The Effects of Serotonin and Catecholamine Depletion on Attentional Control and Response Inhibition

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Declaration

I declare that this report does not incorporate without acknowledgement any material previously submitted for a degree in any University, College of Advanced Education, or other educational institution; and that to the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text.

I further declare that the ethical principles and procedures specified in the School of Behavioural and Social Sciences Human Research Ethics Committee document have been adhered to in the preparation of this report.

Name: Kirsty Scholes

Signed

______________________________
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To my family and friends, thank you for the support, understanding and encouragement throughout this hectic year. And to Glen, without your love, and understanding, I don’t think I would have remained so dedicated to this project.
Abstract

The present study aimed to expand upon our knowledge of the role of brain monoamines on executive functioning by exploring the effects of serotonin depletion, dopamine depletion, and combined monoamine depletion, on attentional control and response inhibition. Ten healthy male participants completed the Stroop task under four treatment conditions; a) placebo control treatment, b) tryptophan depletion treatment, c) tyrosine/phenylalanine depletion treatment, and d) combined monoamine depletion treatment. The prediction that under tryptophan depletion there would be decreased Stroop interference and reaction times was not supported. However, the hypothesis that there would be no difference in the number of errors made under tryptophan depletion was supported. In addition, it was found that there was no difference in facilitation under tryptophan depletion. Concerning tyrosine/phenylalanine depletion, the predictions that there would be increased interference and reaction times, were not supported. However, the hypotheses that there would be no difference in facilitation or the number of errors made, were supported. Furthermore, under combined monoamine depletion, no difference in any of the Stroop task measures was observed. It was concluded that attentional control and response inhibition, as assessed by the Stroop task, are not affected by modulation of dopamine or serotonin with the use of amino acid depletion techniques.
1.1 Overview

Schizophrenia is an acute and disturbing clinical disorder prevalent in approximately 1% of the world’s population (American Psychiatric Association, APA, 1994). In addition to the florid psychotic symptoms evident in most schizophrenic patients, there is also often severe disturbances to cognitive and executive functioning (Abi-Dargham, 2004; Andreasen, 1994). One such disturbance to executive functioning is an impaired ability to control attention and to inhibit irrelevant or unwanted responses in cognitive tasks (Andreasen, 1994; Barch, Cohen, & Carter, 2004; Kuperberg & Heckers, 2000). Although the actual etiology of schizophrenia and such cognitive symptoms is unknown, the catecholamine neurotransmitter dopamine has been specifically implicated in the pathophysiology for many years now, and more recently so too has the neurotransmitter serotonin (Abi-Dargham, 2004; Abi-Dargham, Laruelle, Aghajanian, Charney, & Krystal, 1997; Kapur & Remington, 1996).

Therefore, the present study intends to increase our understanding of the influence of these neurotransmitters on executive functioning, by modulating brain dopamine and serotonin in healthy participants. With an increased understanding of the consequences of specific neurochemical disturbances on
cognitive functioning in healthy participants, we are nearer to identifying the precise underlying disturbances associated with clinical disorders such as schizophrenia. Many researchers have investigated the effects of modulation of brain neurotransmitters on executive functions such as memory (Hughes, Gallagher, & Young, 2002; LeMarquand et al., 1998; Rubinsztein et al., 2001), however of particular importance to schizophrenia, there is little research investigating the effects of such modulations on attentional control and response inhibition. Thus the present study will attempt to provide clarification of the effects of neurochemical modulation on attentional control and response inhibition. The current paper will begin by introducing executive functioning and in particular the Stroop task; the means by which attentional control and response inhibition can be assessed. The literature detailing disturbances associated with schizophrenia will then be reviewed. Following will be a discussion of the process in which brain neurochemicals can be modulated, along with an exploration of the effects of such treatments on executive functioning.

1.2 Executive functions

Central to human autonomy and conscious experience is the ability to integrate and control cognitive functions (Royall et al., 2002). The term executive function has been increasingly employed in neuropsychology to
describe such processes, although exact operationalisation of this phrase has been somewhat under debate (Tranel, Anderson, & Benton, 1994). A comprehensive definition envisaged by Robbins (2000) describes executive functions as a number of cognitive control mechanisms that work to optimize performance in complex tasks. Many researchers consider executive function as comprising multiple components, and factor analytic studies differentiate these into four underlying factors (for a review see Royall et al., 2002). These four dimensions of executive function are thought to be: rule discovery as assessed by tasks such as the Wisconsin Card Sort Task; working memory as assessed by tasks such as the Tower of London; attention as assessed by measures such as the Continuous Performance Task; and response inhibition/attentional control as assessed by measures such as the Stroop Colour-Word Interference task (Royall et al., 2002).

1.3 Attentional control and response inhibition: The Stroop task

The Stroop Colour-Word Interference task is a traditional measure of attentional control and response inhibition which is used frequently in the cognitive science literature. In this task participants are presented with words printed in different ink colours and are told to name the print colour and to ignore the stimulus word. Since the classic study by Stroop (1935) there has been a plethora of literature examining traditional Stroop effects as well as
investigating the consequences of modifications to this basic paradigm (for a review see MacLeod, 1991). The task employed by Stroop (1935) and in many consequent studies, was that known as the card version (MacLeod, 1991). In the card version participants are presented with a series of cards, with each card containing only one type of stimulus. Participants are asked to consecutively name the ink colour of each stimulus on a particular card without stopping, thus the total time taken per card is viewed as a measure of performance for that particular type of stimulus (Henik & Salo, 2004; MacLeod, 1991; Stroop, 1935).

In more recent times of technological advance, researchers have employed different stimulus presentation methodologies (see MacLeod, 1991 for a review). The most commonly utilized version in the contemporary literature is that known as the single-trial version, and in this methodology stimuli are presented on a computer screen one at a time, in a random order (Henik & Salo, 2004; MacLeod, 1991). Participants are required to name the ink colour of the individual stimulus that is printed on the screen (Henik & Salo, 2004; MacLeod, 1991). Use of this task allows for measurement of response times to individual stimuli, as opposed to the summation of response times across the whole set of stimuli (Henik & Salo, 2004). This methodology is also advantageous as errors in naming stimuli can be omitted when
calculating mean response times to particular types of stimuli, whilst additionally these errors can be analyzed separately as variables of interest (Henik & Salo, 2004). This version of the Stroop task is also valuable in that it enables researchers to study both Stroop interference and Stroop facilitation (Henik & Salo, 2004; MacLeod, 1991; MacLeod & Dunbar, 1988), both of which will be discussed below.

The concept of *Stroop interference* was established in Stroop’s (1935) original investigation of colour-word interactions. In the Stroop task when the word and the ink colour conflict, that is they are incongruent (for example, the word red printed in blue ink), participants are slower to respond than when there is no such conflict (Stroop, 1935). This is termed interference and is a very robust effect (MacLeod, 1991). Interference is commonly thought to be the result of our strong automatic and obligatory predisposition for word reading over colour naming, which in turn disrupts our colour naming performance (MacLeod, 1991; MacLeod & Dunbar, 1988). Thus, interference is considered to occur at the perceptual stage of processing, as a function of selective attention (Mead et al., 2002). In contrast, the more recently observed phenomenon, referred to as *Stroop facilitation*, occurs when participants are faster to respond to stimuli when the colour is congruent with the semantic meaning of the word (for instance, the word red printed in red ink) than to
neutral stimuli such as patches of colour (Barch, Carter, Hachten, Usher, & Cohen, 1999a). Facilitation is considered to arise from the same mechanisms as interference; however as there is no conflict between the required colour naming response and the prepotent word reading response; there is a reduction in the total processing load. Accordingly, a reduction in interference occurs, and therefore processing is faster (Barch et al., 1999a; Burt, 2002). However, facilitation is considered to be a somewhat weaker phenomenon than interference. As a result occasionally some studies have only found a weak effect size for facilitation, whilst others have failed to find a significant facilitation effect at all in healthy participants (MacLeod, 1991)

1.4 Models of Stroop performance

Many researchers have attempted to provide theoretical models of Stroop task performance (for a review see MacLeod, 1991). In correspondence with Stroop’s (1935) interpretation of his original data, the relative speed of processing view of Stroop performance was one of the earlier accounts provided to explain the Stroop effect (Cattell, 1886; MacLeod, 1991). This view posits that words are read faster than colours are named. Therefore, when two potential responses compete for production, such is the case when naming the ink colour of the incongruent stimuli, the increased time resulting from this competition is what we term interference (MacLeod, 1991). However, upon
review of the literature and in light of more contemporary work which manipulates factors such as practice, thus in turn influencing relative speed of processing; many researchers have rejected this view as an appropriate theoretical basis to the Stroop effect (see MacLeod, 1991 for a review).

Alternatively, the automaticity account of the Stroop effect, which originates from Cattell’s (1886) early work, proposes that processing one dimension of the stimulus, namely the ink colour, requires much more attentional allocation than does reading of the irrelevant word (MacLeod, 1991). Accordingly, congruent stimuli are named more automatically, and thus faster, than incongruent stimuli. However, this theory too fails to provide an accurate and comprehensive account of the numerous Stroop findings that manipulate the traditional paradigm, particularly those in which there is altered stimulus expectancies and stimuli proportions (for a review see MacLeod, 1991).

In order to account for the deficits in previous theoretical accounts of Stroop processes, Cohen, McClelland and Dunbar (1990b) proposed a Parallel Distributed Processing (PDP) account of Stroop performance which included many of the merits of the previous models but few of the limitations (MacLeod, 1991). This comprehensive and popular connectionist model adopts the idea that processing in the system occurs by activation moving along pathways of different strengths. Therefore in contrast to previous models, strength rather
than speed is of importance in this model (Cohen et al., 1990b). This processing system is comprised of interconnected modules, and within these modules are continuously operating processing units which accept inputs from other units and provide output (Cohen et al., 1990b). An illustration of the PDP model is given below.

Figure 1. Diagrammatic representation of the parallel distributed processing model of Stroop task processing (Cohen et al., 1990b)

As can be seen in Figure 1, individual processing units in the PDP system can be constituents of more than one pathway, which consequently
allows for interactions between processes when the pathways intersect. Furthermore overlapping pathways mediate word reading and colour naming (Cohen et al., 1990b). The phenomenon of Stroop interference is consequently theorized to occur when two pathways are operating concurrently and produce conflicting activation at their intersection (Cohen et al., 1990b). Conversely, when the two pathways have corresponding activation at their intersection, Stroop facilitation is proposed to occur (Cohen et al., 1990b).

Furthermore, our inherent tendency for word reading over colour naming resulting from prior experience (MacLeod, 1991), is represented in the model by stronger pathways for those involved in reading. This in turn helps to facilitate processing in colour naming pathways when the ink colour and semantic meaning of the word are congruent, but conversely interferes with colour naming when ink colour and semantic meaning are incongruent (Cohen et al., 1990b). In addition, given that word reading is inherently more predisposed than colour naming (MacLeod, 1991), attention needs to be intentionally directed towards weaker pathways in order for the naming of incongruent stimuli to occur (Cohen et al., 1990b). Thus, attention is able to modulate the responsiveness of the system, and consequently with practice, the pathways for efficient responding can be learned. In this way, the strength of
colour naming pathways can be increased, thereby improving performance (Cohen et al., 1990b).

Through the application of simulations, this parallel distributed processing model of Stroop performance has been revealed to be able to account for numerous empirical observations, such as Stroop set size effects (Cohen, McClelland, & Usher, 1998) learning effects on Stroop performance (Cohen et al., 1990b), the time course of Stroop processing (Cohen et al., 1990b), the asymmetry of the Stroop processes of facilitation and interference (Lindsay & Jacoby, 1994), and response set effects (Cohen et al., 1990b). Thus, it appears that the parallel distributed processing model of Stroop effects (Cohen et al., 1990b) is a successful model of Stroop performance. Nonetheless it is recognized that there may be deficits in the theorizing and modeling which will require updating as more contemporary research is presented (Cohen et al., 1998)

1.5 *Neural correlates of Stroop task performance*

With the inception of functional neuroimaging techniques such as functional magnetic resonance imaging (fMRI) there has been increasing interest in uncovering the exact brain regions responsible for Stroop task processing. An overwhelming number of neuroimaging studies have found
specific activation of the anterior cingulate cortex and the inferior prefrontal cortex to be associated with performance during the Stroop task (Bench et al., 1993; Carter, Mintun, & Cohen, 1995; Harrison et al., 2005; MacLeod & MacDonald, 2000; Mead et al., 2002). In accordance with such observations, the anterior cingulate has been theorized to be associated with the monitoring and control of conflict in information processing (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Botvinick, Cohen, & Carter, 2004)

1.6 Clinical disorders: Disturbances in attentional control and response inhibition

Many clinical disorders have disturbances in executive functioning, and these disturbances are reflected in the neuropsychological tests that measure such functions. Schizophrenia is characterized by positive symptoms, negative symptoms and cognitive symptoms (Abi-Dargham, 2004). Disturbances in selective attention and cognitive control have long been regarded as a fundamental aspect of the cognitive deficits in schizophrenia (Andreasen, 1994; Barch et al., 2004; Kuperberg & Heckers, 2000). Accordingly, these disturbances are reflected in the Stroop task findings. Previous research utilizing the card version of the Stroop task has indicated that schizophrenic patients display increased interference relative to healthy controls (Baxter & Liddle, 1998; Brebion, Smith, Gorman, & Amador, 1996; Hanes, Andrewes,
Smith, & Pantelis, 1996; McGrath, Scheldt, Welham, & Clair, 1997). These findings have been directly related to the selective attention deficits evident in schizophrenia in which the patients have trouble attending to each specific stimulus on the card containing multiple stimuli (for a review see Henik & Salo, 2004).

However, with the growing number of researchers employing the single trial version of the Stroop task, contrasting evidence has been put forth regarding the exact nature of Stroop deficits in schizophrenia. Specifically, abundant research suggests that schizophrenic patients exhibit increased facilitation and an increased number of errors; but have no difference in interference, when compared to healthy control participants on the single-trial version of the Stroop task (Barch et al., 1999a; Barch et al., 1999b; Barch et al., 2004; Carter, Robertson, & Nordahl, 1992; Chen, Wong, Chen, & Au, 2001; Henik et al., 2002; Nordahl et al., 2001; Perlstein, Carter, Barch, & Baird, 1998; Taylor, Kornblum, & Tandon, 1996). In light of these findings, it has been suggested that the single trial Stroop task and the card Stroop task tap into slightly different processes (Henik & Salo, 2004). As such in the single trial, attentional control and response inhibition are only required for responding correctly to the stimulus; whereas in the card Stroop task attentional control and
response inhibition are required to both block out other stimuli and respond to the correct dimension of each stimulus (Henik & Salo, 2004).

A number of hypotheses have been put forth regarding the exact underlying deficits causing these disturbances in Stroop performance in schizophrenic patients. These such suggestions include the influence of increased automatic spreading activation (Barch et al., 1999b), the general slowing of responses due to word reading (Carter et al., 1992), the influence of an increase in errors (Barch et al., 1999a) or the influence of response set deficits (Barch et al., 1999a). However only one hypothesis has withstood the rigorous tests provided by more contemporary researchers. Thus, it is commonly accepted that the increase in facilitation and errors observed in schizophrenia is due to the patients having deficits in context processing (Barch et al., 1999a; Barch et al., 1999b; Barch et al., 2004; Henik et al., 2002; Henik & Salo, 2004). Context processing is defined as the internal representation of what the task instructions involve, and this function is thought to be localized to prefrontal brain regions (Barch et al., 1999a; Henik et al., 2002). Accordingly, schizophrenic patients are thought to have a decreased ability to use context to overcome the prepotent tendency for word reading. Therefore, when word information is congruent with the ink colour, processing is faster simply because the patients are just reading the word. In contrast, interference is
manifest as an increased number of errors due to this inability to inhibit responding automatically to the word rather than the colour. Thus essentially, it is suggested that dysfunctions in attentional control and response inhibition are responsible for the Stroop task findings.

These disturbances of attentional control in schizophrenic patients are thought to arise from underlying neurochemical dysfunctions in the frontal cortex of the brain. Traditionally, dysfunction of the dopamine system has been primarily implicated in the pathology of schizophrenia. Whilst positive symptoms, such as hallucinations, are generally thought to arise from excessive dopamine release subcortically; both negative symptoms and cognitive symptoms are thought to arise from dysfunction of the dorsolateral prefrontal cortex, resulting in deficient cortical dopamine (for comprehensive reviews see Abi-Dargham, 2004; Laurelle, 1998, 1999). Evidence for such disturbances comes from a multitude of neuroimaging studies (for a review see Laurelle, 1998, 1999) as well as from the observations indicating that typical antipsychotic medications, which are dopamine antagonists, lead to an improvement in positive symptoms but seem to have no reliable effects on negative or cognitive symptoms (for a review see Egan & Weinberger, 1997).
In accordance with these contentions, Cohen and Servan-Schreiber (1992) attempted to provide a model which demonstrated the link between dopamine disturbances and Stroop task disturbances in schizophrenia. This model has more recently been updated by Braver, Barch and Cohen (1999) to specifically explain the link between context representations, dopamine and Stroop performance. The model suggests that dopamine acts as a gating mechanism, and by preserving or increasing the signal-to-noise ratio in the prefrontal cortex, dopamine can help to augment context representations against a background of attentional noise. Therefore with a stronger contextual representation it is easier to keep this present in the mind when completing the task over time, and thus allows for more successful control over the prepotent response tendency of word reading. Hence, according to this model, the proposed deficit in prefrontal cortical dopamine in schizophrenia results in the breakdown of context representations, and consequently a disturbance in Stroop task performance is the result.

Recently, the therapeutic success of newer atypical antipsychotics, which block serotonin receptors (Kahn et al., 1993), has focused researchers attention on the serotonergic system and its interaction with the dopaminergic system in the pathophysiology of schizophrenia (Kapur & Remington, 1996). It is proposed that serotonin plays a role in schizophrenia through its inhibitory
influence on both the firing of dopaminergic cells, and on the synaptic release of dopamine in the cortex (for a review see Kapur & Remington, 1996). Thus given the inhibitory effects of serotonin on the dopaminergic system; decreasing serotonin with the use of atypical antipsychotics in schizophrenic patients would consequently lead to an increase in cortical dopamine, and thus the observed decrease in negative symptoms due to the rebalance in cortical dopamine (Kapur & Remington, 1996). Hence, it seems that in schizophrenia there is a disturbance in both serotonin and dopamine (Abi-Dargham et al., 1997). Thus, it is commonly accepted that an interaction between dopamine and serotonin is a plausible explanation for the symptoms of schizophrenia; particularly the negative and cognitive symptoms (Abi-Dargham et al., 1997).

In summary, it appears that in schizophrenia Stroop task processing is disturbed due to dysfunctional attentional control and response inhibition. Furthermore, it is proposed that the cognitive symptoms of schizophrenia are due to dysfunctional neurotransmission of dopamine and serotonin in the brain. Given that Stroop task processing appears to involve brain areas which are thought to possess dysfunctional neurotransmission in schizophrenia, it is proposed that the disturbances in Stroop processing evident in schizophrenia are as a result of the disturbances in neurotransmission. However, the exact manner in which dopamine and serotonin influence cognitive processing is yet to be
established. An approach which can be used to investigate the exact influence of brain neurotransmitters on cognitive function will be detailed below.

1.7 Modulation of neurochemistry in non-clinical populations

In healthy participants, the monoamines dopamine and serotonin can be modulated to investigate the precise effects of different neurochemical disturbances on human functioning. In particular, modulation of brain neurochemistry in healthy populations can help us to identify the exact nature of the cognitive dysfunctions underlying clinical disorders such as schizophrenia. Modulation of human brain monoamines can be achieved by the administration of receptor agonists and antagonists or the use of inhibitory enzymes; however the most globally effective method that appears to acutely alter central neurotransmission, is that known as amino acid depletion (Hood, Bell, & Nutt, 2005).

The synthesis of brain monoamine neurotransmitters is contingent on the availability of their specific precursors circulating in the blood, therefore the amino acid depletion techniques are based on the premise that acute restriction of the specific precursors decreases the release of the corresponding neurotransmitters (Harrison, Olver, Norman, & Nathan, 2002; Hood et al., 2005; Reilly, McTavish, & Young, 1997; Young, Smith, Phil, & Ervin, 1985).
The availability of precursors to the brain can be reduced by the acute administration of an amino acid load selectively deficient of these precursors (Oldendorf & Szabo, 1976; Pardridge, 1977). There are two main amino acid depletion techniques aimed at depleting different brain neurotransmitters. Tryptophan is the precursor for the production of serotonin, thus tryptophan depletion is directed at depleting global brain serotonin. Conversely, tyrosine and phenylalanine are the precursors for the production of dopamine; thus tyrosine/phenylalanine depletion is aimed at depleting global brain dopamine.

In these depletion techniques, participants ingest a suspension of amino acids, with tryptophan excluded in the serotonin depleting suspension; and both tyrosine and phenylalanine excluded in the dopamine depleting suspension. Administration of the amino acid suspension depletes the precursors by (a) increasing protein synthesis in the body thereby removing the precursors from the blood; and (b) increasing competition with other large neutral amino acids, for active precursor transport into the brain (Fadda, 2000; Oldendorf & Szabo, 1976; Reilly et al., 1997).

In humans, acute tryptophan depletion has been shown to decrease plasma tryptophan levels by as much as 90% after four to seven hours (for a review see Moore et al., 2000; Reilly et al., 1997). Furthermore, considerable
decreases in serotonin metabolites (Carpenter et al., 1998; Williams, Shoaf, Hommer, Rawlings, & Linnoila, 1999) as well as in serotonin synthesis (Nishizawa et al., 1997) have been observed after tryptophan depletion. These findings all offer evidence that tryptophan depletion decreases serotonin function in the brain.

Similarly, acute tyrosine/phenylalanine depletion has been shown to produce reductions in plasma tyrosine and phenylalanine levels (Moja, Lucini, Benedetti, & Lucca, 1996); as well as reductions in catecholamine metabolites (Palmour, Ervin, Baker, & Young, 1998) and decreases in catecholamine synthesis and release (Jaskiw & Bongiovanni, 2004; Leyton et al., 2004; S. F. McTavish, Cowen, & Sharp, 1999; Mehta, Gumaste, Montgomery, McTavish, & Grasby, 2005; Montgomery, McTavish, Cowen, & Grasby, 2003). Therefore, these findings all present evidence in support of the assertion that tyrosine/phenylalanine depletion reduces dopamine function in the brain.

1.8 Cognitive consequences of serotonin modulation

Numerous researchers have investigated the effects of the different depletion techniques on various aspects of cognition, learning and executive functioning (Evers et al., 2005; LeMarquand et al., 1998; Mehta et al., 2005; Rubinsztein et al., 2001; Sobczak et al., 2002). Using the tryptophan depletion
procedure, the Stroop task has only been investigated a handful of times with somewhat mixed findings. The most recent study that investigated the effects of tryptophan depletion on Stroop task performance also included functional magnetic resonance imaging (fMRI) during the task to assess brain activations. This study by Horacek et al. (2005) employed a 100g amino acid suspension to deplete tryptophan, but failed to find any behavioural changes in performance on a blocked card version of the Stroop task. However, changes in brain activation associated with Stroop task performance were observed after tryptophan depletion, which was interpreted to signify evidence for central depletion of serotonin. However the researchers suggested their lack of behavioural findings may have been due to the fact that their participants exhibited superior Stroop performance compared to population norms.

Similarly, a study by Sobczak et al. (2002) did not find any significant effects of tryptophan depletion on Stroop task performance measures such as interference and reaction time. However, the researchers did note a trend towards increased attention following depletion, that is they observed that mean interference tended to decrease, although this was not significant. It was suggested that the failure for this trend to reach significance was possibly due to the heterogeneous population included in the study. More specifically, this study included participants with a wide age range and some who had family
histories of psychiatric illness; all of which could have had differential effects on Stroop task performance. Similarly, a study by Gallagher, Massey, Young and McAllister-Williams (2003) seemed to find an analogous improvement in Stroop task performance after tryptophan depletion, however this study suffered from severe methodological flaws with practice effects inhibiting accurate and confident interpretation of their results.

Thus, to date only one methodologically sound study has been presented which provides evidence in line with the action of atypical antipsychotic medications in schizophrenic patients; that is that a decrease in serotonin function results in improved cognition. This study by Schmitt and colleagues (2000) provided well founded research that documented changes in Stroop task performance after tryptophan depletion. These researchers used a 100g amino acid mixture and participants completed the card version of the Stroop task (among other tasks) at five hours after ingestion of the amino acids. The researchers found that after tryptophan depletion, participants demonstrated less Stroop interference as well as faster reading times for both the incongruent and neutral cards, when compared to the placebo control condition. The number of errors made on the task however was not affected by tryptophan depletion.
Schmitt and colleagues (2000) suggested that this improved reaction time and interference performance could be attributed directly to the reduction in serotonergic function that is assumed to occur after tryptophan depletion. More specifically, they proposed that with a reduction in serotonin, there is a decrease in the inhibitory actions of the serotonergic system on cortical arousal and attention, as well as over other neurotransmitters such as dopamine. Therefore, with the decrease in inhibitory function over dopamine, an increase in dopaminergic function would occur, and consequently an increase in attention would follow. Such reasoning is in accordance with the proposed action of serotonin in schizophrenia (Kapur & Remington, 1996). However as this study utilized a card version of the Stroop task, the effects of tryptophan depletion on facilitation was not addressed.

A number of other studies using alternative neuropsychological measures of attention, have observed findings which they have paralleled with the findings of Schmitt et al. (2000) (Riedel, Klaassen, & Schmitt, 2002; Rubinsztein et al., 2001). One such study is that undertaken by Hughes, Gallagher and Young (2002) which explored the effects of tryptophan depletion on the cognitive function of euthymic bipolar patients. These researchers utilized a 100g amino acid drink, and participants were required to complete a task of vigilance four hours after administration of the amino acid mixture.
This study found that reaction times in the vigil task significantly slowed over time following the placebo control amino acid mixture (that is performance was poorer); there was however no such deterioration after the tryptophan depletion mixture. Thus a contention was put forward that tryptophan depletion maintained and improved attention. As mentioned previously, the researchers attributed these findings to the mechanism described by Schmitt et al. (2000); that is the removal of the inhibitory actions of serotonin in the cortex as a result of the reduced levels of tryptophan and serotonin. Nevertheless, the researchers did admit that this reasoning was somewhat speculative.

Taken together, the above findings suggest that attention, and as a result Stroop task performance, is improved after tryptophan depletion. This leads to the inference that decreased serotonergic function in the human brain results in increased attentional control and thus resulting in improved Stroop task performance, manifest in decreased reaction times and Stroop interference. These findings are perhaps through serotonin’s influence on other monaminergic neurotransmitters such as dopamine.

1.9 Cognitive consequences of catecholamine modulation

Tyrosine depletion, in comparison to tryptophan depletion, is a relatively newer technique, and as a result there is limited research investigating
its effects on cognition and executive functioning. Similarly, to our knowledge, there exists no research that investigates specifically the effects of tyrosine and phenylalanine depletion on Stroop task performance in healthy participants. Therefore, although different measures of executive function arguably are affected differentially by the depletion paradigms (Mehta, Sahakian, McKenna, & Robbins, 1999), it may useful to examine some recent studies which investigate tyrosine and phenylalanine deletion and its implications for executive functioning.

One such novel study by Mehta, Gunmaste, Montgomery, McTavish and Grasby (2005) examined the effects of tyrosine depletion on neuropsychological measures of working memory and planning. These researchers also investigated striatal [11C] raclopride binding in the brain after tyrosine depletion. This technique enables a marker of dopamine to be investigated, and thus levels of striatal dopamine can be established in each participant. The researchers found decreased performance on the measure of planning (the Tower of London task) as well as decreased spatial working memory performance, were associated with increased [11C] raclopride bindings, which is indicative of decreased brain dopaminergic activity. Accordingly these findings suggest that performance on numerous measures of
executive functioning was compromised when brain dopamine levels were decreased after tyrosine and phenylalanine depletion.

Similarly, Grevet et al. (2002) administered a number of mood, attention and memory measures to participants five hours after tyrosine and phenylalanine depletion and found that depletion resulted in decreased performance on the neuropsychological test of memory. However, contrastingly Lythe, Anderson, Deakin, Elliot and Strickland (2005) employed similar methodology and found no significant differences in performance on similar tasks of executive functioning.

Although there is limited research probing dopaminergic function with the use of tyrosine and phenylalanine depletion to examine the consequent effects on cognition; there are numerous researchers who have investigated the cognitive effects of dopamine agonists and antagonists as probes of dopaminergic function. Mehta et al. (1999) conducted such a study in which they investigated the effects of sulpiride (a dopamine antagonist) on cognitive functions such as learning, attentional set shifting and spatial memory. It was found that learning, set shifting, planning abilities and spatial recognition were all impaired after the administration of sulpiride. These deficits were however predominantly observed in the first testing session when the tasks were
relatively novel to the participants. These findings do nevertheless suggest that decreased dopaminergic function in the brain results in decreased cognitive and executive functioning.

Similarly, Luciana and Collins (1997) utilized bromocriptine (a dopamine D₂ agonist) and haloperidol (a dopamine antagonist) to investigate the effects of differing dopamine manipulations on object and spatial working memory. Consistent with the findings of Mehta et al. (1999), it was found that spatial working memory performance was facilitated by an increase in dopaminergic functioning associated with the administration of bromocriptine; whilst there was impairment to spatial working memory by the decrease in dopaminergic functioning associated with the administration of haloperidol. Thus this again provides support for the contention that decreased brain dopaminergic function results in decreased executive function performance. These researchers however found no such effects on object working memory suggesting that although alterations to performance can occur with alterations to dopamine functions, these effects are very specific and are only evident in certain processes and certain tasks.

This specificity in neurochemical effects is also evident in a similar study conducted by Kimberg, D’Esposito and Farah (1997). These researchers
administered bromocriptine to participants who were then required to complete a speeded and more difficult version of the Wisconsin Card Sort Task (WCST), a measure of set shifting. It was found that participants with high working memory capacity performed poorer after administration of bromocriptine; whilst for low working memory capacity participants performance was improved.

Thus, due to these inconsistent findings, the recent study by Roesch-Ely et al. (2005) sought to clarify the effects of different dopaminergic modulations on executive functioning. This study is of particular importance to the current research as it was one of few studies which included the Stroop task in its battery of neuropsychological tests. Participants were administered bromocriptine and were then required to complete a number of tasks, one of which was a single-trial version of the Stroop task. The researchers found that when compared to the placebo treatment, after bromocriptine treatment participants demonstrated decreased Stroop interference while there was no difference in facilitation. In addition, there was no difference in the number of errors made between the two conditions. Hence, these findings suggest that Stroop task performance is improved by increasing dopaminergic function in the brain. However, dopamine modulation appears to have no effect on facilitation.
Likewise, Barch and Carter (2005) adopted a slightly different technique to probe dopaminergic functioning while finding coherent results. These researchers administered D-amphetamine, which increases brain dopamine functioning, to healthy individuals. Participants were required to complete a single-trial version of the Stroop task, and it was found that after amphetamine participants demonstrated faster reaction times on the Stroop task, when compared to performance under the placebo control treatment. There were however no differences in facilitation or interference effects. Thus participants appeared to be performing more rapidly with increased brain dopaminergic functioning, however the pattern of Stroop effects was not altered under this state.

Taken together, these findings using different dopaminergic probes can be used to make inferences about Stroop task performance after tyrosine and phenylalanine depletion. Accordingly, it would appear that decreasing dopamine function using tyrosine depletion would result in poorer performance, manifest as increased Stroop interference and reaction times. This is in line with the previously observed disturbance in neuropsychological performance associated with decreased dopamine (Luciana & Collins, 1997; Mehta et al., 2005), and is the inverse of the findings suggesting improved performance with increased dopaminergic function (Barch & Carter, 2005; Roesch-Ely et al.,
2005). However, evident from the above discussion, facilitation and the number of errors made on the task appear to be insensitive to dopamine modulation.

1.10 A new technique for modulating catecholamines and serotonin simultaneously

Recently a new technique has been developed and validated which depletes tryptophan, phenylalanine and tyrosine simultaneously (Nathan, Hughes, McInerney, & Harrison, 2004). Upon validation of this combined monoamine depletion technique, it was found that plasma levels of all three precursors were significantly reduced to levels that are expected to affect brain monoamine function (Nathan et al., 2004). Therefore it is assumed that this method is able to deplete serotonin and dopamine concurrently (Nathan et al., 2004). As mentioned previously, dopamine and serotonin are both implicated in the pathophysiology of schizophrenia (Kapur & Remington, 1996), thus this new technique is a valuable tool in that it enables examination of the effects of simultaneous dopamine and serotonin depletion. With increased knowledge of the interaction of these two neurochemicals, and their combined effects on executive functioning, we may gain more insight into the underlying dysfunctions that are thought to cause the cognitive disturbances in clinical disorders such as schizophrenia.
As this combined monoamine depletion technique is novel, there is very limited research into its effects on cognitive and executive functioning. To our knowledge there is only one study that investigates the cognitive effects of combined monoamine depletion, however this study did not include the Stroop task in its battery of tests. This research by Matrenza et al. (2004) did nevertheless include a measure of vigilance which could possibly be comparable to processing associated with the Stroop task. After the combined monoamine depletion, it was found that participants demonstrated decreased accuracy and increased reaction time on this task. Thus it appears that the combined depletion was detrimental to sustained attention and vigilance. Further research is required to extend these findings and examine the effects of the combined monoamine depletion technique on other measure of executive functioning, such as the Stroop task.

1.11 Research aims and hypotheses

Following from the above discussion, the current study aimed to clarify previous research by investigating the effect of tryptophan deletion, and tyrosine/phenylalanine depletion on attentional control and response inhibition using the Stroop Colour-Word Interference task. It was also of aim to investigate for the first time the effects of combined monoamine depletion on
Stroop task performance. The current study will use a repeated measures design to test the following hypotheses.

1.11.1 Tryptophan depletion. Evident from the preceding discussion, the hypotheses regarding tryptophan depletion are drawn from the findings of Schmitt et al. (2000) and the proposed effects of the serotonergic system on cortical dopamine. Thus it was hypothesized that when compared to the placebo control treatment, after tryptophan depletion participants would exhibit
(a) decreased Stroop interference, with interference conceptualized as a significantly longer reaction time to incongruent stimuli than neutral stimuli
(b) no difference in the number of errors made during the Stroop task,
(c) decreased reaction times to neutral, congruent and incongruent stimuli

Due to the absence of previous research concerning Stroop facilitation and tryptophan depletion, no specific hypotheses were made; however it was a research aim to investigate whether there was any change in Stroop facilitation under tryptophan depletion, when compared to the placebo control treatment. Stroop facilitation will be conceptualized as a significantly faster reaction time to congruent stimuli than to neutral stimuli

1.11.2 Tyrosine/phenylalanine depletion. The following hypotheses regarding tyrosine depletion are driven by the combined findings of Roesch-Ely
et al. (2005) and Barch and Carter (2005) who noted changes to Stroop performance after modulation of dopamine in healthy participants. Hence, it was predicted that after tyrosine/phenylalanine depletion, when compared to the placebo control treatment participants would exhibit
(a) increased Stroop interference,
(b) no difference in Stroop facilitation
(c) no difference in the number of errors made
(d) increased reaction times to congruent, incongruent and neutral stimuli

1.11.3 Combined monoamine depletion. Due to a lack of previous research, the current study posed a research question that entailed investigating the effects of combined monoamine depletion on attentional control and response inhibition using the Stroop task
Chapter 2: Method

2.1 Participants

The sample of the current study comprised 10 healthy non-smoking male participants, aged 21-38 years (M=26.30 years, SD=5.01 years). Seven additional male participants began involvement in the study, but after one testing session (n=6) or two testing sessions (n=1) they withdrew due to adverse side effects from the amino acid treatments. Furthermore, one other participant completed involvement in the study, but was excluded because of >30% missing values. The inclusion of only male participants was in accordance with previous research suggesting that there may be gender differences in serotonin metabolism (Bell, Abrams, & Nutt, 2001; Nishizawa et al., 1997). Additionally, males rather than females were chosen due to the extended time commitment involved with testing female participants at the same time in the menstrual cycle for each testing session (Harrison et al., 2004).

Participants were recruited for the study through university advertisements, and were considered for inclusion if they were not currently taking any medications, had no personal or family history of psychiatric disorders, had no history of substance abuse, and had no history of head injury. All participants underwent a medical examination by a medical physician prior
to participation, in order to verify that they were physically and psychiatrically healthy and that they satisfied the inclusion criteria. Furthermore, all participants gave written informed consent for participation in the study, which was approved by the Swinburne University Human Research Ethics Committee.

2.2 Study Design

The present study employed a double blind, placebo controlled, repeated measures design in which participants were tested under four treatment conditions, these being: (a) 100g nutritionally balanced placebo control treatment, (b) tryptophan depletion treatment, (c) tyrosine and phenylalanine depletion treatment, and (d) tyrosine, tryptophan and phenylalanine depletion treatment (combined monoamine depletion). Individual assignment for the order of completion of each treatment condition was randomized according to a Latin square design, and each treatment condition was separated by a minimum 7-day washout period for each participant.

2.2.1 Amino acid mixture composition. The amino acid mixtures were based on the 100g balanced mixture developed by Young, Smith, Phil and Ervin (1985). In the current study, the balanced placebo control mixture consisted of 5.5g of L-alanine, 3.2g of glycine, 3.2g of L-histidine, 8.0g of L-isoleucine, 13.5g of leucine, 11.0g of L-lysine monohydrochloride, 5.7g of L-
phenylalanine, 12.2g of L-proline, 6.9g of L-serine, 6.5g of L-threonine, 2.3g of L-tryptophan and 6.9 g of L-tyrosine. L-Arginine (4.9g), L-cysteine (2.7g) and L-methionine (3.0g) were encapsulated in 18 gelatin capsules and were administered separately due to their unpleasant taste. All treatment mixtures were identical in composition to the balanced mixture, however in the tryptophan depletion condition the mixture was deficient of L-tryptophan; in the tyrosine depletion condition the mixture was deficient of L-tyrosine and L-phenylalanine; and in the combined monoamine depletion condition the mixture was deficient of L-tryptophan, L-tyrosine and L-phenylalanine (Nathan et al., 2004).

2.3 Materials

The current study employed the Stroop Colour-Word Interference Test to measure attentional control and response inhibition. The Stroop task used in this study was in accordance with the task designed by Barch, Carter, Hatchen, Usher and Cohen (1999a) to investigate disturbances in Stroop performance associated with schizophrenia. This task was a single trial version which consisted of 96 trials; with 24 (25%) congruent trials, 24 (25%) incongruent trials, and 48 (50%) neutral trials. Each trial consisted of a stimulus printed in one of four colours: red, green, blue or purple. The congruent stimuli consisted of each of the four colour names printed in its own colour (e.g. the word red
printed in red ink). The incongruent stimuli comprised each of the four colour words printed in one of the three remaining colours (e.g. the word red printed in blue ink). The neutral stimuli consisted of four colour unrelated words (dog, bear, tiger, monkey) presented in one of the four colours. These neutral words were from a single semantic category in order to eliminate semantic confounds (MacLeod, 1991). Additionally, these neutral words matched the response set colour words in terms of number of letters and frequency of occurrence in the English language (Francis & Kucera, 1982).

The use of these animal words as the neutral stimuli, rather than patches of colour, was due to previous research suggesting that these neutral stimuli are fairly robust in eliciting a significant facilitation effect in healthy participants (Barch & Carter, 2005; Barch et al., 1999a; Barch et al., 2004). This particular Stroop task has also been shown to reliably produce significant facilitation and interference effects in healthy participants and schizophrenic patients (Barch & Carter, 2005; Barch et al., 1999a; Barch et al., 1999b; Barch et al., 2004).

In each testing session, participants were seated 60 cm from a computer screen. Participants were told that they would be presented with a series of stimuli, one at a time, and that their task was to name the colour in which the stimulus was printed as quickly and accurately as possible (Barch et al., 1999a).
Each stimulus was presented on the screen for 2000 ms, and was then replaced by a fixation cross for 2000 ms. Regardless of the participant’s reaction time to respond, a new trial began 4000 ms after the onset of the previous stimulus. This presentation was employed to ensure the task was a fixed pace for all participants (Barch et al., 1999a). Furthermore, presentation of the stimuli was in a pseudo random order.

Participants were required to wear a headset with an attached microphone that recorded (and relayed to the computer) the reaction time for onset of the verbal responses. The verbal responses were monitored for accuracy (with the recording of errors in the naming of ink colour) by the experimenter. Each participant also completed a short practice version of the task (consisting of 25 stimuli) on two occasions before testing on the day of the first treatment session. These practice sessions were included as both theoretical (Cohen, Dunbar, & McClelland, 1990a) and empirical (Mehta et al., 1999; Roesch-Ely et al., 2005) research highlights the importance of practice, and detriment to performance that can occur without practice on the Stroop task and other measures of executive function. A copy of the error recording sheet is included as Appendix A. The Stroop task and the practice Stroop task are included as Appendix B.
2.4 Procedure

On the day before each testing session, participants were required to adhere to a low protein diet, with their total protein consumption to be less than 20g (Young et al., 1985). In addition, participants were also required to fast from 19:00 hours that evening (with the exception of the consumption of water). This procedure has been employed in many previous studies as it has been suggested that it may enhance the effect of monoamine depletion and lessen the variability in baseline monoamine levels (Bel & Artigas, 1996; Bell et al., 2001; Harrison et al., 2004; Hood et al., 2005; Reilly et al., 1997). On arrival for testing at the Neuropsychopharmacology laboratory at the Brain Sciences Institute, participants signed the informed consent forms. Following this, participants were administered the amino acid drink and capsules. The powdered amino acids were mixed with 180 ml of orange juice a few minutes prior to oral administration. Participants consumed the 18 capsules, and then swallowed the amino acid suspension immediately after. The participants were advised to drink this as quickly as possible given the unfamiliar and unpleasant taste. Upon completion of administration of the amino acids, participants were provided with sugar free chewing gum and a glass of water to cleanse the mouth of the unpleasant tastes. The process of amino acid administration took approximately 10 minutes.
Participants were then required to rest for the following four hours, to enable depletion to occur. During this time, participants were allowed to consume water freely, but were refrained from any physical activity. At two hours post amino acid administration, participants were provided with a low protein snack of carrots and apples. At four hours post ingestion, participants completed the Stroop task which took approximately 10 minutes. This four hour latency period for testing was chosen to coincide with the timing of maximal monoamine depletion determined in previous research detailing the time course of monoamine depletion in rats (Bel & Artigas, 1996; S. F. B. McTavish, Callado, Cowen, & Sharp, 1999), human plasma (S. F. B. McTavish et al., 1999; Moja et al., 1996; Sheehan, Tharyan, McTavish, Campling, & Cowen, 1996) and cerebrospinal fluid (Carpenter et al., 1998; Williams et al., 1999).

Upon conclusion of the testing procedure, participants were provided with high protein snacks in order to replenish their amino acid levels. Participants resumed their normal diet between each of the testing sessions.
Chapter 3: Results

Preliminary data analysis was conducted initially to assess the data and prepare it for detailed analysis. Firstly, the data set was examined for the presence of any missing data. It was evident that one participant was missing all reaction time data under the tyrosine depletion treatment, and this constituted more than 30% missing data. Hence, this participant was excluded from the analysis. The data was then examined for deviations from normality and the presence of outliers. Boxplots and histograms with normal distribution curves were generated for the Stroop reaction time data, all of which appeared to be normally distributed. This was confirmed upon inspection of the Kolmogorov-Smirnov and Shapiro-Wilks statistics, and by examination of the skewness statistics at the critical value of 1.98.

However, the normality statistics for the error data of both the tryptophan and the combined monoamine treatments indicated that these variables were significantly skewed. Upon inspection of the boxplots for these error variables it was evident that each of these variables were skewed because of the presence of a number of outliers which were greater than three standard deviations away from the mean. Upon examination of the data set it was evident that the majority of participants had not made any errors under each of
the treatment conditions, and the participants who had made errors, made no more than one error under each treatment. Therefore, those participants who had made one error were consequently statistical outliers. However, these outliers were determined to be genuine as all errors were personally recorded and noted by the researchers. Thus it was evident that in terms of errors, there was somewhat of a ceiling effect in this Stroop task, in the current sample of healthy participants. Therefore, as the error data did not approximate interval level, and consequently was not normally distributed, it was therefore analysed non-parametrically.

After preliminary data screening, detailed data analysis was undertaken. Firstly, validation of the Stroop task used in the current study, in order to assess the presence of the basic Stroop effects of interference and facilitation, will be presented. This will be followed by the analysis of reaction times, Stroop interference and facilitation effects under each treatment condition. Lastly, the analysis of the number of errors made in the Stroop task, under each treatment condition, will be presented.

3.1 Stroop descriptives and validation of basic Stroop effects

To enable examination of the Stroop reaction time data, mean reaction times to each type of Stroop stimulus under each treatment condition were
generated, with the exclusion of those trials in which errors in naming were noted. These descriptive statistics are presented in Table 1.

**Table 1**  
*Means and Standard Deviations of Reaction Times to each Stroop Stimulus under each Treatment Condition*

<table>
<thead>
<tr>
<th>Treatment condition</th>
<th>Stroop Stimulus</th>
<th>$M$</th>
<th>$SD$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo control treatment</td>
<td>Incongruent</td>
<td>944.59</td>
<td>156.53</td>
</tr>
<tr>
<td></td>
<td>Congruent</td>
<td>835.32</td>
<td>132.88</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>863.00</td>
<td>169.49</td>
</tr>
<tr>
<td>Combined monoamine depletion</td>
<td>Incongruent</td>
<td>879.21</td>
<td>151.56</td>
</tr>
<tr>
<td></td>
<td>Congruent</td>
<td>809.10</td>
<td>138.62</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>825.70</td>
<td>144.58</td>
</tr>
<tr>
<td>Tryptophan depletion</td>
<td>Incongruent</td>
<td>906.71</td>
<td>180.74</td>
</tr>
<tr>
<td></td>
<td>Congruent</td>
<td>834.34</td>
<td>208.18</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>868.75</td>
<td>180.99</td>
</tr>
<tr>
<td>Tyrosine depletion</td>
<td>Incongruent</td>
<td>916.98</td>
<td>161.41</td>
</tr>
<tr>
<td></td>
<td>Congruent</td>
<td>863.44</td>
<td>173.52</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>882.32</td>
<td>176.11</td>
</tr>
</tbody>
</table>

$N=10$
In order to assess whether the task used the in the present study elicited the basic Stroop effects of interference and facilitation, a one way repeated measures ANOVA, with reaction times to the three types of Stroop stimuli (neutral, congruent and incongruent) as the within subjects factors; was conducted on the data from the placebo control treatment only. The use of only the control treatment data enabled elimination of any variance from the depletion treatments, in determining the presence of such Stroop effects. Prior to analysis, Mauchly’s test of sphericity was examined for violations to the assumption of homogeneity of covariance. This revealed no significant violation, thus sphericity was assumed in the subsequent inspection of the ANOVA. The inspection of the ANOVA revealed a significant main effect of stimulus type ($F(2,18)=12.95, p<.001, \text{partial } \eta^2=.59$). In order to further investigate this significant main effect, simple planned contrasts were carried out. These confirmed the presence of a significant Stroop interference effect ($F(1,9)=46.74, p<.001, \text{partial } \eta^2=.84$), however there was no significant Stroop facilitation effect evident ($F(1,9)=1.15, p>.05, \text{observed power}=.16$).

3.3 The treatment conditions and Stroop effects

To enable examination of whether the treatment conditions had any effect on Stroop interference, facilitation or reaction times in general, a
4 (treatment condition) by 3 (Stroop stimulus type) repeated measures ANOVA was conducted. Initial investigation of Mauchly’s test of sphericity indicated non-violation of the assumption of homogeneity of covariance; hence sphericity was assumed in the examination of the ANOVA results. The repeated measures ANOVA revealed no significant main effect of treatment ($F(3,27)=1.45, p>.05, \text{observed power}= .34$) indicating that there was no effect of the treatment conditions on Stroop stimuli reaction times; however there was a significant main effect of Stroop stimulus ($F(2,18)=16.11, p<.001, \text{partial } \eta^2=.64$). In addition, no significant treatment by Stroop stimulus interaction was evident ($F(6,54)=1.68, p>.05, \text{observed power}= .59$). In order to investigate the significant main effect of stimulus type, simple planned contrasts were performed. These indicated that overall across all treatments, there was no significant Stroop facilitation effect ($F(1,9)=2.39, p>.05, \text{observed power}= .28$), however there was a significant Stroop interference effect ($F(1,9)=51.83, p<.001, \text{partial } \eta^2=.85$).

3.4 The treatment conditions and Stroop error rates

As participants in the current study only made errors in naming the incongruent stimuli, there was no need to investigate differences in the number of errors made, to the different types of stimuli. Therefore, the present study
will examine errors in general, rather than to specific types of stimuli. Thus, in order to assess any differences between the depletion treatments and placebo control treatment, in the number of errors made on the Stroop task, a non parametric one way repeated measures ANOVA (Friedman’s test) was conducted with the number of errors made under each treatment as the within subjects variable. The means and standard deviations of this analysis are presented in Table 2.

Table 2

*Means and Standard Deviations of the Number of Errors made during the Stroop Task under the Different Treatment Conditions*

<table>
<thead>
<tr>
<th>Treatment Condition</th>
<th>$M$</th>
<th>$SD$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo control treatment</td>
<td>.36</td>
<td>.51</td>
</tr>
<tr>
<td>Combined monoamine depletion</td>
<td>.18</td>
<td>.41</td>
</tr>
<tr>
<td>Tryptophan depletion</td>
<td>.18</td>
<td>.41</td>
</tr>
<tr>
<td>Tyrosine depletion</td>
<td>.36</td>
<td>.51</td>
</tr>
</tbody>
</table>

$N=10$
This analysis revealed no significant difference in the number of errors made on the Stroop task, between any of the treatment conditions ($\chi^2(3)= 2.40$, $p>.05$).
4.1 Overview of research aims and findings

The aim of the current study was to expand upon our understanding of the role of monoamines in executive functioning, by exploring the effects of serotonin depletion, with the use of tryptophan depletion; dopamine depletion, with the use of tyrosine/phenylalanine depletion; and combined monoamine depletion, on attentional control and response inhibition in healthy participants, using the Stroop task.

The findings of the current study were in partial support of the hypotheses. The prediction that under tryptophan depletion participants would demonstrate decreased Stroop interference, when compared to the control treatment, was not supported. Similarly, the hypothesis that tryptophan depletion would result in a decrease in reaction times to all types of stimuli, when compared to reaction times under the control treatment, also failed to gain support. Furthermore, as no previous research has addressed the effects of tryptophan depletion on Stroop facilitation, exploration of this was attempted in the current study. It was found that there was no difference in facilitation between the control and tryptophan depletion treatments. Additionally, as anticipated there was no difference in the amount of errors made in the Stroop
task, between the control and tryptophan treatments, however this should be interpreted with caution as will be addressed below.

Regarding tyrosine/phenylalanine depletion, the prediction that under the tyrosine depletion treatment participants would demonstrate increased Stroop interference, when compared to the control treatment, did also not gain support. Furthermore, the prediction that reaction times to all Stroop stimuli would be increased under tyrosine depletion when compared to the control treatment was also not supported. However, as anticipated there was no difference in Stroop facilitation or the number of errors made during the task, between the tyrosine depletion and control treatments. Once again, these findings concerning errors must be considered carefully, as will be discussed below.

Finally, the exploration for any differences in Stroop performance after combined monoamine depletion revealed no difference in Stroop interference, Stroop facilitation, reaction times to Stroop stimuli, or the number of errors made; between the placebo control treatment and the combined monoamine depletion treatment. The findings concerning each depletion treatment will be addressed separately in full detail below.
4.2 Serotonin depletion and Stroop task processing

In the current study, depletion of serotonin with the use of tryptophan depletion had no effect on Stroop interference or reaction times to Stroop stimuli, when compared to the control condition. These findings are inconsistent with the findings of Schmitt et al. (2000) who found decreased interference and reaction times with tryptophan depletion; but consistent with a large number of more recent studies who have found no such effects (Gallagher et al., 2003; Horacek et al., 2005; Sobczak et al., 2002). There are number of possibilities for the differences between the current study’s findings, and that of Schmitt et al. (2000). Firstly, Schmitt and colleagues used a blocked card version of the Stroop task whereas the current study employed a single-trial version. The two versions of the Stroop task can be conceived as tapping into slightly different processes; as in the card version participants must ignore the surrounding stimuli on the card as well as the irrelevant word information, in order to correctly name the ink colour; whilst in the single-trial version there is only the irrelevant word information which must be ignored (Henik & Salo, 2004; MacLeod, 1991). Therefore, due to the differential attentional load of the two tasks, Stroop performance may be differentially affected by tryptophan depletion.
This assertion is also supported by the observation of differences in performance between the card and single trial versions of the Stroop task, in schizophrenic patients (see Henik & Salo, 2004 for a review). As such, in schizophrenia, there is increased interference noted in the card version of the Stroop, whereas in the single-trial version research suggests schizophrenic patients exhibit increased facilitation and an increase in the number of errors made (for a review see Henik & Salo, 2004). However this explanation is unlikely to be the primary reason for the difference in findings between the current study and that of Schmitt et al. given that a number of more recent studies have also used the card version of the Stroop task and failed to find any effect of tryptophan depletion on Stroop interference and reaction times (Gallagher et al., 2003; Horacek et al., 2005; Sobczak et al., 2002).

Furthermore, the study by Schmitt et al. (2000) utilized a placebo control amino acid suspension with the same proportions of amino acids as in the present study, that is with the exception of the amino acid tryptophan. Importantly, the current study included 2.3 g of tryptophan in the placebo treatment, whilst the study by Schmitt et al. used 4.6 g of tryptophan. This may have accentuated serotonin synthesis in the placebo condition in the study by Schmitt et al., in turn possibly affecting Stroop performance and consequently allowing for overestimation of the difference between the placebo and the
tryptophan depletion conditions. Importantly, the authors also admit that there is the possibility that the amount of tryptophan used in their placebo condition may have allowed for overestimation of the effects of the depletion on Stroop performance.

Therefore, when considering the findings of the current study in conjunction with the consistent findings of Horacek et al. (2005), Gallagher et al. (2003) and Sobczak et al. (2002), and the fact that there appeared to be an overestimation of the effects of tryptophan depletion on Stroop performance in the study by Schmitt et al. (2000); it seems that Stroop performance is insensitive to alteration of serotonin with the use of tryptophan depletion in healthy participants. This is possible, given the apparent selectivity of tryptophan depletion in producing changes in performance on different cognitive tasks (Harmer, Bhagwagar, Cowen, & Goodwin, 2002; Harrison et al., 2004; Hughes et al., 2002; Murphy, Smith, Cowen, Robbins, & Sahakian, 2002; Rubinsztein et al., 2001). As such, detriments to cognitive function have consistently been observed in measures of learning and memory consolidation after tryptophan depletion (Evers et al., 2005; Harmer et al., 2002; Harrison et al., 2004; Schmitt et al., 2000); but not in measures of sustained attention (Harmer et al., 2002; Harrison et al., 2004; Hughes et al., 2002) Therefore, we can also assume that tryptophan depletion can reliably reduce central serotonin
function to levels that would effect behavioural performance given that there have been these consistent changes noted in some cognitive domains. Thus it appears that the effects of serotonin depletion are dependant on the task administered. Hence, this accumulating evidence lends weight to the argument that depletion of serotonin with the use of tryptophan depletion has no effect on attentional control and response inhibition, as measured by the Stroop task. This is also consistent with research that has used selective serotonin reuptake inhibitors (SSRI’s) and found that such serotonergic manipulation appears to have no effect on Stroop processing (Kerr, Fairweather, Mahendren, & Hindmarch, 1992).

As discussed previously, Stroop facilitation, has to our knowledge never been investigated after tryptophan depletion as all previous studies have utilized the card version of the Stroop task (Horacek et al., 2005; Schmitt et al., 2000; Sobczak et al., 2002), thus not enabling measurement of facilitation. Hence, the current study posed a research question which entailed investigating any changes in Stroop facilitation after tryptophan depletion. The findings of the present study suggest that when compared to placebo control treatment, Stroop facilitation is also not affected by tryptophan depletion. However, it should be noted that although the current study failed to find a significant basic facilitation effect with the task used in the present sample, it is evident upon inspection of
the means that reaction times to congruent stimuli were faster than those to neutral stimuli, which indicates a facilitator effect. Thus, although the facilitation effect in the current sample was only very weak, the differences in reaction times between congruent and neutral stimuli are in the correct direction. Therefore, for the purpose of the current paper, this difference will be referred to as facilitation. Thus, this study does nevertheless suggest that Stroop facilitation is not affected by modulation of central serotonergic function with the use of tryptophan depletion.

There are a number of possibilities as to why this is the case. Firstly, consistent with the previously discussed findings, it is possible that Stroop performance, and thus accordingly Stroop facilitation, are insensitive to modulation of central serotonin. This is probable given the above-mentioned consistent specificity in the effects of tryptophan depletion on different cognitive tasks (Gallagher et al., 2003; Harmer et al., 2002; Harrison et al., 2004; Kimberg & D'Esposito, 2003; Luciana & Collins, 1997; Schmitt et al., 2000). Alternatively, it may be that facilitation specifically is not affected by serotonergic manipulation. However, it is unlikely that facilitation alone could be affected, given that as mentioned previously, a number of researchers have failed to find changes in Stroop reaction times or interference after typrophan depletion (Gallagher et al., 2003; Horacek et al., 2005; Sobczak et al., 2002).
Similarly, a number of researchers have also failed to find changes to sustained attention and vigilance (Harmer, McTavish, Clark, Goodwin, & Cowen, 2001; Harrison et al., 2004; Hughes et al., 2002) after modulation of serotonergic function. Thus it appears that attention in general, and therefore facilitation too, is not affected by modulation of serotonin with the use of tryptophan depletion.

Furthermore, the analyses indicated that consistent with the hypothesis, there was no difference in the amount of errors made during the Stroop task, between the control and tryptophan depletion treatments. These observations are coherent with the findings of Schmitt et al. (2000), however due to the apparent ceiling effects evident in the current study, these results should be viewed with caution. It may be that if the current study had utilized a Stroop task difficult enough to elicit more errors, a difference in the treatment conditions may have been observed. The current findings do nevertheless provide some evidence that tryptophan depletion does not influence the number of errors made on the Stroop task. This could be interpreted, consistent with the above-mentioned inferences regarding the other Stroop measures, as reflecting tryptophan depletion’s inability to modulate Stroop performance in healthy participants. Alternatively, coherent with the findings of Schmitt et al. it may be that, given the selectivity in the effects of tryptophan depletion, the processes
involved specifically in inhibiting the irrelevant response in order to avoid errors, were not affected by tryptophan depletion (Schmitt et al., 2000).

Hence, overall, the findings from the current study suggest that modulation of central serotonin function with the use of tryptophan depletion has no effects on any measures of Stroop performance. This implies that attentional control and response inhibition, as measured by the Stroop task, are insensitive to alteration of central serotonin functioning in healthy humans with the use of tryptophan depletion. Although serotonin has been implicated in the pathophysiology of schizophrenia (Abi-Dargham et al., 1997; Kahn et al., 1993; Kapur & Remington, 1996), the present findings suggest that disturbances to central serotonin function are not the basis for the disturbances in Stroop task performance evident in schizophrenic patients. In addition, although atypical antipsychotics are thought to act on serotonergic function (Kapur & Remington, 1996), they also act dopaminergic receptors and cholinergic muscarinic receptors in the brain (Cash, 1997). In addition, by normalizing dopamine function, the atypical antipsychotics also indirectly affect glutamine function (Cash, 1997). Hence the findings of the current study suggest that the improvement in cognitive function, specifically in attentional control and response inhibition, with the use of atypical antipsychotics in schizophrenia may be a result of their effect on these other neurotransmitters systems, rather
than their effect on the serotonergic system. Hence, drugs that target these systems may be beneficial in treating the attentional control deficits in schizophrenic patients.

4.3 Dopamine depletion and Stroop task processing

The findings of the current study indicated that, in contrast to the hypothesis, tyrosine depletion has no effect on Stroop interference. These findings are incompatible with the findings of Roesch-Ely et al. (2005), Luciana and Collins (1997) and Barch and Carter (2005). These previous researchers all gained findings which imply that decreasing of brain dopamine results in impairments to executive function, and Stroop performance in particular. However, coherent with the current findings, the study by Kimberg and D’Esposito (2003) also found no change in Stroop interference after administration of the dopamine receptor agonist pergolide. There are a number of possible explanations as to why the current study failed to find changes in Stroop interference consistent with those described by Roesch-Ely et al. (2005).

Firstly, Roesch-Ely et al. (2005) used a dopamine D₂ receptor agonist which is thought to influence dopaminergic functioning by stimulating D₂ receptors which are located primarily in the striatum (Joyce & Meador-Woodruff, 1997; Seeman, 1992); whilst the current study used
tyrosine/phenylalanine depletion which is thought to affect global brain
dopamine via modulating its synthesis (Fadda, 2000; Oldendorf & Szabo, 1976;
Reilly et al., 1997). Therefore, as these two dopaminergic modulations act on
different brain areas and in different manners, it is possible that they could
influence Stroop processing differentially. However, this is an unlikely
explanation as to why the current study observed findings different to those of
Roesch-Ely et al, given that, consistent with the present results, the study by
Kimberg and D'Esposito (2003) also failed to find any change in Stroop
performance, after the administration of a dopamine receptor agonist.

Alternatively, the failure of the current study to find a significant
decrease in Stroop interference after tyrosine depletion, when compared to the
placebo treatment, could possibly be because Stroop performance is not
influenced by tyrosine depletion. There are a number of potential reasons as to
why tyrosine depletion does not influence Stroop performance. Firstly, it is
possible that the effects of tyrosine depletion are task dependant. This is
feasible given that researchers such as Harrison et al. (2004) and Harmer et al.
(2001) have found impairments to working memory performance after tyrosine
depletion, along side no differences on measures of attention and short term
memory. Accordingly, it is possible that performance on the Stroop task
specifically is not affected by modulation of central dopamine. However, many
researchers have consistently implicated the deficient cortical dopamine in schizophrenia with the disturbances to Stroop task processing (Barch et al., 2004; Braver et al., 1999; Cohen, Braver, & Brown, 2002; Cohen & Servan-Schreiber, 1992). Furthermore, recent studies using neuroimaging to assess dopamine function in the brains of patients with schizophrenia and Parkinson's disease (also characterized by decreases in dopamine function) has revealed that impaired performance on the Stroop task in these patients is associated with decreased brain dopamine (Bruck et al., 2001; McGowan, Lawrence, Sales, Quested, & Grasby, 2004; Rinne et al., 2000). Therefore it appears implausible that the current study should make such inferences.

Therefore, alternatively the lack of change to Stroop performance after tyrosine depletion in the current study may be because tyrosine depletion may not affect brain dopamine function to levels that can reliably affect Stroop processing in all participants. This assertion is drawn from the recent findings of Mehta et al. (2005). These researchers observed no overall effects of tyrosine depletion on neuropsychological measures of working memory and planning, however when levels of striatal dopamine in each participant were examined together with their behavioural performance on these tasks, it was found that the degree of dopamine depletion in the striatum was related to poorer performance on the neuropsychological tasks. Thus each participant was
differentially susceptible to the effects of tyrosine depletion on dopaminergic function, and therefore behavioural performance was differentially affected. Such a contention is supported by the literature concerning tyrosine depletion and cognitive function, which although fairly limited, has been very inconsistent. For instance, whilst some researchers have found impairment to working memory when employing tyrosine depletion (Harmer et al., 2001; Harrison et al., 2004), other have found no such effects (Ellis, Mehta, Liley, Wesnes, & Nathan, 2003; McLean, Rubinsztein, Robbins, & Sahakian, 2004; Mehta et al., 2005; Roiser, McLean, Ogilvie, Blackwell, & Sahakian, 2004). Thus it appears that the effects of tyrosine depletion may be very inconsistent, most probably due to the inconsistency in its effects on dopaminergic function.

Similar to the findings regarding Stroop interference, in contrast to expectations, no differences in reaction times to neutral, congruent or incongruent stimuli were found between the placebo and tyrosine depletion conditions. These findings are inconsistent with the findings of Mehta, et al. (2005) who found decreases in reaction times to all types of stimuli with the administration of D-amphetamine. This difference in findings could most probably be attributed, as detailed previously in relation to Stroop interference, to the possible inability of tyrosine depletion to alter central dopaminergic function to levels that would consistently affect Stroop performance.
In contrast, the current study’s hypothesis that there would be no difference in Stroop facilitation between the tyrosine depletion treatment and the placebo control treatment, was supported. Such findings are consistent with that of Roesch-Ely et al. (2005) who also found no differences in facilitation after administration of bromocriptine. As discussed previously in relation to tryptophan depletion, although the current study failed to find a significant facilitation effect, the difference in reaction times to neutral and congruent stimuli was in the expected direction. Therefore, these findings do nonetheless suggest that Stroop facilitation is not altered by dopaminergic modulation with the use of tyrosine depletion. As with the previous discussion, there are a number of possibilities why tyrosine depletion did not induce changes in Stroop facilitation. Firstly, it may be that due to the asymmetry between facilitation and interference (MacLeod, 1991), facilitation specifically may not be affected by dopaminergic modulation. This is possible given that other studies have also found no effects on facilitation with the modulation of dopaminergic function, together with significant changes to Stroop reaction times and interference (Barch & Carter, 2005; Roesch-Ely et al., 2005). However, taken together with the inconsistent findings concerning the effects of tyrosine depletion on cognitive function (Ellis et al., 2003; Harmer et al., 2001; Harrison et al., 2004; Mehta et al., 2005), as well as the research by Mehta et al. (2005), and the fact that dopamine has been consistently implicated as the basis for the Stroop
deficits in schizophrenia (Barch et al., 2004; Braver et al., 1999; Cohen et al., 2002; Cohen & Servan-Schreiber, 1992), it is most probable that the current study observed no change in Stroop facilitation due to the inability of tyrosine depletion to decrease dopamine function to levels that consistently affect Stroop performance.

Concerning the prediction regarding errors made during the Stroop task, coherent with the current study’s hypothesis and the findings of Roesch-Ely et al. (2005), there was no difference in the number of errors made under the tyrosine depletion treatment when compared to the control treatment. However, these findings should be interpreted with caution due to the ceiling effect noted in the task. As most participants made no errors, and those who did only made one error, it is difficult to ascertain whether the lack of difference between treatments is because the task was too easy, or because the treatments did not influence the processes involved in error making. As mentioned previously in relation to tryptophan depletion, it may be that if the current study had utilized a Stroop task difficult enough to elicit errors, a difference in the treatment conditions may have been observed. The current findings do nevertheless provide some evidence that tyrosine depletion does not influence the number of errors made on the Stroop task. This could be interpreted, consistent with the above-mentioned inferences regarding the other Stroop measures, as reflecting
the inability of tyrosine depletion to decrease dopaminergic function to levels that could modulate attentional control and response inhibition, and thus Stroop performance, in healthy participants.

In summary, the findings of the current study suggest that attentional control and response inhibition are not affected by modulation of brain dopamine with the application of tyrosine and phenylalanine depletion in healthy participants. However, given that dopamine has been widely implicated in schizophrenia and the associated Stroop task deficits (Barch & Carter, 2005; Barch et al., 1999b; Braver et al., 1999; Cohen et al., 2002; Cohen & Servan-Schreiber, 1992; McGowan et al., 2004), this study can not discount the involvement of dopamine in these processes. This leads to the inference that the technique of tyrosine and phenylalanine depletion is not effective enough to reduce dopaminergic functioning to levels that would affect Stroop task processing in healthy participants.

4.4 Combined monoamine depletion and the Stroop task

The findings of the current study indicated that there was no difference in Stroop facilitation, interference, reaction times to each type of stimulus, or the number of errors made on the Stroop task, between the placebo control treatment and the combined monoamine depletion treatment. As mentioned
earlier, the only other researchers who have investigated the effects of combined monoamine depletion on cognitive function (Matrenza et al., 2004) did not utilize the Stroop task, however they did use a measure of attention which could possibly be comparable. Accordingly, the findings of the current study are inconsistent with that of Matrenza et al. (2004), who found impairment to sustained attention after combined monoamine depletion. Thus taken together, these findings highlight the apparent selectivity of combined monoamine depletion in producing changes in cognitive function. Therefore, the most obvious explanation for the present study’s findings concerning combined monoamine depletion, is that due to the apparent selectivity in its effects, simultaneous depletion of central dopamine and serotonin has no effect on attentional control and response inhibition in healthy participants, as measured by the Stroop task. Alternatively, as suggested with tyrosine depletion, it is possible that the combined monoamine depletion technique may not be able to decrease central monoamine function to levels that would reliably affect Stroop task performance. This is a possibility as, to this date, we have no measure of central monoamine function in human participants, thus we do not definitively know how much central depletion occurs. However, this is nevertheless unlikely given that the previous study by Matrenza et al. (2004) noted selective changes in sustained attention and mood but not learning or memory, after the combined depletion. Thus, this lends further support to the
assertion that attentional control and response inhibition, as assessed by the Stroop task, are insensitive to simultaneous modulation of central dopamine and serotonin. Therefore, although it appears that dopamine alone is strongly implicated in Stroop task processing, given the extensive literature detailing its involvement in the disturbances to Stroop processing in schizophrenia (Barch et al., 2004; Braver et al., 1999; Cohen et al., 2002; Cohen & Servan-Schreiber, 1992; McGowan et al., 2004), this study suggests that the interaction between dopamine and serotonin renders their combined depletion ineffective in modulating Stroop task processing.

4.5 Limitations and directions for future research

In interpretation of the current findings, a number of methodological constraints should be considered. Firstly, the current study utilized only male participants to eliminate the proposed differences in serotonin metabolism between males and females (Nishizawa et al., 1997). This limits the generalisability of the findings to the population. In future it would be beneficial to utilize a sample consisting of both males and females, such to allow comparisons between gender, across the sample in total, and to allow for generalization. Additionally, the Stroop task used in the current study appeared not to be very challenging to the participants. This resulted in a ceiling effect being observed in terms of the number of errors made in the task; and thus
hypotheses regarding error rates could not be reliably addressed. In future research, the use of a Stroop task that has faster presentation times of the stimuli may be valuable in eliciting errors (Barch et al., 2004). This may enable a more accurate examination of the effects of the depletion techniques on the processes involved in error making in the Stroop task. Lastly, whilst not offered earlier as a possible reason for the lack of significant findings, it is possible that the current study did not possess sufficient power. As evident in the results section, the effect sizes of all analyses were quite small, and the power was also generally fairly low; thus these coupled together might have lead to an inability to uncover the expected findings. Power analysis reveals that 496 participants would be needed to uncover an effect size of .15 (such as was the effect size of the treatment by stimulus interaction) in the current study. This lends to the argument that if so many participants are needed to find a significant effect, this effect is not very important. As such, the effect of the treatment conditions on Stroop task performance appears not to be very important.

Furthermore, as mentioned previously, recent research utilizing markers of brain neurochemical activity has suggested that the immense variability in findings utilizing tyrosine depletion is due to the individual inconsistency in the effects of this technique on brain neurochemical function (Mehta et al., 2005). Thus, future research would benefit from coupling Stroop task performance
measures, with neurochemical neuroimaging techniques such as [11C] raclopride PET scans. This would enable examination of the effects of the depletion techniques on individual brain neurochemical levels and Stroop performance. Therefore it would be expected that, consistent with Mehta et al. (2005), those participants in who the depletion resulted in significant alterations to neurotransmitter function would demonstrate significant differences in Stroop performance.

4.6 Implications

The current study expanded upon our understanding of the role of brain monoamines in Stroop task performance. This has implications in terms of the understanding and treatment of clinical disorders such as schizophrenia, which are thought to have disturbances to such neurotransmitter systems. In terms of the findings concerning tryptophan depletion, the current study suggests that serotonin is not involved in the modulation of Stroop task performance. As such, this suggests that the effectiveness of atypical antipsychotics in improving attentional control in schizophrenia is due to the action of these drugs on other neurotransmitter systems such as the dopaminergic and glutaminergic systems. Following from this, in order to improve the effectiveness of these newer antipsychotic drugs in improving attentional control and response inhibition, the
current findings suggest that compounds that target other neurotransmitter systems, rather than serotonergic function, would be of benefit.

Conversely, due to the apparent possible inability of tyrosine depletion to reliably decrease dopaminergic functioning to levels that would affect behavioural performance, the present study could not reliably improve our understanding of the role of dopamine in Stroop task performance. However, stemming from this, the current study offers implications for future research. As such, future research which couples neurochemical imaging techniques with behavioural measures such as the Stroop task, would allow more accurate exploration of the behavioural effects of alterations to brain neurochemicals.

Lastly, the findings of the current study suggest that simultaneous depletion of serotonin and dopamine has no effect on Stroop task performance. Although some researchers have considered such techniques as possible treatment avenues for the neurochemical disturbances in disorders such as schizophrenia (Harrison et al., 2004; Harrison et al., 2002; Matrenza et al., 2004), the current study would suggest that such a technique would not be a suitable means to treat the cognitive and attentional deficits in schizophrenia, as in the depletion of both monoamines the apparent interaction between dopamine and serotonin renders dopamine ineffective in modulating Stroop performance.
4.7 Conclusion

The current study aimed to explore the effects of serotonin depletion, dopamine depletion, and combined monoamine depletion, on attentional control and response inhibition using the Stroop task. The findings of the current study suggest that Stroop performance (interference, facilitation, reaction times to Stroop stimuli and errors) is not affected by modulation of central dopamine with tyrosine depletion; nor by modulation of central serotonin with the use of tryptophan depletion, nor by combined central serotonin and dopamine modulation with the use of combined monoamine depletion techniques. This lends to the proposal that attentional control and response inhibition in healthy participants is not modulated by the depletion of the precursors for dopamine or serotonin.

Furthermore, although the present study cannot reliably confirm or deny that dopamine may be important for Stroop performance, the findings do suggest that systems like the glutaminergic and cholinergic systems may affect Stroop performance rather than the serotonergic system. Hence, drugs targeting these systems may help to improve the deficits in Stroop performance evident in schizophrenia.
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Modulation of Executive Control in Healthy Subjects.

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## APPENDIX A

### AA depletion-Stroop Task- Error recording sheet

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APPENDIX B

Disk containing the Stroop task used in the current study, and the practice Stroop task used in the current study