuroimaging findings have demonstrated hypoactivity in visual processing centers during craving resistance that are modulated as a function of visual attention. Volkow et al. (2010) reported a decrease in activity in the left fusiform gyrus (Heinze et al., 1994; Vuilleumier et al., 2001) while participants made efforts to inhibit their craving. While another recent study (Brody et al., 2007), in which smokers were instructed to resist craving during exposure to cigarette cues, reported lower activation bilaterally in the cuneus and occipital gyrus (Corbetta et al., 1991; Hillyard and Anillo-Vento, 1998; Le et al., 1998; Martinez et al., 1999).

Thus, in the context of previous observations that resistance to alluring stimuli can be prolonged by re-direction of attention (Mischel and Ebbeson, 1970; Mischel et al., 1972), findings may be suggestive of a strategic, endogenous disengagement of attentional mechanisms in the presence of reward-related cues as a means of reducing the craving associated with them. Based on the following constraining factors however, results derived from recent craving resistance studies (e.g., Brody et al., 2007; Kober et al., 2010; Volkow et al., 2010) may require some further clarification. First, the authenticity of participants' efforts to suppress craving or allow craving in response to a cue is difficult to corroborate without behavioral verification. Without this, results are vulnerable to the “white bear” effect, in which paradoxically, participants may be liable to reflect more strongly on a topic when requested to suppress thoughts about it (Wegner et al., 1987; Wylie et al., 2004). Although self-report measures have been utilized post-cue presentation, these are subject to their own artifacts such as social desirability bias (Nederhof, 1985) and experimenter expectancy effects (Rosenthal, 1976). Second, the finding in previous studies of activation of PFC regions implicated in cognitive control during strategic resistance over reward-related cues has no comparison with activation during standard cognitive control. It is therefore unclear whether recruitment of these regions can be differentiated from that needed during cognitive control over cues which are unrelated to reward. Third, given that participants were instructed to engage in cognitive appraisal strategies, the patterns of activation reported in previous studies may not be completely reflective of a typical everyday act of abstinence over an alluring target in which an explicit strategy is less likely to be employed.

In the present event-related fMRI study, we employed a modified Go/No-go task that required participants to resist responding to an alluring stimulus with immediate response–reward associations in exchange for a larger gain rewarded for consistent inhibitory control performance. By adopting a Go/No-go paradigm and thus eliminating the influence of a “white bear” effect, we aimed to investigate neural mechanisms specific to successful inhibitory control during resistance of smaller gain with immediate feedback in exchange for a larger long-term reward with delayed feedback. Further, inclusion of No-go trials without reward contingencies enabled an assessment of potential differentiation with activation during inhibitory control over a non-alluring stimulus. Moreover, by providing actual monetary gains

contingent on participants' response or non-response, the need for cognitive appraisal strategies was not required, thus allowing for spontaneous processes of self control over an alluring stimulus to be assessed.

Studies of the effect of proximal and long-term gains on decision-making have also demonstrated prominent roles for regions implicated in reward (e.g., NAcc) and cognitive control (e.g., PFC) (Diekhof and Gruber, 2010; Hare et al., 2009). However, such tasks necessitate concurrent presentation of both stimuli regardless of short- or long-term reward contingencies and thus conflate any influence of attentional mechanisms, [unless attention has been exogenously modulated (e.g., Lim et al., 2011)]. With regards to the current task, we hypothesized that successful inhibitory control over a single immediately rewarding stimulus would permit a role for attention. Specifically, successful inhibitory control over a rewarding stimulus would be associated with hypoactivity of visual processing centers involved in attention such as the fusiform gyrus, occipital gyrus and cuneus. Consistent with this interpretation, we hypothesized behavioral modulation analogous to the increased efficiency in Go/No-go performance yielded by individuals who were able delay gratification by directing attention away from rewarding aspects of a stimulus (Eigsti et al., 2006). In addition, consistent with a prefrontal–subcortical balance model of self-regulation, we hypothesized concurrent hypoactivation of ventral and limbic regions associated with reward and emotion processes and increased recruitment of PFC regions implicated in inhibitory control such as the right inferior frontal gyrus.

Materials and methods

Participants

Eighteen healthy volunteers (9 males, mean age, 23) took part in the current study. All of the participants were right-handed, as determined by the Edinburgh Handedness Inventory (Oldfield, 1971), and reported no current or past history of neurological or psychiatric disorders or psychotropic medication use. Participants provided informed consent and procedures were executed in compliance with ethical research institutional guidelines.

Behavioral task

Participants completed a Go/No-go task designed to investigate inhibitory control during resistance of rewarding stimulus with immediate feedback in exchange for a larger reward with delayed feedback (Fig. 1). The alluring reward–response associations of Reward No-go trials were cultivated in two ways. First, failure to perform inhibitory control over them resulted in small monetary rewards for which immediate feedback was provided. Second, Reward No-go stimuli were assigned that had been employed in the previous block as a trial that was monetarily rewarded for rapid responses with immediate feedback. Successful inhibitory control over alluring No-go trials resulted in a larger reward comprising the sum of the longest run of consistent inhibitions. However, performance regarding money gained from successful Reward No-go inhibitory control was not immediately apparent to participants as feedback was delayed until the end of each block.

The task consisted of three types of trials: Go, No-go and Money trials. Go trials consisted of the presentation of white double-digit numbers (different, e.g. 21, 23 but not 22), centrally on a black background for 750 ms, followed immediately by a 1250 ms interstimulus interval (ISI) presenting only the black background. Participants were asked to respond to Go trials by making a single button press response as quickly as possible upon Go trial presentation.

Money trials presented same-digit double-digit numbers (e.g., 11, 22 or 33) and required participants to make a single button press response as quickly as possible. The stimulus was presented for 750 ms, followed by a feedback screen for 750 ms and blank-screen ISI (500 ms). Money trials paid monetary rewards in proportion to how quickly

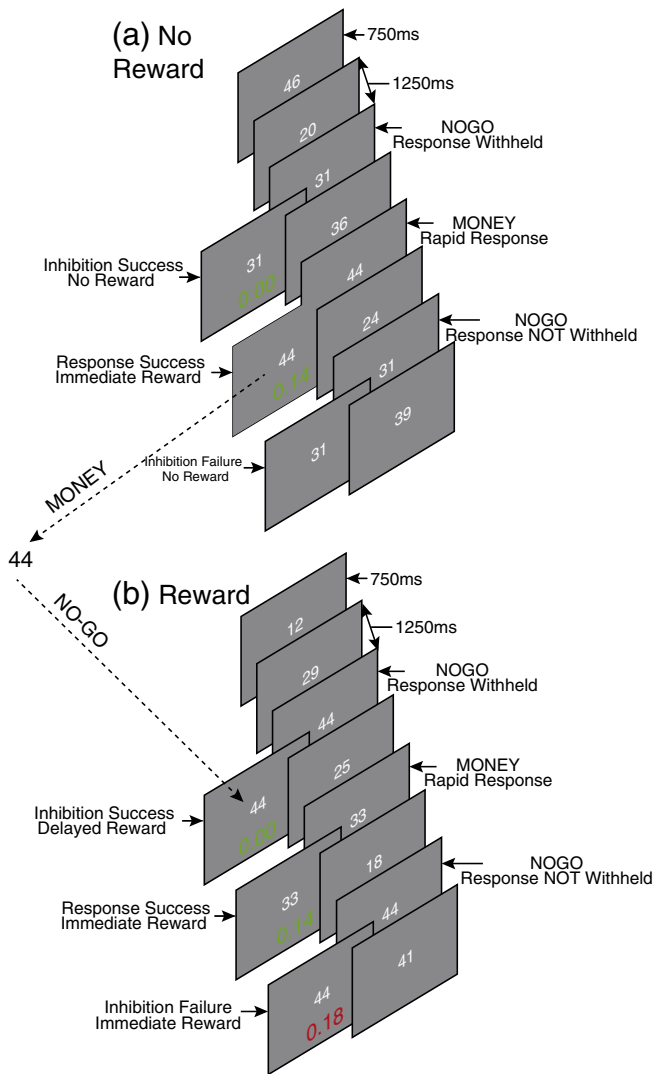


Fig. 1. No-Reward/Reward Go/No-Go task design. The task required participants to (i) respond rapidly to different-digit double-digit numbers (Go trials); (ii) respond rapidly to same-digit double-digit numbers (Money trials) and (iii) withhold response to a designated double-digit number previously employed as a Money trial in the preceding block of trials (No-Go trials). For Money trials, monetary gains were rewarded commensurate with RT speed (maximum gains were 20c) and immediate feedback on performance was provided on the screen. Reward outcomes for successful inhibitory control of No-go trials were contingent on condition: (i) No-Reward No-go inhibition success did not provide a reward; (ii) Reward No-go inhibition success provided a 40c reward. However, rewards were the sum of the longest run of consecutive inhibitions within each block and feedback for amount gained was delayed until the end of a block. Consequently, immediate feedback for No-Go trial performance did not differ between conditions. Feedback for failure to perform inhibitory control was also contingent on condition: (i) No-Reward did not result in monetary reward; (ii) Reward inhibitory control failure resulted in a monetary reward, which like Money trials, was commensurate with RT speed.

participants responded to the Money trial presentation. Two different same-digit double-digit numbers (e.g., 22 and 44) were presented as Money trial stimuli for each block.

No-go trials were pseudo-randomly interspersed throughout the Go trials. The No-go stimulus was presented for 750 ms, followed by a 1250 ms ISI, a 1000 ms feedback screen and 1000 ms ISI. Participants were informed prior to the beginning of each block which double-digit number was designated as the forthcoming No-go stimulus. Participants were asked to withhold their button response upon presentation of this No-go stimulus.

Immediate feedback on performance accuracy and amount gained was provided during the feedback screen that followed Money and No-go trials. Successful button presses for a Money trial stimulus

provided an immediate monetary reward with a maximum value of 20c (AUD). The monetary reward for Money trials was calculated by subtracting the reaction time from the 1000 ms response window duration. For example, if a participant's reaction time was 300 ms in a Money trial, the monetary gain would be 14c $[(1000 - 300)/50] = 14$. Performance accuracy feedback was also provided during the ISI period following successful No-go trial inhibitory control.

Two experimental conditions, Reward and No-Reward, were administered to participants. These were differentiated by their contingencies relating to inhibitory control success and failure during No-go trials. Rather than receiving an immediate reward for successful inhibitory control during the No-go trial, participants were provided with monetary reward feedback at the end of each block based upon the highest number of consecutive successfully inhibited No-go trials during the block, multiplied by 40c. For example, if within one block the highest number of successful consecutive response inhibitions were seven, then the participant was awarded \$2.80 $(7 \times 40c)$. Consequently, immediate feedback for successful inhibitory control of individual No-go trials informed participants that no money had yet been accrued. Such a paradigm was devised to model real-world behavior in which abstinence is required over an immediate and tangible reward (i.e. reward amount is based on reaction time with immediate feedback) in order to obtain a larger yet less tangible reward (i.e. reward amount is based on an accumulation of consecutive inhibitions with no immediate feedback).

During the Reward condition (Fig. 1a), failure to inhibit during a No-go trial led to an immediate reward. Feedback during the ISI period signaled performance failure and a monetary reward commensurate with RT, thereby remaining consistent with the response-reward relationship experienced during Money trials. During the No-Reward condition, no monetary reinforcement was applied to inhibition success or failure, only Money trials were rewarded. In order to maximize the recency and prepotency of the association between the No-go stimuli and monetary reward for Reward, the No-go stimulus for each block was selected from one of the two same-digit double-digit Money trial stimuli from the block preceding it.

Three consecutive blocks of Reward conditions were presented to participants, with a No-Reward condition block preceding and following these. Each block comprised of 120 Go, 20 No-go and 20 Money trials, all of which were pseudo-randomly presented such that No-go and Money trials were always separated by at least two Go trials. To avoid retroactive interference effects, same-digit numbers were not used as a Money trial stimulus in the block immediately following its use as a No-go stimulus.

All aspects of stimulus delivery and response recording were controlled by E-Prime software (version 2.0, Psychology Software Tools, Pittsburgh, PA), running on a laptop PC (Intel 2Ghz, 256mb Nvidia Video Card) that was interfaced with the MR scanner during acquisition of fMRI data. Participants indicated their responses by pressing the appropriate button on the appropriate buttons of a MR-compatible response box (Fibre-Optic response pads, Current Designs, Philadelphia, PA, USA).

Image acquisition

Functional MR images were acquired at the Royal Children's Hospital, Melbourne, using a 3 T scanner (Siemens Magnetom TrioTim, Erlangen, Germany). 183 echo-planar imaging (EPI) sequences providing T2*-weighted blood oxygenation level-dependent (BOLD) were acquired for each functional run with the following parameters: repetition time (TR), 2000 ms; echo time, 35 ms; flip angle, 90°; 32 contiguous slices of 4 mm thickness; in-plane resolution, 3.6 mm \times 3.6 mm \times 4 mm. To allow for steady-state tissue magnetization, each functional run began with two volume acquisitions that were later discarded. Five functional runs were collected for each participant. Activation data were registered to high-resolution T1-weighted isotropic (0.8 mm³) structural magnetization-prepared

rapid-acquisition gradient echo images to localize the pattern of physiological changes with the task time-series.

Data analysis

All analyses were conducted using AFNI software (<http://afni.nimh.nih.gov/afni/>) (Cox, 1996). Following image reconstruction, the time-series data were time-shifted using Fourier interpolation to remove differences in slice acquisition times, and motion-corrected using three-dimensional volume registration (least-squares alignment of three translational and three rotational parameters). Activation outside the brain was removed using edge detection techniques.

To examine the influence of reward on No-go performance, an event-related analysis was performed that estimated activation during No-go trial responses for both Reward and No-Reward conditions. To do this, hemodynamic response functions were calculated using deconvolution techniques for each successful No-go trial response. As the presentation of all epochs of interest was timed to coincide with the beginning of the 2 s temporal resolution cycle, response functions for all regressor events were initiated at individual epoch onsets. To avoid contamination of the baseline and event-related estimates, additional regressors were included to model the activity related to errors and feedback screens related to both correct and incorrect trials. The area under the curve was expressed as a percentage of the area under the baseline. The baseline estimate was the mean activation recorded during the ongoing trial period (Go trials), such that the activation observed during successful No-go trial responses represents activation over and above that required for the ongoing trial period (or Go) responses.

Percentage area (event-related activation) map voxels were resampled at 1 mm³ resolution then spatially normalized to standard MNI space (MNI 152 template) and spatially blurred with a 3 mm isotropic root-mean-squared Gaussian kernel. Group activation maps for the No-go event type were determined with one-sample *t* tests against the null hypothesis of zero event-related activation changes (i.e., no change related to baseline). Significant voxels passed a voxelwise statistical threshold ($t = 3.97, p \leq 0.001$) and were required to be part of a larger 142 μ l cluster of contiguous significant voxels. The combination of probability thresholding and cluster thresholding was used to maximize the power of the statistical test while holding the likelihood of false positives to a minimum. Simulation using the 3D ClustSim function in AFNI (http://afni.nimh.nih.gov/pub/dist/doc/program_help/3dClustSim.html) and an uncorrected voxelwise threshold $P = 0.001$ indicated that cluster size of 142 μ l, given our parameters that occurs < 1% of the time by chance can be selected, given a threshold of $p = 0.01$ (corrected).

Activation clusters from the whole-brain analysis of No-go trials were used to create an activation map including the voxels of activation indicated as significant constituent maps (Reward or No-Reward). The mean activation for clusters in this map was calculated for the purposes of a functionally-derived region of interest (ROI) analysis. Activation estimates between conditions were compared using repeated-measures *t* tests, corrected using a modified Bonferroni procedure for multiple comparisons (Keppel, 1991). Finally, due to a priori interest in the activity of the ventral striatum in response to performance outcomes, anatomically defined ROI analyses were conducted on right (130 μ l; $x = 11, y = 9, z = -8$) and left (157 μ l; $x = -13, y = 9, z = -8$) nucleus accumbens (NAcc), defined by the Montreal Neurological Institute atlas of the AFNI toolbox.

Results

Behavioral results

Reward Go trials yielded significantly faster reaction times (RTs) than No-Reward Go trials (369 ms vs. 380 ms), $t(17) = 2.19, P < 0.05$,

while accuracy for Reward No-go's trials was not lower than No-Reward No-go trials but slightly higher (78% vs. 74%), although this difference was not statistically significant, $t(17) = 1.68, P = 0.11$. That faster Reward Go trial responses were not committed at the expense of inferior inhibitory control (i.e., speed-accuracy trade-off) implies more efficient Go/No-go performance for this condition. The lack of a significant correlation between Reward Go RTs and Reward No-go accuracy ($r = .19, p = .46$) provides further evidence for an absence of such a trade-off for the Reward condition. The speed of responses did not differ significantly between Reward and No-Reward Money trials (368 ms vs. 378 ms). There was no significant influence of gender on behavioral performance.

fMRI BOLD activity

Consistent with previous event-related fMRI research employing Go/No-go tasks, successful inhibitory control was associated with BOLD activity in regions of the right lateralized PFC, namely inferior and middle frontal gyri, and ACC (Aron, 2011; Botvinick et al., 2001; Ridderinkhof et al., 2004; Rubia et al., 2001) (Table 1). In posterior areas, activity was observed in the left fusiform gyrus and superior temporal gyrus (STG), both visual processing centers shown to be susceptible to attentional modulation (Heinze et al., 1994; Pessoa et al., 2002; Vuilleumier et al., 2001). Bilateral activity in multiple sites of the insula and caudate, both implicated in reward and emotion processes (Knutson et al., 2001; Naqvi and Bechara, 2009; Phillips et al., 2008), was also observed.

In comparing activity for each condition in functionally defined ROIs derived from activity during all No-go trials, several regions showed sensitivity to Reward (Table 1). Lower BOLD signal was found during successful Reward No-go trials in visual processing centers in left (fusiform gyrus) and right (STG) hemispheres (Fig. 2). In striatal regions, lower Reward No-go activity was observed in the right caudate (Fig. 2), the same pattern was yielded in the left limbic area by the insula (Fig. 2). Activity encompassing both the right insula and rIFG was anatomically differentiated and successful No-go activity between No-Reward and Reward was compared for both ROIs. Although right insula ($x = 33, y = 19, z = 7$) activity was not modulated

Table 1
Regions of event-related activation during successful No-go trials.

Structure	HS	Volume (μ l)	Center of mass			<i>p</i>
			<i>x</i>	<i>y</i>	<i>z</i>	
Frontal lobe						
Medial	R	250	11	-5	66	
Superior	R	219	21	-8	56	
Middle	R	259	42	2	40	
Temporal lobe						
Fusiform	L	259	-29	-66	-10	NR > R
Superior	R	246	58	-50	18	NR > R
Middle	L	150	-43	-52	-1	
Parietal lobe						
Middle/anterior cingulate	R/L	3659	1	23	36	
Postcentral	L	2828	-40	-29	52	
Supramarginal	L	188	-54	-48	29	
L	L	183	-53	-24	16	NR > R
Insular and subcortical						
Insula/inferior frontal	R	3734	36	18	9	
Insula	L	2014	-30	17	9	
L	L	418	-29	16	19	NR > R
L	L	255	-41	-29	19	
Caudate	R	257	18	-11	20	NR > R
L	L	231	-12	9	3	
R	R	151	14	9	2	
L	L	150	-13	-1	20	
Thalamus	R	163	3	-4	10	

HS, Hemisphere; L, Left; R, Right. Center of mass in MNI co-ordinates. *p*, significant difference between R, Reward and NR, No-Reward ($p < 0.05$ corrected).

by Reward, activity in the rIFG ($x=45, y=18, z=13$) was reduced for Reward No-go trials (Fig. 2). In addition, greater deactivation of the left supramarginal during Neutral No-go trials was observed. For the comparison of anatomically defined NAcc regions, no significant differences were found.

Discussion

In the present study participants were required to refrain from responding to a rewarding stimulus with immediate feedback. Moreover, successful consistent inhibitory control over immediately rewarding targets contributed to larger monetary gains with delayed feedback. We found that the Reward No-go condition was associated with improved inhibitory control efficiency, that is, greater speed on Go trials without compromised performance during No-go trials. This enhancement is comparable to Go/No-go performance demonstrated by individuals with an ability to effectively direct attention away from tempting aspects of rewards in a delay-of-gratification task (Eigsti et al., 2006). By adopting the current approach we were able to build on previous literature examining self-regulatory mechanisms in at least three ways.

First, we investigated the association between attentional mechanisms and the ability to perform inhibitory control over a rewarding stimulus. We observed hypoactivity in both the right superior temporal gyrus (STG) and the left fusiform gyrus during successful inhibition over an alluring No-go target. The right superior temporal region is a visual processing area whose modulation has been thought

to reflect the strategic allocation of attention to relevant features (Williams et al., 2005). Although, the STG has not previously been reported in studies of craving resistance, it has been found to respond differentially to emotional valence as a function of attention (Pessoa et al., 2002), and has recently been implicated in visual attention-guided decision value computations (Lim et al., 2011). The left fusiform gyrus is a region that has demonstrated reduced activity during attempts to strategically inhibit craving over reward-related images (Volkow et al., 2010). This pattern of hypoactivity in visual areas associated with attention is echoed by reports of lower activity in the cuneus and occipital areas during resistance over cigarette cues (Brody et al., 2007). Current results add to previous studies by showing that such a pattern of hypoactivity is also possible during non-simulated resistance over a target with tangible immediate reward potential. We argue that hypoactivation of such areas during resistance over an alluring stimulus is suggestive of a type of attentional disengagement that can be likened to the “cooling” of “hot” appetitive features of an alluring stimulus previously proposed by Mischel and colleagues (Mischel and Ebbeson, 1970; Mischel et al., 1972; Sethi et al., 2000). That is, a reduction in attentional engagement during exposure to an immediately rewarding stimulus can serve to ease inhibitory control exertion. This complements recent research suggesting that stimulus value signals at the time of decision-making can be modulated by visual attention (Lim et al., 2011). Specifically, exogenous guidance of visual attention toward one of two stimulus choices resulted in a bias in decision for the attended option. By presenting images of faces versus scrambled faces in conjunction with rewarding

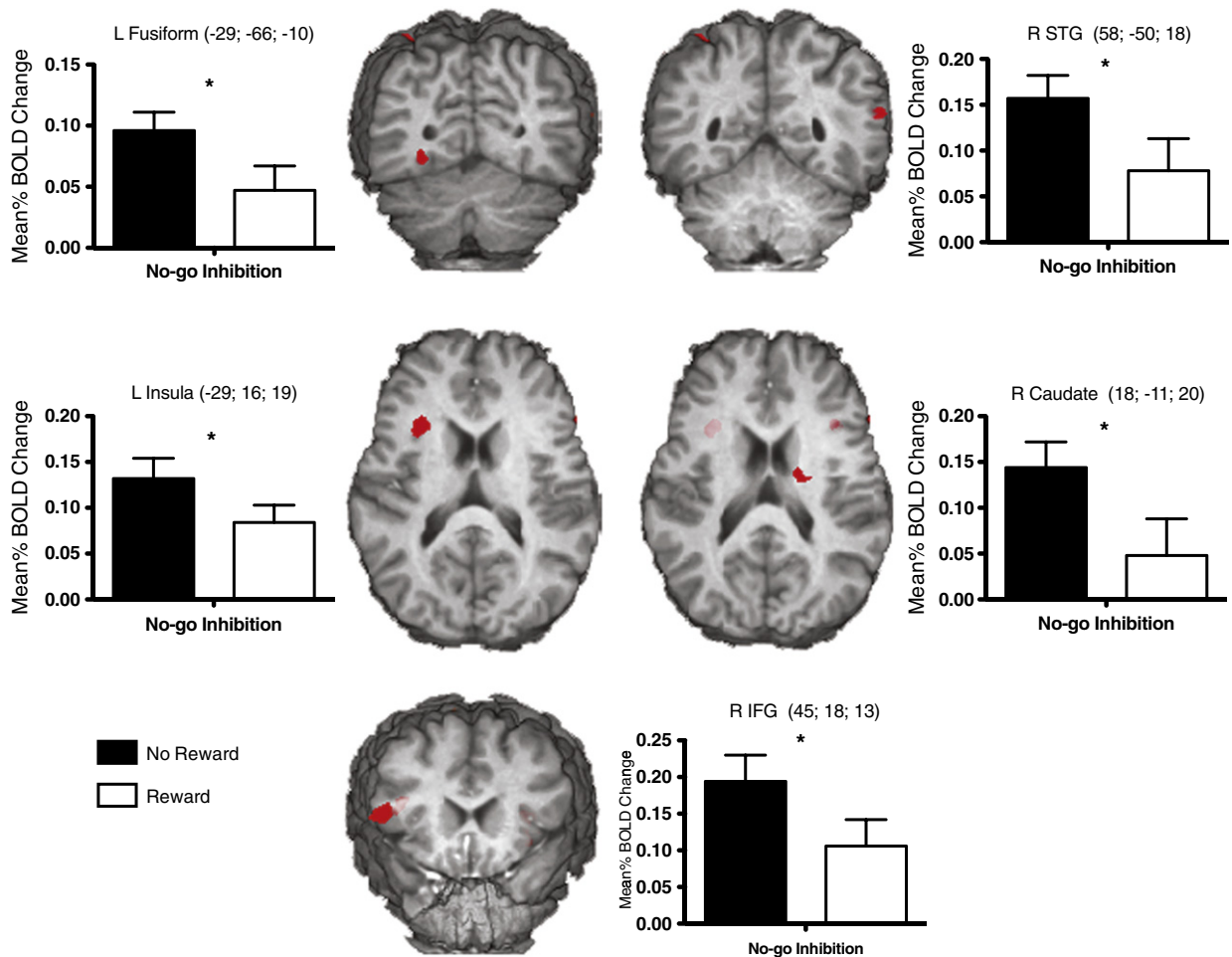


Fig. 2. Regions of brain activity differentiating Reward from No-Reward during successful inhibitory control over No-go trials. Bar graphs represent mean BOLD % signal change (relative to baseline for Reward and No-Reward No-go trials). Error bars represent the standard error of the mean. MNI co-ordinates are listed in each bar graph title. Significant comparisons are indicated by the bar and asterisk notations. R STG, right superior temporal gyrus; R IFG, right inferior frontal gyrus.

or neutral No-go targets, our group is presently further examining the potential for endogenous strategic allocation of attention away from immediately rewarding targets. It is hypothesized that the attention-capturing characteristics of faces may offer an inhibition-enhancing distraction when targets are alluring.

Tradeoffs between speed and accuracy are generally expected during standard inhibitory control task performance, however their effects have previously been found to be attenuated by the influence of motivation through monetary reward (Leotti and Wager, 2010). Present behavioral results showing increased efficiency in cognitive control performance for the Reward condition can be interpreted within a framework of attentional disengagement of Reward No-go targets. In addition to the reduction in prepotency offered by limiting the amount of attentional resources allocated to the processing of alluring No-go targets, this effect may also influence the relative potentiation of Go and No-go pathways such that the detection of Go targets is more efficient (Frank et al., 2004). This improvement in efficiency is consistent with longitudinal research showing that, as adults, preschoolers who tended to direct their attention away from rewarding aspects of a stimulus during a delay-of-gratification task were faster at performing a Go/No-go task without making more errors than those directed attention towards the rewarding aspects of a stimulus (Eigsti et al., 2006).

Second, hypoactivity was found in regions of the left insula and right caudate during successful inhibitory control of Reward No-go trials. The insula, which has been implicated in reward-related urges and decision-making processes that involve risk and reward (Naqvi and Bechara, 2009), has previously shown reduced activity during strategic attempts to inhibit craving over cocaine-cues (Volkow et al., 2010). It has also been cited in studies of emotion processing that propose a potential for disengagement of attention from emotional stimuli (Phillips et al., 2008) and diversion-based approaches to emotion regulation (Ochsner and Gross, 2005). The caudate is a region of the striatum that has previously been associated with impulsivity during response inhibition performance (Brown et al., 2006), reward sensitivity in motivation-influenced cognitive control (Locke and Braver, 2008) and coding for expected reward magnitude (Knutson et al., 2001). In order to successfully refrain from responding to an immediately rewarding stimulus in exchange for a larger delayed reward, inhibition of such a mechanism, as demonstrated in the current study, would appear necessary. Both findings are consistent with a model of self-regulation that posits reduced activity in limbic and striatal regions associated with reward and emotion (see Heatherton and Wagner, 2011 for a recent review).

Third, to our knowledge, no prior studies have examined whether PFC activity related to inhibitory control over an immediately rewarding stimulus differs from that produced during standard inhibitory control performance. In the context of a prefrontal-subcortical balance model of self-regulation (Heatherton and Wagner, 2011) one might predict a corresponding increase in PFC regions implicated in cognitive control. For instance, strategic resistance over cocaine cues showed that reduced activity in the ventral striatum correlated with an increase in lateral PFC activity (Volkow et al., 2010; note however that this increase was the result of a comparison with PFC activity during passive viewing of cocaine cues). In the present study and running counter to a prefrontal-subcortical balance model interpretation, we observed reduced activity in the rIFG during successful inhibitory control over Reward No-go trials compared to No-Reward No-go trials. This suggests, somewhat counter-intuitively, that less top-down regulation was required to inhibit an immediately rewarding stimulus. Thus, in the context of an interpretation of attentional disengagement as an aid to withholding response over an alluring stimulus, the finding of associated hypoactivity in the rIFG is convergent with the notion that “it is easier to avoid temptation than to overcome it” (Baumeister and Heatherton, 1996, p. 4).

A primary aim of the current study was to address a limitation identified in previous self-regulation literature. That is, without an appropriate comparison condition, activity that had been interpreted as characteristic of resistance over an alluring stimulus could also be interpreted as mere resistance. Our proposed solution was to modify the typical format of a Go/No-go task that has been used to examine the neural correlates of general inhibitory control (e.g., Aron, 2011; Botvinick et al., 2001; Garavan et al., 2002; Ridderinkhof et al., 2004; Rubia et al., 2001) in order to model a scenario of inhibitory control that could be likened to that seen in simulated resistance studies. By comparing activity produced by such a model with an unmodified equivalent we attempted to isolate the neural and behavioural correlates of resistance over an alluring stimulus. However, in adopting such a design, Reward No-go trials conflated several confounding characteristics that were not manifest in No-Reward No-go trials. First, Reward No-go trials were the only trials to be recently associated with monetary outcomes contingent on fast responses; second, failure to inhibit Reward No-go trials resulted in immediate reward; and third, withholding responses to Reward No-go trials resulted in rewards with delayed feedback. In addition, Reward blocks were more frequently presented than No-Reward blocks (three vs. two).

So that such conflated factors can be differentiated, future work should adopt a more experimentally nuanced approach. For example, studies involving inhibitory control over rewarding stimuli may benefit from the following design modifications. First, Aron (2011) posits that faster Go trial RT is indicative of a reactive mode of inhibitory control, whereas proactive inhibitory control, which is generated according to participants' goals rather than external signals, is characterized by slower Go trial responses. The faster Go trial RT produced by the current Reward condition may reflect a type of goal-driven reactive control brought about by the conflation of two contrary goal contingencies. That is, a “push” elicited by rewarding responses to No-go trials versus an opposing “pull” elicited by rewarding the inhibition of responses to the same trials. Theoretically, by isolating only one goal contingency, through the introduction of a No-go trial that only rewards inhibition, participants would more likely demonstrate a proactive mode of inhibitory control. Second, presently we can only speculate on its relevance in the context of our study but the orbitofrontal cortex (OFC) may warrant further investigation as a means of exploring the viability of a prefrontal-subcortical balance model of self-regulation (Heatherton and Wagner, 2011). This region has previously been implicated in the calculation of relative preference between stimuli, such that neurons can be more or less activated by a reward depending on which alternative reward is available (Tremblay and Schultz, 1999). Consequently, the OFC may be particularly influential in cases where the act of refraining from responding to an immediately rewarding stimulus produces larger delayed reward benefits. In the context of current findings, an *intra-stimulus* reward relativity calculation may be plausible, whereby exposure to an immediately rewarding stimulus yields modulation of OFC activity because the outcome of not responding to that stimulus is likely to result in a preferred larger delayed reward. In order to substantiate this line of argument, future studies could employ optimized scanning parameters for functional sensitivity in this region and an additional condition in which inhibitory control is required over an immediately rewarding stimulus that has no delayed reward outcome for successful inhibition.

Finally, with respect to clinical contexts, and substance use disorders (SUDs) in particular, present findings complement prominent models that posit a reciprocal relationship between craving and attentional bias, whereby craving can increase as a consequence of increasing attention to substance-related cues (Field and Cox, 2008; Franken, 2003; Kavanagh et al., 2005; Ryan, 2002). Given that healthy participants appear able to disengage from alluring targets in order to abstain from them, it may be worth exploring further whether efforts by individuals with SUD to abstain from craved substances are undermined by a reduction in the ability to disengage attention from their appetitive features.

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References

- Adolphs, R., Tranel, D., Damasio, H., Damasio, A., 1994. Impaired recognition of emotion in facial expressions following bilateral damage to the human amygdala. *Nature* 372 (6507), 669–672.
- Aron, A., 2007. The neural basis of inhibition in cognitive control. *Neuroscientist* 13, 214–228.
- Aron, A.R., 2011. From reactive to proactive and selective control: developing a richer model for stopping inappropriate responses. *Biol. Psychiatry* 69 (12), e55–e68.
- Aron, A.R., Robbins, T.W., Poldrack, R.A., 2004. Inhibition and the right inferior frontal cortex. *Trends Cogn. Sci.* 8 (4), 170–177.
- Ayduk, O., Mendoza-Denton, R., Mischel, W., Downey, G., Peake, P.K., Rodriguez, M., 2000. Regulating the interpersonal self: strategic self-regulation for coping with rejection sensitivity. *J. Pers. Soc. Psychol.* 79 (5), 776–792.
- Baumeister, R., Heatherton, T., 1996. Self-regulation failure: an overview. *Psychol. Inq.* 7, 1–15.
- Botvinick, M., Braver, T., Barch, D., Carter, C., Cohen, J., 2001. Conflict monitoring and cognitive control. *Psychol. Rev.* 108 (3), 624–652.
- Brody, A.L., Mandelkern, M.A., Olmstead, R.E., Jou, J., Tongson, E., Allen, V., et al., 2007. Neural substrates of resisting craving during cigarette cue exposure. *Biol. Psychiatry* 62 (6), 642–651.
- Brown, S.M., Manuck, S.B., Flory, J.D., Hariri, A.R., 2006. Neural basis of individual differences in impulsivity: contributions of corticolimbic circuits for behavioral arousal and control. *Emotion* 6 (2), 239–245.
- Casey, B.J., Somerville, L.H., Gotlib, I.H., Ayduk, O., Franklin, N.T., Askren, M.K., et al., 2011. Behavioral and neural correlates of delay of gratification 40 years later. *Proc. Natl. Acad. Sci. U. S. A.* 108 (36), 14998–15003.
- Collins, A.L., Lapsley, H.M., 2008. The costs of tobacco, alcohol and illicit drug abuse to Australian society in 2004/05. Commonwealth of Australia, Canberra.
- 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. *J. Neurosci.* 11 (8), 2383–2402.
- Cox, R.W., 1996. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Comput. Biomed. Res.* 29 (3), 162–173.
- Damasio, A.R., Grabowski, T.J., Bechara, A., Damasio, H., Ponto, L.L., Parvizi, J., et al., 2000. Subcortical and cortical brain activity during the feeling of self-generated emotions. *Nat. Neurosci.* 3 (10), 1049–1056.
- David, S.P., Munafò, M.R., Johansen-Berg, H., Smith, S.M., Rogers, R.D., Matthews, P.M., et al., 2005. Ventral striatum/nucleus accumbens activation to smoking-related pictorial cues in smokers and nonsmokers: a functional magnetic resonance imaging study. *Biol. Psychiatry* 58 (6), 488–494.
- Diekhof, E.K., Gruber, O., 2010. When desire collides with reason: functional interactions between anteroventral prefrontal cortex and nucleus accumbens underlie the human ability to resist impulsive desires. *J. Neurosci.* 30 (4), 1488–1493.
- Due, D.L., Huettel, S.A., Hall, W.G., Rubin, D.C., 2002. Activation in mesolimbic and visuospatial neural circuits elicited by smoking cues: evidence from functional magnetic resonance imaging. *Am. J. Psychiatry* 159 (6), 954–960.
- Eigsti, I.M., Zayas, V., Mischel, W., Shoda, Y., Ayduk, O., Dadlani, M.B., et al., 2006. Predicting cognitive control from preschool to late adolescence and young adulthood. *Psychol. Sci.* 17 (6), 478–484.
- Field, M., Cox, W.M., 2008. Attentional bias in addictive behaviors: a review of its development, causes, and consequences. *Drug Alcohol Depend.* 97 (1–2), 1–20.
- Frank, M.J., Seeberger, L.C., O'Reilly, R.C., 2004. By carrot or by stick: cognitive reinforcement learning in parkinsonism. *Science* 306 (5703), 1940–1943.
- Franken, I.H., 2003. Drug craving and addiction: integrating psychological and neuropsychopharmacological approaches. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 27 (4), 563–579.
- Franklin, T.R., Wang, Z., Wang, J., Sciortino, N., Harper, D., Li, Y., et al., 2007. Limbic activation to cigarette smoking cues independent of nicotine withdrawal: a perfusion fMRI study. *Neuropsychopharmacology* 32 (11), 2301–2309.
- Garavan, H., Ross, T.J., Murphy, K., Roche, R.A., Stein, E.A., 2002. Dissociable executive functions in the dynamic control of behavior: inhibition, error detection, and correction. *Neuroimage* 17 (4), 1820–1829.
- Hare, T.A., Camerer, C.F., Rangel, A., 2009. Self-control in decision-making involves modulation of the vmPFC valuation system. *Science* 324 (5927), 646–648.
- Hariri, A.R., Bookheimer, S.Y., Mattziotta, J.C., 2000. Modulating emotional responses: effects of a neocortical network on the limbic system. *Neuroreport* 11 (1), 43–48.
- Heatherton, T.F., Wagner, D.D., 2011. Cognitive neuroscience of self-regulation failure. *Trends Cogn. Sci.* 15 (3), 132–139.
- Heinze, H.J., Mangun, G.R., Burchert, W., Hinrichs, H., Scholz, M., Munte, T.F., et al., 1994. Combined spatial and temporal imaging of brain activity during visual selective attention in humans. *Nature* 372 (6506), 543–546.
- Hillyard, S.A., Anillo-Vento, L., 1998. Event-related brain potentials in the study of visual selective attention. *Proc. Natl. Acad. Sci. U. S. A.* 95 (3), 781–787.
- Kamerow, D.B., Pincus, H.A., Macdonald, D.I., 1986. Alcohol abuse, other drug abuse, and mental disorders in medical practice. *JAMA* 255 (15), 2054–2057.
- Kavanagh, D.J., Andrade, J., May, J., 2005. Imaginary relish and exquisite torture: the elaborated intrusion theory of desire. *Psychol. Rev.* 112 (2), 446–467.
- Keppel, G., 1991. *Design and Analysis: A Researcher's Handbook*. Prentice Hall, New Jersey.
- Knutson, B., Adams, C.M., Fong, G.W., Hommer, D., 2001. Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *J. Neurosci.* 21 (16), RC159.
- Kober, H., Mende-Siedlecki, P., Kross, E.F., Weber, J., Mischel, W., Hart, C.L., et al., 2010. Prefrontal–striatal pathway underlies cognitive regulation of craving. *Proc. Natl. Acad. Sci. U. S. A.* 107 (33), 14811–14816.
- Koechlin, E., Ody, C., Kouneiher, F., 2003. The architecture of cognitive control in the human prefrontal cortex. *Science* 302 (5648), 1181–1185.
- Le, T.H., Pardo, J.V., Hu, X., 1998. 4T-fMRI study of nonspatial shifting of selective attention: cerebellar and parietal contributions. *J. Neurophysiol.* 79 (3), 1535–1548.
- Leotti, L.A., Wager, T.D., 2010. Motivational influences on response inhibition measures. *J. Exp. Psychol. Hum. Percept. Perform.* 36 (2), 430–447.
- Lim, S.L., O'Doherty, J.P., Rangel, A., 2011. The decision value computations in the vmPFC and striatum use a relative value code that is guided by visual attention. *J. Neurosci.* 31 (37), 13214–13223.
- Locke, H.S., Braver, T.S., 2008. Motivational influences on cognitive control: behavior, brain activation, and individual differences. *Cogn. Affect. Behav. Neurosci.* 8 (1), 99–112.
- Martinez, A., Anillo-Vento, L., Sereno, M.I., Frank, L.R., Buxton, R.B., Dubowitz, D.J., et al., 1999. Involvement of striate and extrastriate visual cortical areas in spatial attention. *Nat. Neurosci.* 2 (4), 364–369.
- Mischel, W., Ebbesen, E., 1970. Attention in delay of gratification. *J. Pers. Soc. Psychol.* 16, 329–337.
- Mischel, W., Ebbesen, E.B., Zeiss, A.R., 1972. Cognitive and attentional mechanisms in delay of gratification. *J. Pers. Soc. Psychol.* 21 (2), 204–218.
- Mischel, W., Shoda, Y., Peake, P.K., 1988. The nature of adolescent competencies predicted by preschool delay of gratification. *J. Pers. Soc. Psychol.* 54 (4), 687–696.
- Mischel, W., Shoda, Y., Rodriguez, M.I., 1989. Delay of gratification in children. *Science* 244 (4907), 933–938.
- Naqvi, N.H., Bechara, A., 2009. The hidden island of addiction: the insula. *Trends Neurosci.* 32 (1), 56–67.
- Nederhof, A.J., 1985. Methods of coping with social desirability bias: a review. *Eur. J. Soc. Psychol.* 15, 263–280.
- Ochsner, K.N., Gross, J.J., 2005. The cognitive control of emotion. *Trends Cogn. Sci.* 9 (5), 242–249.
- O'Doherty, J., 2004. Reward representations and reward-related learning in the human brain: insights from neuroimaging. *Curr. Opin. Neurobiol.* 14 (6), 769–776.
- Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9 (1), 97–113.
- Pessoa, L., Kastner, S., Ungerleider, L.G., 2002. Attentional control of the processing of neural and emotional stimuli. *Brain Res. Cogn. Brain Res.* 15 (1), 31–45.
- Phillips, M.L., Ladouceur, C.D., Drevets, W.C., 2008. A neural model of voluntary and automatic emotion regulation: implications for understanding the pathophysiology and neurodevelopment of bipolar disorder. *Mol. Psychiatry* 13(9) (829), 833–857.
- Ridderinkhof, K., van den Wildenberg, W., Segalowitz, S., Carter, C., 2004. Neurocognitive mechanisms of cognitive control: the role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning. *Brain Cogn.* 56 (2), 129–140.
- Rosenthal, R., 1976. *Experimenter Effects in Behavioral Research*. Irvington, New York.
- Rubia, K., Russell, T., Overmeyer, S., Brammer, M.J., Bullmore, E.T., Sharma, T., et al., 2001. Mapping motor inhibition: conjunctive brain activations across different versions of go/no-go and stop tasks. *Neuroimage* 13 (2), 250–261.
- Ryan, F., 2002. Detected, selected, and sometimes neglected: cognitive processing of cues in addiction. *Exp. Clin. Psychopharmacol.* 10 (2), 67–76.
- Schultz, W., Apicella, P., Scarnati, E., Jungberg, T., 1992. Neuronal activity in monkey ventral striatum related to the expectation of reward. *J. Neurosci.* 12 (12), 4595–4610.
- Schultz, W., Tremblay, L., Hollerman, J.R., 2000. Reward processing in primate orbitofrontal cortex and basal ganglia. *Cereb. Cortex* 10 (3), 272–284.
- Sethi, A., Mischel, W., Aber, J.L., Shoda, Y., Rodriguez, M.L., 2000. The role of strategic attention deployment in development of self-regulation: predicting preschoolers' delay of gratification from mother-toddler interactions. *Dev. Psychol.* 36 (6), 767–777.
- Shoda, Y., Mischel, W., Peake, P., 1990. Predicting adolescent cognitive and self-regulatory competencies from preschool delay of gratification: Identifying diagnostic conditions. *Dev. Psychol.* 26, 978–986.
- Tremblay, L., Schultz, W., 1999. Relative reward preference in primate orbitofrontal cortex. *Nature* 398 (6729), 704–708.
- Volkow, N.D., Fowler, J.S., Wang, G.J., Telang, F., Logan, J., Jayne, M., et al., 2010. Cognitive control of drug craving inhibits brain reward regions in cocaine abusers. *Neuroimage* 49 (3), 2536–2543.
- Vuilleumier, P., Armony, J.L., Driver, J., Dolan, R.J., 2001. Effects of attention and emotion on face processing in the human brain: an event-related fMRI study. *Neuron* 30 (3), 829–841.
- Wegner, D.M., Schneider, D.J., Carter III, S.R., White, T.L., 1987. Paradoxical effects of thought suppression. *J. Pers. Soc. Psychol.* 53 (1), 5–13.
- Williams, M.A., McClone, F., Abbott, D.F., Mattingley, J.B., 2005. Differential amygdala responses to happy and fearful facial expressions depend on selective attention. *Neuroimage* 24 (2), 417–425.
- Wylie, G.R., Javitt, D.C., Foxe, J.J., 2004. Don't think of a white bear: an fMRI investigation of the effects of sequential instructional sets on cortical activity in a task-switching paradigm. *Hum. Brain Mapp.* 21 (4), 279–297.