The impact of the 5:2 intermittent fasting diet on cognition in healthy adults

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D.Clin.Psy. thesis (Volume 1), 2019

University College London

UCL Doctorate in Clinical Psychology

Thesis declaration form

I confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Overview

Intermittent Fasting (IF), where individuals restrict their food intake on several days per week, while eating normally on other days, has recently become a popular strategy for weight loss and health improvement. Knowledge of which areas of cognition might be impaired by IF can inform researchers and clinicians, with the potential to prevent impairment and influence advice regarding clinical interventions.

Part One of this thesis is a conceptual introduction that examines the current research and interest in the role of calorie restriction and fasting in human health and cognition. A brief review of the research literature suggests that numerous specific areas of cognitive performance are impacted by a reduction in calorie intake. Continuous calorie restriction (CCR) studies were more likely to report cognitive improvements with more deficits reported in total fasting studies (where participants consumed water only). Specific areas affected by calorie restriction and fasting are discussed, alongside methodological issues and future directions for research.

Part Two presents empirical research into the impact of the 5:2 intermittent fasting diet on cognitive function. Results suggest that on fasting days, working memory, prospective memory, and cognitive flexibility was impaired for those who were following the 5:2 diet for longer than four weeks. Overall composite scores show that accuracy and response time was impaired on fasting days. Furthermore, when compared with a group who were following CCR diets, those in the 5:2 group performed worse in tasks designed to measure psycho-motor speed and cognitive flexibility with overall composite scores indicating slower reaction time. Limitations to the interpretation of the results and potential alternative explanations are considered. Future recommendations for research and potential clinical applications are discussed.

Part Three presents a critical appraisal of the research process. Difficulties experienced during the recruitment process and personal reflections about the method are discussed along with particular aspects of ethical research.

The empirical research in Part Two was completed as part of a joint research project. The details of the other part of this project can be found in Donaldson, F (2019). Comparing the effects of intermittent fasting diets and continuous calorie restriction on symptoms of eating disorders and mood in healthy adults. Clinical Psychology Doctorate Thesis.

Impact statement

With the cost of obesity in the NHS estimated by Public Health England to be £6 bn per annum, there is a drive by the government to reduce UK calorie consumption by 20% by 2024. In response, the NHS now encourages the use of dieting regimes and in 2013 referred 69,000 people who were classified as overweight to commercial weight management schemes. The physical health benefits for the growing numbers of people who successfully follow calorie restricted diets have been widely acknowledged, yet our understanding of their impact on cognitive function is in its infancy. Further, little is known about any potential cognitive impact of intermittent fasting diets such as the 5:2 fasting diet which continues to rise in popularity.

This study sought to understand the impact of the 5:2 diet on specific areas of cognition. This research presents novel findings about the impact of intermittent fasting on cognition, finding impairments to cognitive performance for those following the 5:2 diet. The dissemination of this study via scholarly journals will add to existing specialist research that investigates the specific areas of cognitive performance thought to be affected by calorie restriction. This research has the potential to add to knowledge that may assist in the development of guidelines for the safe use of continuous and intermittent calorie restriction for weight loss.

Moreover, for healthy individuals who are following diets or considering which diet to follow, being informed about the impact of intermittent fasting diets on cognition may enable them to avoid potential cognitive impairments, thus preventing a decline to their quality of life.

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Acknowledgements

I would like to thank both Dr Lucy Serpell and Dr Sam Gilbert for providing supervision, support and guidance during this project. Thanks also to my research partner Freya Donaldson, for her assistance during the initial stages of the project. I am hugely grateful to the gatekeepers of the very many online websites that provided access to recruiting the participants required for this study. I would particularly like to acknowledge all those individuals who took part in this research, without which this study would not have been possible. Finally, I am enormously indebted to my wife Natalie and to my children Amber and Seth, who have provided me with endless encouragement and motivation to complete this research.

Part 1: Conceptual Introduction.

Investigating the impact of calorie restriction

on health and cognition

Abstract

Research into the effects of calorie restriction continues to excite those interested in its potential to allow humans to live longer and healthier lives. Animal studies of continuous calorie restriction and fasting have demonstrated significant advantages to health and longevity yet concerns remain over the impact of restricting calorie intake for human health and cognition.

Section 1 examines the literature to show why there is such interest in the restriction of calorie intake, and how intermittent fasting has become popularised as a potential route to longer and healthier lives in humans. The literature reveals mixed findings regarding the impact on human health and cognition suggesting further research is required to understand the costs and benefits of calorie restriction.

Section 2 investigates the relationship between varying degrees of calorie restriction and human cognition. The results show a trend for impaired performance in fully fasted states, with more improvements reported in continuous calorie restriction studies. Further, specific areas of cognition appear to be influenced by the degree of restriction.

Section 3 Summarises these findings, the limitations of the study and states the aims of the empirical study.

Investigating the impact of calorie restriction on health and cognition

Introduction

This project aims to increase knowledge about the impact of intermittent fasting diets (IF) on cognition. By examining differences in cognition between people who are using popular IF diets, and those who are on continuous calorie restricted (CCR) diets, the study aims to inform both current and potential dieters about the risks or benefits of intermittent fasting to cognition.

Researchers interested in the impact of CCR and IF diets on health have reported numerous positive physical health benefits for humans. Thus, there is growing support for adherence to several dieting regimes, with champions of CCR and IF offering evidence that following calorie restriction and fasting diets yields significant health benefits. These include an increase in lifespan and protection from conditions such as dementia and Alzheimer's disease.

Among the most popular of intermittent diets in the UK is the 5:2 diet, recently promoted by proponents such as Dr Michael Mosely. This form of IF diet encourages severe calorie restriction for two days each week whilst eating normally for the remaining five. Despite its popularity, there is currently very little evidence regarding the impact of this diet on cognition in humans. Indeed, to our knowledge there are currently no peer reviewed publications that have examined the potential impact of engaging with the 5:2 dieting regime on cognitive function. This study will attempt to address this knowledge gap by comparing the results of cognitive online tasks for those who subscribe to the 5:2 diet and those engaging with CCR diets. Specifically, the project will seek to investigate differences in psycho-motor speed, set shifting capabilities and mental flexibility, working and prospective memory capacity, and reflective impulsivity. A between-participant, quasi-experimental

design will be used to compare the scores taken from online tests of cognition between 5:2 and CCR groups. In addition, differences in cognition between fasting and non-fasting days over one week will be determined for those who are on the 5:2 diet. This will allow us to measure any impact on cognition of short term fasting. This work has the potential to contribute to a body of evidence regarding the pros and cons of intermittent fasting.

The following introduction to the project will provide an overview of our current understanding of the potential benefits and costs of calorie restriction for humans. A systematic literature review will focus on relevant research looking at the relationship between calorie restriction and cognition. The results and recommendations for future studies will be discussed alongside the rationale for the empirical paper.

Section 1

An introduction to calorie restriction

Calorie restriction (CR)

The desire to discover the secret of immortality has long been the dream of humanity. Science now claims to have found a way to unlock some of the secrets of longevity and health through the process of calorie restriction. But while scientific research continues to explore the mechanisms of calorie restriction and their contributions to aging and health research, less is known about its impact on cognition.

Calorie restriction (CR) refers to the intentional reduction in energy intake. Those who follow a CR regime typically reduce their daily energy intake by between 15-30%. This form of dietary intervention has been studied with growing interest as the measured limitation of food intake whilst maintaining optimum nutrition has been shown to extend lifespan in a variety of organisms and improve general health (Van Cauwenberghe, Vandendriessche, Libert, & Vandenbroucke, 2016).

More than 80 years ago, Macay and colleagues used an experimental design to show that healthy rodents who had their daily energy intake reduced lived longer when compared to a control group that could feed ad libitum (Macay, Crowell, & Maynard, 1935). Since then numerous experimental studies have confirmed this observation in insect and mammal species (Hanjani & Vafa, 2016). For instance, fruit flies and worms have been widely used and both species have benefitted from an increased lifespan following CR (Clancy et al., 2001; Houthoofd & Vanfleteren, 2007). The scientific community quickly realised that studying short lived species, such as insects provided easy and low-cost methods for researching longevity. In addition, such studies avoid complex ethical considerations that would be attached to human experimental participation.

The benefits of CR that are observed in insects appear to be conserved in mammal species. Mice that restrict calories in early life, as well as those who begin CR later have benefited from longer and healthier lives (Weindruch, Walford, Fligiel, & Guthrie, 1986). CR in rodents appears to suppress genes that might otherwise encourage the onset of age-related disease such as cancers and cardiovascular disease (Higami et al., 2006). Despite questions about the translation of results from short lived species to humans, key findings may be relevant to exploring mechanisms for aging in non-human primates (Colman & Anderson, 2011). Non-human primate studies provide an important link between these short-lived species and humans. The rhesus monkey lives for approximately 40 years in captivity and their genetics, lifecycle and susceptibility to age related disease is similar to that of humans (Uno, 1997). Two major studies that tested the impact of CR on rhesus monkeys suggest that CR in non-human primates has distinct health benefits and can delay the effects of aging (Colman et al., 2009; Mattison et al., 2012).

Although the exact mechanisms that explain the relationship between CR and increased health and longevity are not yet fully elucidated, these findings have captured the attention of those interested in similar effects within human populations. Incidences of cancer are lower in short-lived CR species such as rodents (Weindruch, & Walford, 1988), and also longer-lived CR species such as rhesus monkeys (Colman et al., 2009; Mattison et al., 2012) suggesting that CR protects against tumours across species. Given that the rhesus monkey shares over 90% of its genetic sequence identity with humans (Gibbs et al., 2007; Zimin et al., 2014), the additional findings that CR rhesus monkeys benefit from lower incidences of cardiovascular disease and diabetes (Colman et al., 2009; Mattison et al., 2012), adds further evidence to suggest that such benefits may be observed in humans.

The study of long term CR in humans is neither practical nor ethical due to the potentially harmful health consequences of starvation under experimental

conditions, while the study of health and cognitive impairments in countries where food deprivation is common raises not only ethical concerns but also inhibits the generalisability of the results due to confounding factors such as war, extreme stress and displacement (Jones, Duncan, Brouwers, & Mirsky, 1991). Under these circumstances optimum nutrition is unlikely to be preserved.

The recent CALERIE (Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy) study of short term sustained CR in humans reports a reduction in weight, a reduced risk of cardiovascular disease and improvements to glucoregulatory function (Fontana et al., 2007; Heilbronn et al., 2006; Lefevre et al., 2009; Racetteet al., 2006; Redman et al., 2007; Weiss et al., 2006). These findings are comparable in CR rhesus monkeys (Edwards et al., 2001; Gresl et al., 2001; Rezzi, Martin, Shanmuganayagam, Colman, Nicholson, & Weindruch, 2009; Yamada et al., 2013), adding further support to the idea that both species elicit the same primary response to CR.

Whilst research continues to examine the short-term benefits of CR to humans, the long-term effects are unknown. Epidemiological studies have added to speculation that humans can live longer and remain in comparatively better health by consuming fewer calories. Whilst these studies are not scientifically controlled experiments and are therefore lacking in validity, it is worth mentioning one that is relevant. The inhabitants of the Japanese Island of Okinawa have one of the highest longevity rates in the world (Rosenbaum, Willcox, Willcox, Suzuki, & Okinawa, 2010). The island was once known to contain more centenarians than anywhere else in Japan (Kagawa, 1978). Okinarians were known to consume less calories than those on the main island, a reduction of between 20-40% with inhabitants benefitting from a reduction in morbidity from vascular disease and cancers, as well as reduced overall death rates (Roth, Ingram & Lane, 1999). Whilst CR may be a factor in this lifespan extension, other factors such as diet might also explain these

effects. The Okinarian diet was derived from 9% protein, 85% carbohydrate, and very little fat (Le Couteur et al., 2016). Interestingly, younger inhabitants of the island appear to be losing this advantage and life expectancy is now lower at birth compared to Japanese living on the mainland (Gavrilova & Gavrilov, 2012). This change has coincided with the introduction of a more western diet where younger generations of Okinawans now have access to western style fast food outlets, leading to a gradual increase in individual energy consumption, and a decrease in energy expenditure (Gavrilova & Gavrilov, 2012). These changes to diet and energy consumption have led to the islands inhabitants no longer recognised as being in a calorie restricted state and current demographic data suggests that the longevity phenomenon for those inhabitants is now a thing of the past (Gavrilova & Gavrilov, 2012).

National interest in CR

Interest in CR extends beyond the realms of the scientific community, as public awareness about its benefits continue to grow steadily. In the UK there was a decrease in caloric consumption at the individual level of between 5-6 percent between 2001 and 2011 (Office of National Statistics, 2016). This suggests that among other factors such as socio-economics, people are becoming more conscious of the relationship between calorie intake and health. The potential benefits of this relationship have become the focus of a UK government drive to reduce obesity. Despite the reported individual decrease in calorie consumption, almost two thirds of adults in the UK and one fifth of children were classified as obese in 2015 (Public Health England, 2017). The scale of the problem is becoming more evident. Obesity in the UK is thought to be responsible for more than 30,000 deaths each year, and it is estimated that people who are obese will die on average 9 years prematurely (Public Health England, 2017). Thus, public health bodies such

as the National Health Service (NHS) have realised the risks of failing to address the upward trend in obesity, which is estimated to cost the NHS over £6 billion annually. This figure is forecast to rise to 9.7 billion by 2050 (Public Health England, 2017).

In response the NHS have launched health focussed initiatives, one of which is the NHS Weight Loss Plan (NHS, 2016). Their 12-week diet and exercise plan is designed to encourage safe and sustainable weight loss by reducing and thereafter maintaining a recommended daily calorie intake. The plan is based on guidelines which state that safe weight loss should be achieved by a daily reduction of 600 calories (NICE, 2014). In addition, The UK government now advises health professionals to refer people who are overweight to weight management services. In 2013, the National Health Service (NHS) referred approximately 69,000 people to two large commercial weight loss programmes, Weight Watchers and Slimming World (NICE, 2014). Despite the growth of health plans that are designed to encourage CR, levels of obesity worldwide continue to rise. Obesity is caused by multiple complex factors but the environment, particularly the excessive availability of calorie rich foods is believed to be a major reason why people find it more difficult to choose and maintain a healthy lifestyle (Foresight Report, 2007).

Intermittent fasting (IF)

All living organisms depend upon food for their survival and reproduction, and many species have evolved to survive during periods where food is scarce (Mattson, Longo & Harvie, 2017). For example, yeast can enter a dormant stage when food is unavailable, and similarly bears will hibernate during winter seasons to conserve energy (Calixto, 2015). Bears and other mammals have evolved to allow them to function physically and mentally when they are in a fasted state (Mattson,

2015). These intermittent fasting regimes are common in the natural world, but interest has grown in the benefits of such regimes in mammals and humans.

One form of CR that is becoming more popular is known as intermittent fasting (IF). IF describes a cycle of eating, followed by non-eating or reduced eating. The method by which IF takes place can vary. For instance, IF might include absolute fasting every other day. Alternatively, IF might involve eating normally for five consecutive or alternate days in seven and then reducing energy intake substantially during the remaining two days.

Despite differences in IF procedures, varying degrees of benefits are reportedly common to all regimens. In animal studies numerous effects of IF include a reduction in levels of body fat (Varady, Roohk, Loe, McEvoy-Hein, & Hellerstein, 2007) and a lean mass retention in rodents that is greater than those who are on daily CR regimes (Gotthardt et al., 2016). Similarly, heart rate and blood pressure are reduced in rodents following one week on an IF diet (Mager et al., 2006). This appears to be the result of IF and not solely CR, as IF rodents that restricted their calorie intake by 15-30% exhibited greater reductions than those subjected to a 40% daily calorie restricted diet (Mager et al., 2006). Other studies using rats suggest that IF has the capacity to prevent and reduce the symptoms of type 2 diabetes (Mattson, Longo, & Harvie, 2017), drastically reduce the risk of cardiovascular disease (Ahmet, Wan, Mattson, Lakatta, & Talan, 2005) and it has been suggested that in mice, IF can delay the progression of cancers (Raffaghello et al., 2008). Although the vast majority of studies that examine the impact of IF on health report positive findings, some studies report differences between continuous calorie restriction (CCR) and IF regimes, as well as negative effects of IF. CCR appears to demonstrate superior decreases in body weight (Barnosky, Hoddy, Unterman, & Varady, 2014) when compared with IF and may also be more effective for the retention of lean mass in humans (Varady, 2011), whilst there are adverse

effects on the reproductive system in rats subjected to IF regimes (Kumar & Gurcharan, 2013).

IF in Humans

IF as a form of energy restriction has seen a recent increase in popularity, and diets such as Dr Michael Mosely's 5:2 diet have grabbed the attention of the media and public (Mosley & Spencer, 2013). Subscribers of the 5:2 diet are required to severely restrict their calorie intake by 75% (600 for men, 500 for women) for two days each week, whilst eating normally for the remaining five (Mosley & Spencer, 2013). Given that the potential benefits of IF regimes such as the 5:2 diet may be at least equal to continuous calorie restriction (CCR) regimes such as weight watchers, the prospect of gaining the same health benefits by more radical but less frequent CR methods may be preferred, thus offering a potential increase in compliance for those who choose to adopt the 5:2 method.

The mechanisms by which IF diets are purported to work include: 1) the body converts fat to energy during periods of IF, reducing overall adipose mass resulting in cumulative benefits over time to health; and 2) the effect of nutritional stress results in cell-based regeneration, and metabolic rejuvenation. This prevents the effects of aging by protecting neurons from aged related genetic and environmental decline, reduces cardiovascular risk factors, and acts on glucose metabolism (Horne, Muhlestein, & Anderson, 2015). Initial reports suggest that IF can match CCR diets for health benefits such as weight reduction and improved insulin sensitivity (Mattson, Longo, & Harvie, 2017).

Despite this, evidence supporting the health benefits of IF for humans is limited to handful of randomized controlled trials and observational studies (Horne, Muhlestein, & Anderson, 2015), suggesting that further research is required before

IF can be recommended in clinical guidelines to facilitate health and wellbeing in humans. A recent systematic review of intermittent fasting and its benefits to humans found that most studies concentrated on weight loss, with secondary outcomes such as cognitive performance requiring additional clinical research (Seimon et al., 2015). Further research examining the effect of IF on cognition would provide important information to health care providers about the potential merits and risks of recommending the regime to patients.

CR and brain function

Given there are consistent positive health indicators during the restriction of calories in humans, questions have arisen regarding the potential impact of CCR and IF on the brain. One theory described by Mattson (2015) explores the possibility that the human brain has evolved to provide an advantage over competitors during periods where food is scarce, by ensuring optimal brain functionality when searching for nutrients. The neuronal stress during these periods engages signalling pathways which optimise cell and organ functionality and resists age related disease.

Researchers investigating the link between CR and age-related disease have reported preventative effects of CR on neurocognitive decline in conditions such as Parkinson's disease and Huntington's disease (Hanjani & Vafa, 2016). Similarly, a reduction in food intake has been linked with the slowing of symptoms which are associated with Alzheimer's disease (Van Cauwenberghe, Vandendriessche, Libert & Vandenbroucke, 2016), a neurodegenerative disorder characterised by progressive memory loss and deficits in executive function. Interest therefore in the impact of fasting on conditions such as Alzheimer's has been rising and with over half a million people in the United Kingdom currently living with the condition (Alzheimer's society, 2017), it is important to understand whether

caloric restriction could assist with preventing the disease. However, given the evidence that suggests CR impacts the brain this raises the question as to whether CR might also be detrimental to some areas of cognitive function.

CR and cognitive function

Cognitive function describes numerous mental processes that assist our ability to gain knowledge, and comprehension. It allows humans to perceive, reason, store and manipulate information, and to solve problems based on the information available to them.

Evidence suggests that weight may play an important part in cognitive function. Cognitive impairments are significantly associated with obesity, particularly within elderly populations (Smith, Hay, Campbell, & Troller, 2011). Furthermore, a recent systematic review suggests that obese individuals are impaired on behavioural tasks of executive functioning such as problem solving, decision making memory, planning and verbal fluency (Fitzpatrick, Gilbert, & Serpell, 2013). It is important however not assume that obesity is a cause of cognitive dysfunction. It is possible that pre-existing impairments in cognitive function could help to explain the pattern of dysregulated eating often observed in obesity people. Impairments to executive function can result in a decreased ability to control automatic impulses (such as to eat) which can lead to undesired behaviours, such as uncontrolled eating, Hoffman et al., 2012). Response inhibition is an executive function and refers to the ability not to respond, or to overrule automatic intentions, and numerous studies have found that obesity is associated with a decrease in response inhibitory control (Nederkoorn, Braet, Van Eijs, Tanghe, & Jansen, 2006; Guerrieri, Nederkoorn, & Jansen, 2012). Furthermore, a decrease in response inhibition is also associated with unsuccessful dieting. A study of obese

children with poor response inhibition skills showed that they lost less weight during a cognitive behavioural weight loss programme compared with children who had had better inhibitory control (Kulandran et al., 2012).

Although it is difficult to determine whether cognitive deficits are a cause of obesity or if the opposite is true, researchers are becoming more aware of the influence of calorie restriction on cognition, and although animal studies have demonstrated that CR of around 30% can improve cognition (Brownlow et al., 2014; Vitousek, 2004; Witte, Fobker, Gellner, Knecht & Floel, 2009), the impact on humans is less clear. Understanding which regions of cognition are sensitive to a reduction in calorie intake in humans may increase our knowledge of the link between weight and cognitive impairment.

Our understanding of any causal link between a reduction in calories and cognition would benefit from the inclusion of potentially related physiological mechanisms. Numerous models have attempted to explain why cognition might change following a decrease in energy intake. For instance, it has become firmly established that when the brain is engaged in activity, there is an increase in the demand for glucose in specific brain areas, whereas reduced brain activity utilises less glucose in the same areas (Hertz & Dienel, 2002).This suggests that a reduction in calorie consumption, which would result in less glucose might impair cognitive function. Similarly, glycogen is the major reserve for glucose in the brain (Ibrahim, 2013), and more glycogen is delivered to brain regions when glucose levels decrease (Waitt, Reed, Ransom & Brown, 2017), therefore a reduction in glycogen might also impact cognition. Other proposed mechanisms of how CR might influence cognitive ability includes the potential role of cortisol. Cortisol is a stress hormone which is released in greater quantity during moments of elevated stress or anxiety. For many people, dieting can be a stressful experience. Research suggests that in both rodents and humans short term calorie restriction results in

significant increases in cortisol (Dubuc, Phinney, Stern, & Havel, 1998) and in humans, high levels of cortisol have been found to impair some regions of brain function (Arnsten 2009).

Section 2

Literature review: **Investigating the relationship between calorie restriction and cognition**

This review aims to explore the evidence that varying degrees of calorie restriction impacts human cognition. Its purpose is to provide information about the potential costs and benefits of CR for human cognition. This might better inform researchers who are interested in the advantages and disadvantages to people who engage with dieting regimes.

Method

To evaluate the literature on the impact of calorie restriction and fasting on cognition a PsychInfo database (https://www.apa.org/pubs/databases/psycinfo/) search was conducted during October 2018. Search terms were discussed with the project supervisor and taken from previous literature. The following search terms were used: (5*2 diet OR 2 day fast OR alternate day fasting OR calorie restriction OR periodic fasting OR intermittent energy restriction OR Fasting OR fasted OR intermittent fasting OR intermittent diet OR 2-day fast OR alternate day fasting OR low-calorie OR starvation OR calorie restraint OR dietary restraint OR restricted eating) AND cognition OR executive function OR decision making OR set-shifting OR reflective impulsivity OR psycho-motor OR working memory OR prospective memory OR Trail making OR perception OR visuospatial memory OR neuropsychology OR neuro OR memory OR brain OR attention OR central executive OR inhibition OR processing speed) or variants of these terms. The initial search yielded a total of 936 results. These were reduced to 25 when accounting only for experimental studies that have measured cognition following the manipulation of total energy intake. For inclusion, the studies included human adult

(>18) participation and did not include experimental designs with food-related stimuli where attentional food bias might have accounted for changes in cognition.

Findings

The findings highlight studies that assessed varying degrees of calorie restriction and references to fasting studies are those with zero food intake, while references to CR studies are those with less than 100% restriction. Given this is not a full systematic review, it is likely that some domains that have been assessed will not be included. Of those reviewed here 14 are taken from CR studies and 11 are from fasting studies. From the total of 25 studies, nine used between-participant designs and the remainder used within-participant designs. The effects of calorie restriction and fasting on all cognitive domains described have been summarised in tables 1 (calorie restriction) and 2 (total fasting). Significant improvements in a particular domain are represented by an upward arrow, whilst significant impairments are represented by a downward arrow. Between-subject designs are indicated by a ‘B’ in the appropriate column, whereas within-subjects repeated measures designs are indicated by a ‘W’. For studies that used between-subject designs, only the findings from the appropriate energy manipulation groups were used. The cognitive task used to measure the domain has been reported below each finding. Further details on each of these studies can be found in the text below.

Table 1

Effect of continuous calorie restriction on cognition

Study	Sample Population	Duration (days)	Between or Within subject (B/W)	Energy reduced (%)	Attention	Inhibition	Cog Flex	Processing Speed	Working Memory	Psycho-Motor abilities
Martin et al, 2007	24 overweight adults	168	B	25	No change Conner's Continuous Performance Test-II	_____	_____	_____	No change Rey Auditory and Verbal Learning Test	_____
Cheatham et al, 2009	42 overweight adults	180	W	30	No change Scanning Visual Vigilance Test	_____	_____	No Change Four Choice Visual Reaction Time	_____	_____
Kretsch et al, 1997	14 healthy adult women	105	W	50	No change MEL 1.0 Psychology Software	_____	_____	↓ MEL 1.0 Psychology Software	_____	_____
Makris et al, 2013	47 obese adults	168	W	25	No change Continuous performance task	↑ Stroop	No change Wisconsin Card Sorting Test	_____	_____	_____
Pearce et al, 2012	44 obese adults	56	W	30	No change Digit Symbol Substitution Test	_____	_____	No Change Digit Span	No Change Digit Span	_____
Wing et al, 1995	21 overweight women	28	W	80	No change Digit Vigilance Task	↑ Stroop	_____	_____	_____	_____
Witte et al, 2009	19 overweight elderly	84	W	30	No change Trail Making Tasks	_____	_____	_____	_____	_____
Wardle et al, 2000	52 middle-aged	84	B	17	↓ Bakan Vigilance Task	_____	_____	_____	_____	_____
Bryan & Tiggemann, 2001	42 overweight momen	84	B	20	↑ WAIS III Digit Symbol Coding	No change Stroop	_____	_____	No change Digit Span	_____
Siervo et al, 2012	50 obese adults	116	W	40	↑ Trail Making Tasks	_____	_____	_____	_____	_____
Solianik et al, 2018	9 obese adults	2	W	75	_____	_____	↓ Two Choice Reaction Time Task	_____	↑ Matching-to-sample test	No change Simple Reaction Time Test
Brinkworth et al, 2009	32 overweight adults	365	B	28	_____	_____	_____	No Change Inspection time task	↑ Digit Span	_____
Buffenstein et al, 2000	9 overweight adults	30	W	60	_____	_____	_____	↑ Reaction Time Test	_____	_____
Halyburton et al, 2007	93 obese adults	56	B	30	_____	_____	_____	↑ Inspection Time Task	↑ Digit Span	_____

Table 2

Effect of total fasting on cognition (no food or calorie containing fluids allowed, water only)

Study	Sample Population	Duration (hours)	Between or Within subjects (B/W)	Energy reduced (%)	Attention	Inhibition	Cog Flex	Processing Speed	Working Memory	Psycho-Motor abilities
Green et al, 1995	21 female students	24	W	100	No change Focussed Attention Task	_____	_____	_____	No change Bakan Vigilance Task	↓ Tapping Task
Tian et al, 2011	18 Male athletes	12	W	100	↑ Identification Task	_____	_____	↑ Detection Task	No change One-back Memory Task	_____
Doniger et al, 2006	40 university students	16	W	100	_____	No Change Stroop	_____	↓ Staged Information Processing Speed test	_____	↓ Catch Game Task
Stewart & Samoluk, 1997	32 university students	6	W	100	_____	No change Stroop	_____	_____	_____	_____
Owen et al, 2012	30 university students	12	W	100	No change Stroop	_____	_____	_____	No change Computerised Serial Threes Task	_____
Pender et al, 2014	60 healthy adults	18	W	100	_____	_____	↓ Rule Change Task	_____	_____	_____
Solianik et al, 2016	9 male amateur weight-lifters	48	W	100	_____	_____	↑ Two Choice Reaction Time Task	_____	No change Memory Search Task	_____
Bolton et al, 2014	60 healthy adults	16	W	100	_____	_____	↓ Rule Change Task	_____	_____	_____
Harder et al, 2017	10 healthy males	14	W	100	_____	_____	_____	_____	No change Rey Auditory and Verbal Learning Test	_____
Benton et at, 1998	15 female students	14	B	100	_____	_____	_____	_____	No change Trigram Memory Test	_____
Green et al, 1997	20 healthy students	4	W	100	_____	_____	_____	_____	No change Recognition and Free Recall Tasks	↓ Tapping Task

Note. Findings for both tables have been categorised according to the sample population, and duration. Significant improvements are represented by an upward arrow. Significant impairments are represented by a downward arrow. A dash indicates that the domain was not measured in the study. The cognitive task used to measure the domain has been reported below each finding.

Attention

The vast majority of things that we do in our daily lives require us to take notice of discrete stimuli, and often involve the need to sustain our attention or to redirect it where necessary until a task is complete. There are risks associated with poor attention in certain occupations, such as those which involve machinery or medical procedures, hence understanding the impact of CR on this domain is important. Almost all cognitive tasks involve an element of attention to complete the test successfully. Several studies have specifically investigated the impact of reduced energy intake on attention resulting from continuous calorie restriction (CCR), or from fasting.

CCR studies

Ten studies looked at attention, seven of which found no change. Two found significant improvements whilst one found significant impairments (see table 1). For the most part, there have been no significant changes in attention for participants following CCR. For instance, a study of overweight individuals who restricted their calories by 25% over a period of 168 days reported no changes when compared with three other groups, weight maintenance, CCR plus exercise, and low carbohydrate diet followed by weight maintenance (Martin et al., 2007). This study used the Conner's Continuous Performance Test-II (Rosvold, Mirsky, Sarason, Bransome, & Beck, 1956) which is designed to measure attention, concentration, inattention, and impulsivity. Similar studies, using within-subjects methods and a variety of cognitive tests have failed to find significant differences in attention during CCR. (Cheatham et al., 2009; Kretsch, Green, Fong, Elliman, & Johnson, 1997; Makris et al., 2013; Pearce, Noakes, Wilson, & Clifton, 2012; Wing, Vazquez & Ryan 1995; Witte et al., 2009).

One study demonstrated a decrease in attention for healthy adults during CCR (Wardle et al., 2000), whilst attention improved for participants in two other studies (Bryan & Tiggemann, 2001; Siervo et al., 2012). Participants who restricted their energy intake over 12 weeks whilst assigned to either a low fat or Mediterranean diet performed significantly worse on the Bakan vigilance task of sustained attention when compared to those on the waiting list control group (Wardle et al., 2000). However, the impairment was greatest among those with the largest decrease in cholesterol level prompting the authors concede that a reduction in cholesterol may have been a contributing factor.

Attention increased in a study which used Weschler's WAIS III digit symbol coding subtest (Weschler, 1997) to test attention in overweight women over a 12-week period who had their calorie intake reduced by 20% (Bryan & Tiggemann, 2001). However, this increase was also apparent in the weight maintenance control group, suggesting practice effects may have been responsible for the change. A further study by Siervo et al. (2012) used the Trail Making Tasks (parts A and B) to test attention. The Trail making tasks (TMT) require the participant to join consecutive sequential numbers (Part A; i.e., 1,2,3 etc) and consecutive but alternating numbers and letters (Part-B; i.e. 1, A, 2, B etc). The TMT is widely used to measure several cognitive domains, including problem solving, and psychomotor speed. Results from these tasks showed that participants who restricted their calorie intake by 40% over 16 weeks performed significantly better than prior to restriction (Siervo et al., 2012).

Fasting Studies

Three studies investigated the effects of fasting on attention (see table 2). One study reported an increase (Tian, Aziz, Png, Wahid, Yeo, & Png, 2011), whilst two more reported no changes (Green et al., 1995; Owen et al., 2012).

Reaction time increased following a 12 hour fast for participants in Tian and colleague's within-subjects study (2011). They used an identification task to measure attention, which formed part of a neuropsychological test battery (CogState software, version 1.0). Participants were presented with a playing card on a computer screen. They were required to press "yes" for cards which were red in colour, or "no" for those that were not. Participants were measured at 0900 hours and at 1600 hours on separate days. There was an interesting 'time of day' effect with the study reporting quicker reaction times when participants fasted at 0900 when compared to the non-fasting period. It is notable that the study did not account for the effect of lowered blood glucose levels which would almost certainly decline during the afternoon when fasting.

In another study, focussed attention was assessed using a modification of the Eriksen & Eriksen (1974) procedure (Green at al., 1995). Subjects were required to press the correct key on a keyboard when letters appeared on screen. The letters would appear either alone or accompanied by a distractor, in the form of crosses or letters which were either identical or different from the target letter. No differences in this within-subject study were reported after 24 hours between fasted and non-fasted conditions. A further within-subjects study by Owen et al. (2012) found no significant changes following 12 hours of fasting when participants were assessed for selective attention using the Stroop Task.

The literature search revealed no studies that measured attention for participants who are involved in intermittent fasting regimes such as the 5:2 diet.

Inhibition

Inhibition describes the ability to restrain or curtail a behaviour, response or process.

CCR Studies

Three CCR studies measured inhibition, with two finding significant improvements, and one finding no change (see table 1). These have all used the Stroop task or a modified version of the same. The Stroop task is used widely in psychology to measure a person's ability to supress an automatic response. Participants are presented with a sheet of paper with 176 colour names which are printed in various colours on the page. They are required to first read the colour names aloud, before being asked in the next trial to read aloud the colour of the ink in which the word has been printed. Time taken to complete the trials, as well as incorrect responses are common measures.

Three published studies reported improvements in inhibition. One study reported a significant increase in Stroop reaction time both for the 20% CR group and for the control group (Bryan & Tiggemann, 2001) but as mentioned earlier this was likely due to practice effects. An improved performance over time was reported in a within-subjects design, with an increase in correct responses reported following a 25% reduction in calorie intake over six months (Makris et al.,2013), whilst Wing et al. (1995) reported an increase in the number of words read, for participants following CCR of 80% over a period of one month. Neither of these studies included a control group which limits the conclusions that can be drawn about the effect of calorie restriction when compared with those who have made no dietary alterations.

Fasting Studies

Studies researching the effect of fasting on inhibition are similarly scarce. Of three known published studies, all of which used the Stroop test and were reported in Benau et al.'s (2014) review paper, none found a significant effect on inhibition (Doniger et al.,2006; Stewart & Samouk, 1998; Owen et al., 2012). All used within-

subjects designs, measuring inhibition following periods of fasting ranging between 6-16 hours.

Cognitive Flexibility

Cognitive flexibility describes a person's capacity to adapt to rule change. Among the most popular test used in psychology is the Wisconsin Card Sorting Test or WCST (Grant & Berg, 1948). The test requires participants to classify cards according to certain criteria (number of shapes on the card, colour, and shape of the symbols on the card) and to state whether the classification is correct or not. After 10 cards are shown the rule of classification changes thus requiring the participant to recognise and adapt to the rule change.

CCR Studies

Two CCR studies have measured cognitive flexibility, one finding no change and one finding impairments (see table 1). Studies investigating the impact of CCR on mental flexibility have reported mixed results. Using the Wisconsin Card Sorting Test (WCST), participants in a within-subjects design who restricted their calorie intake by 25% over 3 months showed no change (Makris et al., 2013).

Solianik et al. (2016) used a repeated measures within-subjects design to assess set-shifting abilities in participants following a 2 days of severe calorie restriction using the Two Choice Reaction Time Task (TCRT). Part of a computerised neuropsychological test battery, this subtest measures mental flexibility. During the test, one of two stimuli are presented on screen, either a "*" or "o". The test instructs participants to respond rapidly to one of two stimuli by pressing the left mouse button on a computerised screen each time a "*" stimulus

appears, or the right mouse button when the “o” stimulus appears. They measured the accuracy and mean response time, finding that severe calorie restriction for 2 days which mimics the 5:2 diet (500Kcal per day for women, 600kcal per day for men) resulted in a significant decrease in mental flexibility. Although an increase in reaction time was not significant, there was a significant decrease in accuracy

Fasting Studies

Three fasting studies have measured cognitive flexibility, two finding improvements and one finding impairments (see table 2).

Set shifting is the ability to move flexibly between different tasks and can be measured in a variety of ways. Much like the WCST, set-shifting involves the capacity to adapt to rule change. Solianik (2016) used the TCRT to measure set-shifting in participants who had fasted for 48 hours. Their results showed a significant decrease in response time, suggesting there is an increase in mental flexibility following fasting. This study used a within-subjects repeated measures design and recruited a small sample of amateur weightlifters. Their results support a link between a cardiovascular response and cognition, but the results should be viewed in the context of the small sample size which may have contributed to sampling error.

Using a novel computerised rule-change task, Pender et al. (2014) used a within-participant repeated measures design to compare individuals at two time points, when satiated, and when fasted for 18 hours. Participants were presented with up to six identical non-food images on a computer screen. They were required to respond to one of four questions using Yes or No response keys. The questions ask the participants to judge if the pictures were Odd, Even, High (4 or more pictures) or Low (3 or Less pictures). The questions were switched periodically

without warning for one third of each trial. The study reported a greater cost of switching rules in the fasting condition when compared to the satiated condition, suggesting short-term food deprivation significant impairs set shifting abilities. This was a repeat of an earlier study which used the same experimental design, but presented pictures that were a mix of foodstuffs, or inedible items. For this study, set shifting costs significantly increased after fasting, regardless of the food/non-food stimuli (Bolton et al., 2014). For both studies set-shifting cost was measured by calculating the mean difference in reaction time between "shift" and "stay" trials.

Processing Speed

Processing speed refers to the ability to make sense of, and to respond to information within the amount of time taken to execute a given task. Processing speed requires an element of attention and typically measures reaction time.

CCR Studies

Six studies measured processing speed, with three reporting no change in reaction, two showing an increase in reaction and one reporting a decrease (see table 1).

Buffenstien et al. (2000) studied nine overweight women who were restricted in their energy intake to 800Kcals per day over one month. The participants undertook a complex reaction time test which involved tapping one of five brass discs, each corresponding to one of five small red lights. Participants were required to tap the correct disc when a corresponding light was illuminated. They measured both speed and accuracy and reported significantly faster mean reaction times and greater accuracy following calorie restriction. Given that this was a within-subjects study and therefore did not have a control group, it is again important to consider the possibility that these results may reflect practice effects.

Halyburton et al. (2007) used a larger sample size (n=93) of obese participants during an eight-week clinical trial where participants were randomly assigned to diets with either high or low levels of carbohydrates. They used an 'Inspection Time' test which required participants to identify the shorter of two lines of visual stimuli, when both lines were presented together. A 30% energy restricted diet (6300 kJe6600 kJ/day) either high (45%) or low (4%) in carbohydrate content showed significant improvement in the time taken to identify the target stimulus.

The only study of CCR that reported impairment in processing speed used a computerised finger tapping task to measure the simple reaction time of 14 women, restricted to 50% energy intake over 4 months (Kretsch et al., 1997). This repeated measures within-subjects study showed that reaction time was significantly slower, and interestingly it continued to slow (by 10%) following a 3-week weight stabilization period. The authors were unable to determine the cause of the apparent inability to restore processing speed following weight stabilization.

Fasting Studies

Two fasting studies exclusively measured processing speed, one showing impairments whilst the other showed improvements (see table 2). One study used the Staged Information Processing Speed test (SIPS) which comprises of multi-level arithmetic problems that the participant is required to solve (Doniger et al., 2006). As the levels progress in difficulty, participants are required to respond using the left and right mouse buttons to determine if the result is greater, equal or less than four. Using a repeated measures within-subjects design, 46 university students were tested on fasting (12-16 hours) and non-fasting days, over an average of 35 days. They found that reaction time was more impaired on fasting days for participants on medium difficulty tasks. This suggests that some tasks with certain psychometric

properties may be more sensitive in detecting any negative impact on processing speed.

Conversely, processing speed improved for a sample of male athletes who fasted for 12 hours. Tian et al. (2011) used a detection task test, which formed part of a cognitive battery. The Detection task uses playing cards on a computerised screen, all of which are red or black jokers. Participants are required to press a key as soon as the centre card on screen is turned. The mean reaction times are recorded with lower scores equalling better performance. Significantly faster reaction times were reported following a period of fasting.

Working memory

Working memory describes a cognitive function which allows short term information to be held temporarily for processing.

CCR Studies

The impact on working memory from CCR is similarly mixed with 3 studies reporting improvements whilst 2 report no changes (see table 1).
Several studies used a Digit Span task. Digit span is used often in psychology as a measure of short-term numerical memory. The task requires the participants to recall a series of numbers in the correct order immediately following their presentation. Digit span backwards requires the participant to recall the numbers presented, but in reverse order.

One study measured digit span for participants who were either in a low fat or low carbohydrate group, both of which had their energy restricted by 30% (Halyburton et al., 2007). They found that digit span backwards significantly improved following 8 weeks of CCR, but a lack of control group increases the possibility that any change is due to practice effects, rather than calorie restriction. In a follow-up Brinkworth et al. (2009) found that after 1 year, the low carbohydrate

and low-fat groups both maintained improvements in the backward digit span task. They concluded that numerical working memory improved following CCR, and that this improvement was likely due to energy restriction alone, rather than dietary change in carbohydrate or fat content.

The study performed described above by Bryan and Tiggemann (2001) which also used the backward digit span task, found no significant change to numerical working memory for those on CCR diets of 20% restriction. Similarly, no change was reported in numerical working memory using the digit span task for elderly participants who restricted their calorie intake by 30% over 3 months (Witte et al., 2009). These finding were echoed in a further repeated measures within-subjects study which also used the digit span task to measure performance in obese adults with CCR of 30% over 6 months (Pearce et al., 2012).

Martin et al. (2007) measured non-numerical working memory using the *Rey Auditory and Verbal Learning Test-RAVLT (*Rey, 1996). Participants who had their energy intake restricted by 25% improved after 3 months, but not after 6 months, when compared to a weight maintenance group and a CCR plus exercise group. The small effect size (generalized eta squared =0.07), led the authors to conclude that practice effects were likely responsible for any change over time. Improvements were also found in visuo-spatial working memory in a study where nine obese adults participants were measured following two days of severe calorie restriction (75%) using a matching-to-sample test (MTST). The test requires participants to remember a pattern presented on screen. After 2 seconds the pattern disappears and is replaced by 2 other patterns side-by-side. The participant must state (by pressing one of two buttons) if the left or right pattern matched the original. Mean response time and accuracy both improved with the latter showing a 4.7% improvement (Solianik et al., 2018).

Fasting Studies

Seven fasting studies looked at working memory(WM), all of which reported no significant change (see table 2). For instance, Benton & Parker (1998) showed that participants who missed their first meal performed worse in a trigram memory test (recalling a sequence of 3 letters after counting backwards by 3 for an allotted time) than those who had either eaten breakfast or drunk glucose. This suggests the glucose drink nullified the effects of missing breakfast. Overall, the impairments in WM for those who missed their meal were not significant.

A more recent study by Harder-Lauridsen et al. (2017) used the RAVLT in a repeated measures within-subjects design to measure WM in participants who fasted using the Ramadan model. This model involves 28 consecutive days of daytime fasting lasting approximately 14 hours. No significant changes were found. However, it is notable this was a small non-randomised study of 10 healthy men below the age of 35. Thus, future studies working within this model would improve upon the validity of this test by accounting for age, gender and sample size. Another within-subjects study that recruited a small sample (18) of healthy male participants found no significant effect on WM following 12 hours of fasting (Tian et al., 2011).

Two further studies reported no changes in WM. The Bakan Vigilance Task measured WM in a sample of 21 female subjects who had fasted for up to 24 hours prior to testing (Green et al., 1995). The Bakan vigilance task requires subjects to press a key on a computer keyboard when they detect a string of numbers in a sequence of either three odd or three even numbers. Up to nine numbers are presented on a computer screen in a continuous stream and the subject should respond as quickly as possible to the tasks. The number of correct hits were recorded, and no differences were observed.

The Rapid Visual Information Processing task which closely resembles the Bakan Vigilance task measured 20 healthy participants directly following the

absence of one meal. No significant differences in WM were found between fasted and non-fasted conditions (Green, Elliman, & Rogers 1997).

Psycho-motor ability

CCR studies

One CCR study measured psycho-motor abilities showing no effect (Solianik et al, 2018). The Pursuit Tracking Test (PTT) was used to measure fine psycho-motor ability in nine obese women during a 2-days CR which mimicked the popular 5:2 diet, reducing calorie intake by 75% (Solianik et al, 2018). The PTT requires subjects to track a moving box across a computer screen, ensuring that as the box moves across the screen in a circular pattern, the mouse cursor remains inside the box. The study observed no effects following two consecutive fasting days.

Fasting Studies

Three fasting studies measured psycho-motor abilities, all of which found significant impairments in healthy acutely fasted adults (see table 2).

Using a between-subjects repeated measures design, psycho-motor speed was measured following a 16 hour fast, using both Catch Game task and a tapping task (Doniger et al., 2006). The Catch Game tests for hand-eye coordination and response speed. The task requires participants to move a “paddle” at the bottom of a screen so that it can catch objects that are falling. No differences were observed between fasting and non-fasting days in the tapping task, however the time until first move was significantly longer on fasting days for the Catch Game task.

A separate within-subjects study that also used a tapping task found psycho-motor speed decreased for 21 healthy female students following a 24-hour fasting period when compared with two other levels of food deprivation, missing either one or two meals prior to testing (Green et al., 1995). Using a sample of 21 healthy

female participants, the two-finger tapping task involved the pressing of the “1” and “2” buttons on a keyboard alternately using the first and second fingers of the preferred hand until reaching 300 presses. The outcome was measured by ‘taps per second’. There was a significant effect of food deprivation on tapping rate. A further study by Green et al. (1997) using the same experimental design and finger tapping task with 20 healthy students also reported the same effect following short term food deprivation (missing one meal prior to testing when compared with satiated condition).

Section 3

Discussion

Of the 24 studies reviewed, nine significant improvements to cognitive function were reported for CCR studies, with three studies reporting significant impairments. For fasting studies, three reported significant improvements to cognitive function, with six reporting significant impairments.

Overall, CCR studies were more likely to report cognitive improvements whilst more deficits were reported in fasting studies, suggesting that the degree of CR may play an important role in affecting the direction of any impact on cognition.

Despite variation across the domains the results suggest that calorie restriction benefits inhibition, processing speed and working memory with some impairments in cognitive flexibility. The results of fasting studies suggest that fasting is associated with impairments in cognitive flexibility and psycho-motor abilities. Measures of attention and processing speed reported varied outcomes for fasting studies whilst inhibition and working memory appeared unaffected. Inconsistent findings were reported in all cognitive domains across the studies, likely due to variations in fast duration and tasks used.

Most impairments were observed in the domains of cognitive flexibility (two from fasting, and one from CCR) and psycho-motor abilities (three from fasting, and one from CCR). For studies measuring cognitive flexibility, two of these were from fasting studies that were comparable in sample size, duration and sample population (Bolton et al., 2014; Pender et al., 2014). One study from the literature on calorie restriction reported impairments following severe CR (75%) over two days (Solianik et al., 2018). This most closely resembles the 5:2 intermittent fasting (IF) diet in which calorie intake is restricted by 75% for two days each week. This suggests that the extent of calorie restriction may play an important role in changes to cognitive flexibility during dieting. The only other study resembling the 5:2 diet for

the percentage energy reduction (80%) measured cognition following continuous CR over 28 days (Wing et al., 1995). Whilst cognitive flexibility was not measured in Wing and colleagues study, the impact on cognitive function for those who diet intermittently, rather than continuously, and who also severely restrict their calorie intake for longer than 28 days remains unknown.

Of the three fasting studies that had discretely measured psycho-motor abilities (PMA) all reported significant impairments. Notably these studies recruited healthy university students and their findings were similar to those examining the cognitive processing profile of young people with anorexia nervosa (Kjaersdam Telléus et al., 2015). Therefore, further research investigating the effect on PMA after engaging in a cycle of severe fasting and eating would add to our understanding of a potential cognitive profile for eating disorders. Thus, future studies should seek to understand the impact of intermittent fasting using cognitive tests that measure both PMA and cognitive flexibility. Furthermore, despite it being generally accepted that younger people perform better in accuracy and speed than older people (Krampe, 2002), the evidence suggests a detrimental impact for PMA following severe CR for young people. Less is known about the impact for adults beyond the typical university age.

The singular study from the CCR literature that measured PMA was Solianik and colleagues' 5:2 comparable study which recruited a small sample of obese adults, finding no significant impact of CCR (Solianik et al., 2018). Thus, further research is needed to explore the impact of severe calorie restriction on PMA for healthy adults across the age range.

Most improvements were observed in the domains of inhibition, working memory and attention (9 in total), the majority of which were from continuous calorie restriction research. This suggests encouraging cognitive changes following continuous energy reduction. From an evolutionary perspective these results appear logical given that it would be evolutionarily adaptive for the brain to function at its

best when hungry, maximising the chance of success in seeking and acquiring food (Mattson, 2015). However, there was no change in inhibition or working memory in fasting studies with only one fasting study reporting an improvement in attention (Tian et al., 2011). This suggests that there may be a differential impact on cognitive function that varies according to the degree of energy intake.

There were inconsistent findings from the literature regarding the impact of continuous calorie restriction and fasting on processing speed. Significant improvements were reported in two CCR studies (Buffenstein et al., 2000; Halyburton et al., 2007) with one reporting impairments (Kretsch et al., 1997) and a further three reporting no changes (Brinkworth et al., 2009; Cheatham et al., 2009; Pearce et al., 2012). This is likely influenced by great deal of variability in the design of the studies reviewed.

The variability in methodology makes it difficult to directly compare the results of the studies for any of the cognitive domains. For instance, whilst some used a combination of selective tasks to measure cognition (Green et al., 1995), others have used more extensive cognitive batteries (Doniger et al., 2006). Further, cognitive domains have been measured in numerous ways. For instance, processing speed was measured differently in two of the studies with contrasting results (Doniger et al., 2006; Tian et al., 2011). Additionally, the studies reviewed contain a mix of within-participant and between-participant designs. Within participant designs require participants to repeat tasks to see if there is a difference following experimental manipulation. This design is useful for reducing the number of participants required and is therefore more practical and cost efficient. Such designs reduce variance and thus increase power as the participants act as their own controls. However, the advantages of between-participant designs (where two groups perform tasks just once) include minimising the learning and transfer of knowledge across conditions (practice and/or order effects). Thus, each study

design has distinct advantages and disadvantages, the advantages of a within-participants design tending to be disadvantages in a between-participant design and vice versa.

Few studies account for major confounds such as exercise, diet and time of day. For instance, two of the studies reviewed found that performance improved in the afternoon (Doniger et al., 2006; Tian et al., 2011). In addition, research indicates a close link between dietary intake, exercise and cognition with experimental studies reporting improvements in neurocognitive function following a combination of aerobic exercise with dietary manipulation and caloric restriction (Smith et al., 2010). Consequently, future research should account for these factors and others such as stress and sleep patterns.

The impact of reduced blood glucose on cognition has not been considered in many of these studies. Benton, Parker, and Donohoe (1996) discuss the psychological and physical symptoms associated with low levels of blood glucose (hypoglycaemia). They found that cognitively demanding tasks deplete the brain of glucose and therefore those with low blood glucose levels (hypoglycaemia) will likely perform significantly worse in cognitive tests than those with higher levels of blood glucose reserve. Despite the widely accepted effect of glucose of cognition, fewer than half of the studies reviewed here take this into consideration (Benton et al., 1998; Cheatham et al., 2009; Green et al., 1997; Harder et al., 2017; Owen et al., 2012; Pearce et al., 2012; Solianik et al., 2018; Witte et., 2009). Moreover, a reduction in fasting peripheral insulin can increase insulin sensitivity (Witte et al., 2009). This means the body becomes more efficient in assisting the regulation of insulin transport at the blood-brain barrier. It has been suggested that improving insulin signalling in the brain has neuro-protective effects (Witte et al., 2009). A decrease in peripheral insulin has been observed following CR in a study by Witte et al. (2009), which also reported improved memory performance in older adults, demonstrating that improvements in insulin regulation can positively effect cognition.

Future work should account for blood glucose and insulin levels as potential confounding factors when measuring changes in cognition.

The majority of these studies are laboratory based. Under these conditions motivation is likely to be extrinsic, that is they are likely to be motivated by outside sources such as financial gain. Given diets are costly, most dieters are intrinsically motivated, meaning that they strive to reach a level or goal for personal satisfaction or achievement. Intrinsic motivation is usually more successful in changing long term behaviour (Harpine, 2015), thus studies that recruit participants who are already dieting outside of laboratory conditions with likely have higher external validity and reduced dropout rates.

Finally, all the studies reviewed here examine the impact of continuous calorie restriction (CCR) on cognition. Whilst such studies add to our existing knowledge of the role of CCR in cognitive function, there has been marked neglect of research that investigates any potential cognitive changes resulting from intermittent, as opposed to continuous fasting regimes. A popular version of intermittent fasting is the '5:2' diet which has been heavily promoted in the UK media as an evidence-based method for losing weight and improving health. Whilst one study reviewed above mimics the design of the 5:2 (Solianik et al., 2018), the results should be interpreted with care, given the study's duration (2 consecutive days) does not reflect a realistic weekly cycle of intermittent calorie-reduced eating and fasting. To gain a better understanding of the potential effects of the '5:2' diet on cognition, it is necessary to measure cognition for participants who are already engaged with the diet over a longer duration.

Limitations

This literature review focussed on experimental studies that manipulated total calorie intake. The findings presented are from studies which were necessarily

limited by the restraints of writing a conceptual introduction. A full systematic review would have undoubtedly uncovered further studies and allowed for greater depth of discussion. Searching the literature systematically would have reduced bias, thus producing a more objective review of the literature. A more thorough search that included 'grey literature' such as theses, unpublished studies, and non-peer reviewed journals, as well as those outside of the psychological mainstream such as lifestyle and pharmacological approaches to weight loss would have improved the quality of the review. In addition, with the current review not being systematic, there is an absence of a list of generic (common to all research studies) and particular (specific to the topic) aspects of quality, against which to judge each trial (Greenhalgh, 1997). Furthermore, unlike a full systematic review, a more basic literature review contained within a conceptual introduction would not wholly consider the external validity of each of the trials that are included, thus care must be taken when interpreting the results and the extent to which they are generalisable to the target population.

Aims of the empirical study

There appears to be a large gap in the literature as none of the studies reviewed have explored the effect on cognitive function for those following intermittent fasting (IF) regimes. The primary aim of the empirical study will be to measure changes in cognition for those following IF diets. The 5:2 diet will be chosen due to its popularity. Whilst recent evidence suggests that IF diets such as the 5:2 are at least as beneficial to human health as continuous calorie restricted (CCR) diets (Mattson, Longo, & Harvie, 2017), there is a paucity of research exploring any potential cognitive effects. Given that the studies reviewed have reported that most cognitive deficits have been observed following severe CR

(between 75-100%) it is possible that the 5:2 diet, which encourages a severe reduction in calories might be detrimental to some domains of cognition.

By comparing the results of cognitive tasks for those who are on the 5:2 diet to those who are on CCR diets, (as well as comparing performance on fasting and non-fasting days for 5:2 participants), any disparities in cognitive function may provide essential information for those who are considering the costs and benefits of following the 5:2 regime. Furthermore, the results from cognitive studies designed to investigate healthy participants who choose to adopt a regular pattern of severe calorie restriction and normal eating, may be beneficial to our understanding of clinical presentations for those with eating disorders. For instance, deficits in cognitive flexibility have been found in those with anorexia (Lena, Fiocco, & Leyenaar, 2004) which might account partially for the difficulties they often experience when switching from thinking about things one way, to thinking about them differently. This is often particularly evident for more complex or deeply embedded behaviours. Should deficits be found for those engaging in the 5:2 diet, but not for those on CCR diets, then we might expect cognitive flexibility to improve following a change from IF to CCR. If this is the case, then it is possible that prioritising changes in the pattern of energy intake for those with anorexia could reduce cognitive rigidity and accelerate recovery.

The empirical study will seek to consider some of the confounds discussed such as insulin/glucose sensitivity and time of day, whilst also using online tasks as part of a worldwide study to improve the external validity of any significant findings. Further, given that within and between-participant designs both have costs and benefits to experimental design this study will employ both. A within participant design will be used to measure any differences in cognition for those on the 5:2 diet following fasting and non-fasting days within a seven-day period. This will help to establish any short-term changes. Furthermore, the studies reviewed above that resemble the 5:2 diet in terms of the degree of calorie restriction, have not

continued beyond 28 days (Solianik et al., 2018; Wing et al., 1995). Those who choose the 5:2 diet will often remain on it for much longer, therefore it is important to determine any differences in cognition following a longer duration. Thus, the empirical study will only recruit those who have been following their diets for longer than one month.

In summary, the empirical study will aim to explore differences in cognition between those who are already engaged with the 5:2 diet and those engaged with CCR diets, as well as comparing performance on fasting and non-fasting days for 5:2 participants. Any knowledge gained will be helpful for those considering which diet to choose or maintain, and for researchers and clinicians with an interest in eating disorders.

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Part 2: Empirical Paper

The impact of the 5:2 intermittent fasting diet on cognition in healthy adults.

Abstract

Objectives:

Research suggests that a reduction in calories may impact cognitive functioning in healthy adults. Despite studies that demonstrate changes to cognitive function following periods of fasting and continuous calorie restriction, any potential impact for those who follow intermittent fasting (IF) diets remains unclear. Among the most popular IF diet is the 5:2 fasting diet. Proponents of this dieting regime claims that it has numerous benefits to general health. Less in known about the impact of this diet on cognition. Given that some studies have shown cognition is impaired following acute fasting, concerns remain about the impact of a fasting diet that encourages high levels of intermittent calorie restriction. This study sought to understand the impact on specific areas of cognition for healthy adults who follow the 5:2 diet.

Methods:

Part A

Using a within-subjects repeated measures design, 36 healthy adults who were following the 5:2 diet for more than four weeks were measured for cognitive performance on fasting and non-fasting days using a range of online cognitive tasks. Specifically, we measured cognitive flexibility, working and prospective memory, reflective impulsivity and psycho-motor speed.

Part B

Using a between-subjects design, mean performance on the cognitive tasks for healthy adults following the 5:2 diet (n=36), was compared to those following CCR diets (n=30). Both groups had been following their diets for more than four weeks.

Results:

Part A

Cognitive flexibility, working and prospective memory was impaired on fasting days along with a reduction in impulsivity. Overall composite scores revealed impaired reaction time and accuracy on fasting days.

Part B

Participants following the 5:2 diet performed worse than those following CCR diets in tasks designed to measure psycho-motor speed and cognitive. Overall composite scores revealed impaired reaction time for those following 5:2 diets, compared with those following CCR diets.

Conclusions

Research that investigates the impact of calorie restriction and fasting on cognitive function should also consider the potential risks of cognitive impairment for those who choose to follow intermittent fasting diets. Future studies would benefit from longer term measurement of cognition for those following IF diets whilst accounting for potential confounding variables.

Introduction

Calorie restriction (CR) without malnutrition improves general health and extends the lifespan of numerous non-human organisms (Van Cauwenberghe, Vandendriessche, Libert, & Vandenbroucke, 2016). In non-human primates, research has established that CR can increase health span (time free from disease) and reduce mortality, with researchers suggesting these benefits may extend to humans (Martin et al., 2016). The opportunity for people to live longer and healthier lives by reducing their energy intake has captured public interest, but whilst dieting regimes increase in popularity, little is known about the impact of CR on human cognition.

Animal studies focussed on cognitive changes during CR, have established that a daily reduction in calorie intake of around 30% has the potential to improve cognitive function (Brownlow et al., 2014; Vitousek, 2004; Witte, Fobker, Gellner, Knecht, & Floel, 2009). Human studies have shown that a similar short-term percentage reduction in calories can significantly improve cognitive performance in areas such as processing speed, inhibition, and working memory (Buffenstein, Karklin, & Driver, 2000; Brinkworth, Buckley, Noakes, Clifton, & Wilson, 2009; Bryan & Tiggemann, 2001; Halyburton et al., 2007; Makris et al., 2013).

Absolute fasting is distinct from caloric restriction as it involves total calorie deprivation. Unlike CR, numerous short- term fasting studies appear to demonstrate a trend towards impairments in cognitive performance, with poorer performance reported in processing speed, cognitive flexibility (set-shifting), and psychomotor abilities. (Bolton et al., 2014; Doniger, Simon, & Zivotofsky, 2006; Green, Elliman, & Rogers, 1995; 1997; Pender, Gilbert, & Serpell, 2014). Additional fasting studies have reported no changes in working memory (Benton & Parker, 1998; Green et al., 1995; 1997; Harder et al., 2017; Owen et al., 2012; Solianik, Sujeta, Terentjeviene,

& Skurvydas, 2016; Tian, Aziz, Png, Wahid, Yeo, & Png, 2011), with one reporting improved performance in cognitive flexibility (Solianik et al., 2016).

Despite a lack of consensus regarding the impact of fasting on cognition (Benau, Orloff, Janke, Serpell, & Timko, 2014) concerns remain about the potential effect on human cognition for those who choose to adopt intermittent fasting (IF) regimes. IF fasting regimes have become popular for those wishing to lose weight or to maintain a healthy lifestyle, and usually involve a cycle of fasting and ad libitum intake (normal eating) over a defined period.

Among the most popular forms of IF in the UK is the 5:2 fast-diet (Mosley & Spencer, 2013). This diet encourages subscribers to reduce their calorie intake by 75% for two days each week (from 2400 to 600-650 calories for men, and from 2000 to 500 calories for women). Champions of the 5:2 diet have claimed the regime is as beneficial as continuous calorie restriction, reporting improved insulin sensitivity and weight loss (Mattson, Longo, & Harvie, 2017). However, existing studies of IF in humans have mostly investigated the impact on physical health (e.g. Harvie et al., 2010) whilst few have looked at the potential effect of IF diets on cognition.

To our knowledge, just one published study has investigated the impact of calorie restriction on human cognition whilst following the same guidelines for the degree of calorie restriction as those recommended for the 5:2 diet (Solianik, Sujeta, & Čekanauskaitė, 2018). Cognitive changes were measured in 9 obese females following a 2-day very low-calorie diet, reporting improved performances in working memory, and a reduction in cognitive flexibility. However, the authors concede that considering the small number of participants it is difficult to determine if these changes are meaningful. In addition, the study length of two days does not reflect an intermittent fasting regime. Given that most people who follow the 5:2 diet are likely to engage with it for longer, studies that measure cognitive function after a

longer period are necessary to add to our existing knowledge about its potential impact.

One further unpublished study measured changes in cognitive performance on fasting and non-fasting days for participants who had been following the 5:2 diet for four weeks (Mahony, 2016). No differences were found on any measures between the two conditions, suggesting that following the 5:2 diet for four weeks did not lead to cognitive impairments on fasting days. However, participants recruited to the study were new to the 5:2 diet and so may not have been committed to adhering to the strict dietary guidelines for calorie reduction. Current research within UCL's Eating Disorder Research Group, that examined the food diaries of the participants recruited for Mahony's study suggests that 50% did not comply with calorie recommendations on fasting days (F. Cook, personal communication, May. 31, 2019). In addition, Mahony's study measured cognition after a relatively short time period, when compared with numerous studies that reported significant cognitive changes following periods of CR lasting between 56-365 days (Brinkworth et al., 2009; Bryan & Tiggemann, 2001; Halyburton et al., 2007; Kretsch, Green, Fong, Elliman, & Johnson, 1997; Makris et al., 2013; Siervo et al., 2012; Wardle et al., 2000).

Several studies have highlighted changes in specific areas of cognitive function in humans following a reduction in calorie consumption. Research into the effects of CR on cognitive flexibility have reported impairments following acute severe restriction (Solianik et al., 2018), as well as in individuals with anorexia nervosa (Reville, O'Connor, & Frampton, 2016), while deficits in set-shifting have been evident following acute fasting (Bolton et al., 2014; Pender et al., 2014). Reflective impulsivity has previously been shown to reduce after short-term fasting (Howard, 2015), whilst deficits in psychomotor speed using simple two-finger tapping tasks were reported in two separate studies for participants who were in an

acutely fasted state (Green, Elliman, & Rogers, 1995,1997). Working memory has been shown to improve following CR (Brinkworth et al., 2009; Halyburton et al., 2007; Solianik et al., 2018) whilst research suggests that glucose ingestion may improve prospective memory performance (Riby, Law, Mclaughlin, & Murray, 2011).

The current study aims to establish whether cognitive performance on measures of cognitive flexibility, reflective impulsivity, working memory, prospective memory and processing speed, is impacted on fasting days for those engaged with the 5:2 diet. Given that previous research recruited participants who were new to the diet and their cognitive performance was not measured beyond 4 weeks (Mahony, 2016; Solianik et al., 2018), this study will recruit established users of the 5:2 diet who have been engaged with the regime for at least 4 weeks.

If there are observed differences in cognitive performance between fasting and non-fasting days, this will raise important questions about the relationship between nutrition and cognition. Firstly, it may help to further understand the mechanisms by which severe intermittent calorie restriction effects cognitive function. Furthermore, any differences might add to our existing knowledge regarding which brain systems are affected by a reduction in calorie intake. In addition, potential deficits in cognitive abilities may inform researchers and clinicians with an interest in eating disorders (EDs) by adding to existing research that seeks to understand the role of energy restriction in their maintenance.

Given that the evidence base for the safety and effectiveness of the 5:2 diet is limited, it is important to establish if there are any overall differences in cognitive performance between the 5:2 and CCR diets. The NHS advise that people wishing to lose weight should follow NICE guidelines which recommend CCR to reduce obesity (NICE, 2014). IF regimes such as the 5:2 continue to be used as a popular method for weight reduction and are promoted on NHS websites as an alternative to CCR. To our knowledge there are no published studies comparing cognitive

function between these two different types of dieting regimes, thus little is known about the costs and benefits to cognition of choosing either.

Given our research questions, this study required two separate designs. By using a within-subjects design whereby the cognitive performance of participants on the 5:2 diet is measured on fasting and non-fasting days, much of the variance from individual differences in task performance can be controlled for, whilst also increasing the power of the study to detect differences, with participants acting as their own controls. By using a between-subjects design to investigate differences in cognitive performance between participants on the 5:2 and CCR diets, it is possible to compare the cognitive profile of individuals following these two different dieting regimes.

Hypotheses.

1. There will be a difference in cognitive performance on fasting days when compared with non-fasting days for participants who have been engaged with the 5:2 diet for a minimum of 4-8 weeks. More specifically, in line with previous research we would predict improvements on fasting days in working memory and a reduction in reflective impulsivity, with deficits predicted in set-shifting and psycho-motor speed. Given that, to our knowledge, there is no pre-existing research on the impact of calorie restriction on prospective memory, no prediction was made for the impact of intermittent fasting on this area of cognition.
2. Given the general trend that fasting appears to impair cognition when compared with CCR (see conceptual introduction), we would predict that those following the 5:2 intermittent fasting diet will perform worse overall in tasks designed to measure cognitive performance than those following CCR

diets. In the absence of existing published studies comparing the two diet regimes, no further prediction was made regarding which areas of cognition may be affected.

Methodology

Participants

The planning procedure for the study took place alongside another trainee as part of a joint project (see appendix I for further details). A healthy adult sample was recruited for the study (n=98). Participants were eligible for the study if they were aged between 18-60 and were fluent English speakers. Fifty-three participants were following a continuous calorie restricted diet (CCR) with a daily reduction in calories of between 15-25%, whilst 45 were following the 5:2 IF diet. Recruitment was through online platforms such as the official 5:2 diet forum (https://thefastdiet.co.uk/forums/), social media platforms, twitter accounts, and community poster adverts (see Appendix II for recruitment advertisement). All permissions were sought in advance from the relevant site administrators. 80.61% of participants completing the study were currently residing in the UK, with China, India, Canada, and the USA each contributing 3.06% of participants. The remaining participants were resident in Europe, Asia, or Central America. The mean age of participants completing the study was 43.19 years (SD=11.32). 90.91% were female and 9.91% were male. 53.06% reported their ethnicity as Mixed ethnicity (White or Caucasian 40.81%, 4.08% Asian, 2.04% Afro-Caribbean). Mean body mass index at the start of the study was 28.32 (SD=3.80).

Participants were eligible if they were fluent in English, computer literature, had normal (or corrected) visual acuity, and had internet access. Those with difficulties that would impair their ability to engage easily with online tasks were excluded. This included those with learning difficulties (such as dyslexia/dyscalculia) and those with other current mental health problems. In addition, the exclusion

criteria included those with any current or past eating disorder, those who were pregnant, diabetic, and those who lived with any other medical or physical condition where taking part in the fasting study would place them at risk of harm. All those who responded to the recruitment adverts were screened prior to being accepted for the study (see Appendix III for screening form). To incentivise participation and reduce attrition, participants were entered into a prize draw for Amazon vouchers that ranged in value from £20-£100.

Power calculation

Part A of this study was designed to examine any differences in cognitive function on fasting versus non-fasting days for those engaged in the 5:2 diet. The power analysis was informed by a study similar in design (Watkins & Serpell, 2016). A power calculation was conducted using G Power (Faul, Erdfelder, Lang, & Buchner, 2007), giving an estimated sample size of 34 participants to provide 80% power to detect a medium effect size with an alpha level of 0.05. This was based on a dependent means matched-pairs design.

Part B was designed to examine the differences in cognitive function between two diets (5:2 and CCR). The power analysis was informed by a similar study using a similar design (Lopez, Tchanturia, Stahl, & Treasure, 2009). A power calculation was conducted using G Power (Faul, Erdfelder, Lang, & Buchner, 2007), giving an estimated sample size of 45 per group to provide 80% power to detect a medium effect size with an alpha level of 0.05. This assumed the adoption of an independent means design.

Ethics

Ethical approval was sought from the UCL Research Ethics Committee (Project ID 12695/001, see Appendix IV for further details). All participants were

required to have been participating in their dieting regime for at least 4 weeks. This safeguarded against encouraging individuals to use study participation as a reason to begin dieting. Given the severe level of calorie restriction in the 5:2 condition, individuals with a previous history of eating disorders were excluded from the study to prevent the possibility of triggering relapse. All participants were advised to seek medical assistance if at any time during the study they felt unwell.

Study design and procedure

Part A

This study used a within-subjects quasi-experimental design to measure scores on tests of cognitive function at two separate time intervals for those engaged with the 5:2 IF diet. Participants completed the cognitive tasks on two occasions, once on a fasting day, and once on a non-fasting day. Half of the 5:2 participants were instructed to complete the tasks first on a fasting day with the second set of task scores measured on a non-fasting day. This order was reversed for the other half of the sample to reduce potential order effects. Participants were required to complete the tasks on one fasting and one non-fasting day within a 7-day period.

Part B

In addition, the study used a between-subjects independent, quasi-experimental design, where participants from both IF and CCR groups were tested on two occasions. Those in the CCR group were asked to complete the online tasks twice on any two days within a 7-day period. Participants in both groups were asked

to complete the cognitive tasks within the same time frame on testing days, which was set at between 6 and 10pm to minimise time-of-day effects (Benau et al, 2014). All participants were asked to commence their second testing session within thirty minutes of the time they chose on their first testing day. Participants were advised to undertake testing in a quiet location, free from external distractions.

To reduce the impact of glucose depletion on cognition (Feldman & Barshi, 2007) all participants were asked to ensure they had eaten something thirty minutes before commencing cognitive testing. To ensure participants who were following the 5:2 diet were not in a fully fasted state when tested, they were asked to ensure they had consumed at least half of their calorie intake (250-300 calories) on fasting days before starting the cognitive tasks.

Participant's recorded their food intake using a diary prior to commencing the online tasks to encourage compliance by emphasising that researchers were checking their calorie intake on fasting days. The diary was presented to them as part of the online programme, just prior to access to the cognitive tasks. Participants were asked to complete a record of all food and drink consumed on the day prior to their participation in the cognitive tasks. This included the time of consumption, type of food or drink consumed, and the amount consumed. The order in which cognitive tasks were presented was randomised to prevent order effects. The duration of each testing session was approximately 20 minutes.

Individuals who responded to the research posters contacted the researchers via email. All participants were screened for suitability via a return email which also contained information relating to the study and a consent form. Participants were instructed to return the consent form only if they were eligible to take part in the study (For details of information sent to participants see appendices III and V). Upon completion of eligibility screening and receipt of a signed consent form (see appendix VI) all participants were sent an email prompting them to

complete the cognitive tasks. The email included a personalised ID number and weblink to allow participants access to the online cognitive tasks (see appendix VII for further details). Participants were provided with an opportunity to contact the researchers at any point prior or during their involvement via email or telephone to address concerns or to ask questions relating to the study. Access to the cognitive tasks was via participant's own laptop or desktop computer with internet access.

Pilot study

A small convenience sample of four healthy volunteers agreed to take part in the cognitive testing prior to recruitment. This provided important feedback relating to technical difficulties for those completing the tasks. Consequently, rigorous testing of the online platform allowed for the correction of any faults, and qualitative feedback was used to make adjustments to testing procedures (i.e. providing clarity regarding incompatibility with tablets and smartphones).

Measures

Demographics

All participants were asked to provide information relating to their age, gender, ethnicity, current country of residence, native language and highest educational attainment. Self-reported weight and height were used to calculate BMI.

Cognitive tasks.

Participants were provided with instructions on how to complete each task, with an opportunity to practice beforehand. (Further details on the layout and presentation of the online tasks can be seen in appendix VIII). For some tasks (Rule Change and 2n Back), the practice trial included an accuracy threshold set at a level

above that of chance. Those who did not reach the level were required to repeat the trial tasks before proceeding further. The cognitive tasks incorporated touch-key and mouse technology to record the participant's response. A progress bar was displayed in the top-centre of the screen to indicate the stage of the participant's progression in the cognitive battery. The cognitive battery comprised of 5 tasks, each designed to measure various aspects of cognitive function. These were the Trail Making Tests (TMT) Part A&B, Rule Change Task, Tapping Task, a 2n-Back Task with an embedded Delayed Intention (prospective memory) task, and an Information Sampling Task.

Psychomotor speed and processing speed (Tapping task, Trail Making-Part A)

A computerised tapping task was used to measure psychomotor speed. Participants in this study were asked to press the 'M' key on a keyboard as many times as possible within a 15 second period. The time remaining was displayed in the form of an on-screen countdown. This task was completed twice and the total number of taps per trial was recorded as the outcome measure.

The Trail Making Test (TMT) is used widely to measure several cognitive domains, including problem solving, psychomotor speed, visual attention, flexibility, working memory, processing speed and shifting. It is considered sensitive to a variety of neurological processes and impairments and has good psychometric properties (Tombaugh, 2004). As with all our tasks, a computerised version was presented, which may not perform identically to paper versions (Drapeau, Bastian-Toniazzo, Rous, & Cartier, 2007).

Part A of the study is often used to measure processing speed and was included in our test battery for this purpose. TMT-A requires the participant to join consecutive sequential numbers or letters by drawing a line between them (e.g.,

1,2,3, etc.) with the outcome measured as time to complete the task. Participants were presented with two online trails. On both occasions the screen displayed several on-screen yellow circles containing numbers or letters. Trial completion involved clicking on each circle in the correct order, with circles turning green if correct or pink if incorrect (see Figure 1). Average time taken to complete both trials was recorded.

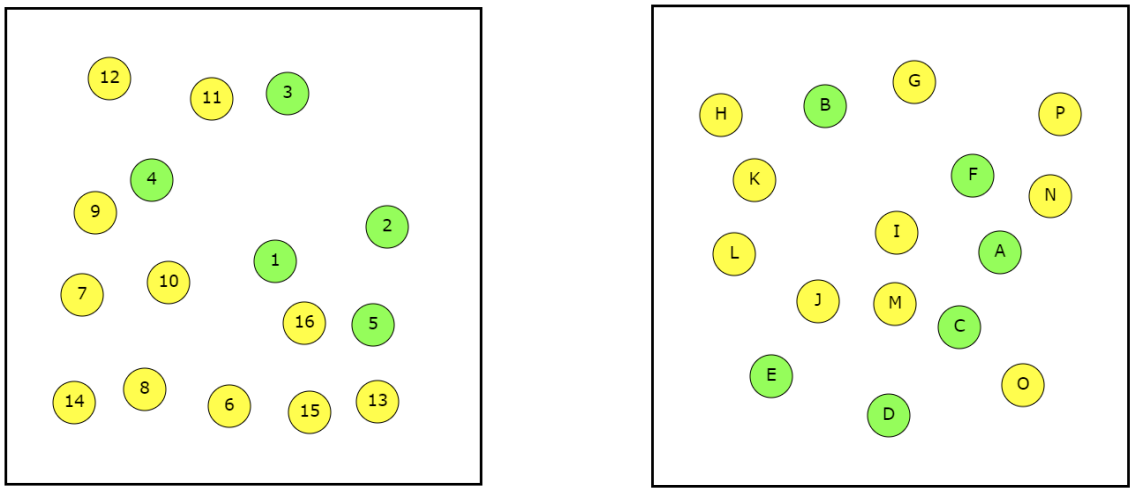

Figure 1- Trail making test – Part A

Set-shifting and cognitive flexibility (Rule Change task, Trail Making-Part B)

The Rule-Change Task (RC) was used to measure set-shifting. Set shifting is the ability to move flexibly between different tasks and involves the capacity to adapt to rule change. The RC task was adapted from an earlier version used by Bolton et al. (2014) who studied set-shifting costs in healthy adult females. Their study showed that set-shifting costs increased following an acute period of fasting in both food and non-food (neutral) trials. Food trials contained stimuli consisting of food items to investigate potential effects of food cues on set-shifting ability, whereas non-food trials contained neutral stimuli.

For this study, participants were presented only with on-screen non-food neutral stimuli in the form of a series of grey boxes. Up to six boxes were presented at any one time and participants were required to indicate whether the number of boxes were high or low (above four = high) or whether the boxes presented were an odd or an even number. The question, Odd?, Even?, High? Or Low?, would appear on-screen (see Figure 2). The rule would stay the same on some consecutive trials (stay trial) with a one in three probability of the next consecutive trial becoming a change trial (shift trial). Participants were required to complete 100 trials with accuracy and reaction time recorded.

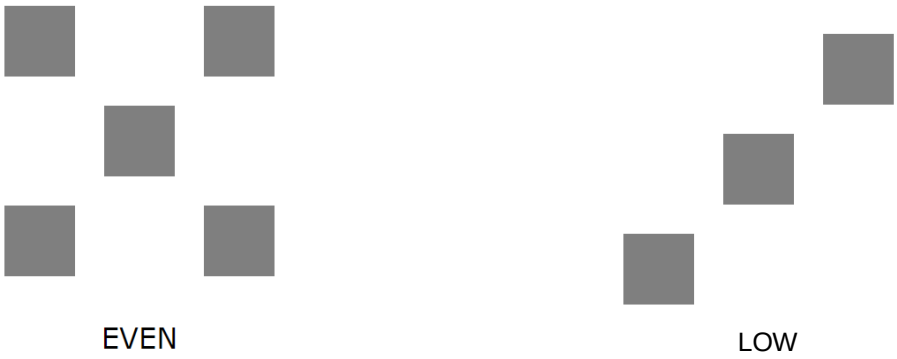

Figure 2- Rule Change Task

The Trail Making Test, part B (TMT-B) was used as a further measure of cognitive flexibility. Part B was adapted for computer use and was administered immediately following Part A. Participants were presented with two online trials. In both trials participants were presented with several on-screen yellow circles containing both numbers and letters. Trial completion involved clicking on each circle in the alternating order (e.g., 1, A, 2, B etc.) with circles turning green if correct or pink if incorrect (See Figure 3). Placement of the circles was randomised for each trial, with average time taken to complete both trials recorded.

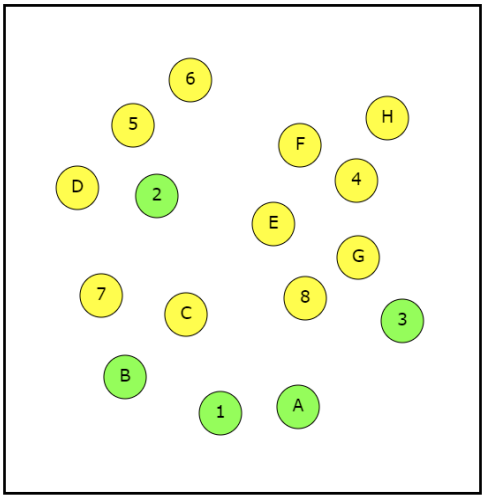

Figure 3-Trail Making Test- Part B

Working memory (2n-Back task)

A 2n-Back task was used to test participant's ability to retain and manipulate working memory. This task requires the ability to remember information from the past and to use it in the present. The 2n-back task lasted 5 minutes and 10 seconds, during which single letters were presented on-screen as neutral stimuli. These stimuli remained on-screen until the participant pressed a key. Using designated "yes" or "no" keys, participants were required to indicate on each trial whether the stimulus matched the item presented two trials previously.

Prospective memory (2n Back Task – clock)

Prospective memory (PM) describes the ability to recall a planned intention or to perform a planned action at a future point in time. Everyday examples of PM include remembering to take medication, cooking, or making social arrangements.

For this study the PM task was embedded in the 2n-Back task, requiring participants to remember to undertake an additional action in the absence of direct prompting. During the 2n-Back task, participants were required to press a key at 30 second intervals (within +/- 3 seconds). Pressing a separate key displayed an on-screen timing clock for 1.5 seconds to support participants with their response accuracy. The number of times that the clock was checked, along with the number of times participants hit the relevant key within the designated time period was measured.

Reflective impulsivity (Information Sampling Task)

Reflective impulsivity describes the process of accumulating and examining information prior to making a decision. An information sampling (IS) task was used to measure reflective impulsivity using a modified version of a trial described by Howard (2015). Research has shown this test to be sensitive to participants in an acute fasting state. Howard and colleagues demonstrated that when compared to a satiated condition, fasted participants who were presented with a matrix of boxes opened more of them before deciding which colour boxes represented the majority (Howard, 2015). This effect only occurred in the fixed-win condition where participants could open as many boxes as they wished without penalty, as opposed to the decreasing win condition where participants lost points for each box opened. Thus, for this study the fixed win condition was used. Participants were presented with an on-screen array of grey boxes which when clicked using a mouse button would reveal either a blue or yellow colour (see Figure 4). Once the participant had decided upon which colour represented the overall majority of boxes, they were instructed to click one of two options below the matrix to select either blue or yellow. Opened boxes remained open to reduce the demand on working memory and participants were required to complete ten trials in total. Measurements included accuracy (number of correct trial decisions), quantity of information sampled (total

number of boxes opened), reaction time for opening each box, and the time taken to complete the task.

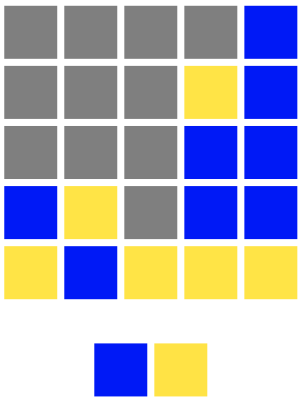

Figure 4-Information Sampling Task

Data Analysis

The data were carefully screened prior to analysis and checked to minimise potential errors. Each variable was scrutinised to exclude responses that were no more accurate than chance. For example, when examining data for the 5:2 only group, one participant's data for the Rule Change tasks was removed from the fasting session because their accuracy was below chance (36%) suggesting they had misunderstood the task. For those who completed the cognitive tasks more than once, dates and times were monitored to ensure that participants completed within the stipulated time frames. All participants completed the two trials within seven days and within a two-hour time period. Data was initially imported into Microsoft Excel prior to transfer to SPSS Statistics V25. Following the same protocol as an unpublished study within our research team which also explored the impact of the 5:2 diet on cognition (Mahony, 2016), outliers were excluded from data analysis if they exceeded 2.5 standard deviations (SD) from the mean, calculated separately for each measure and for fasting vs non-fasting days.

To explore our hypothesis that the 5:2 group will show a difference in cognition on fasting and non-fasting days, data in part A of the study was analysed using mixed analyses of variance (ANOVA). The fasting order (i.e. participants who completed the tasks first when fasting, versus those completed them first when not fasting) was used as the between-subjects variable for all analyses. Upon inspection some variables exhibited a minor violation of assumptions of normal distribution (skewed distribution observed) but given all sample sizes exceeded thirty, the decision was made to proceed with parametric statistics (Norman, 2010; Pallant, 2013). To explore our hypothesis in that there will be a difference in cognition for those following the 5:2 diet compared with those engaged with a CCR diet, data in Part B of the study was analysed using independent t-tests. According to conventions set by Cohen (1992) for effect sizes (ds) for t-tests .80 is large, .50 is

medium and .20 is small. Some variables exhibited a minor violation for the assumption of normality (skewed distribution) but with a sample size exceeding thirty, parametric statistics were used. Levene's test confirmed homogeneity of variance across both groups.

Results

Part A: Comparison of fasting and non-fasting for 5:2 group

Participants

For the 5:2 participants there were 142 initial responses to the study. 17 completed the tasks only once, hence their data was not used in further analyses, and 36 completed them on both a fasting and a non-fasting day. Initial investigations revealed that all those who completed both cognitive testing sessions did so within seven days and within the same two-hour time frame on fasting and non-fasting days. Given they were requested to complete within a four-hour time window, all participants in the 5:2 group (n=36) were considered eligible for analysis.

The mean age of the 5:2 group was 44.52 (SD= 11.46, range = 19 - 60) and the majority were female (n=32: 89%). Most of the participants resided in the UK (n=30). All participants were educated to at least G.C.S.E level, with most educated to degree level or above (N=31: 86%). The largest ethnic group was White British. The mean BMI was 27.39 (SD=3.84, range = 21.12 – 34.16). The most common length of time for participants engaged with the 5:2 diet was 4-8 weeks (n=12) with the remainder engaged with the diet for longer. Of these, 16 had been using the 5:2 diet for more than six months. Although participants were assigned equally to the order in which to complete the two cognitive sessions (i.e completing the first session in either a fasted or non-fasted state), many who initially agreed to take part and were therefore assigned to a particular order did not continue with the study. Consequently, the number of participants in the sample who had completed the first testing session whilst fasted was greater (n=26) than those who had completed the first testing session in a non-fasted state (n=10).

Psychomotor speed

Participant's performance on the TMT- A was examined to assess differences in psycho-motor speed. Table 1 shows the mean task completion time (seconds) in the fasting and non-fasting conditions according to fasting order. A mixed ANOVA was performed with one within-subjects factor (fasting state) and one between-subjects factor (fasting order) and completion time as the dependent variable. There was no significant main effect of fasting order, $F(1,32) = 0.42$, $p=0.52$, $\eta^2p =0.013$ or fasting state, $F(1,32) = 0.07$, $p = 0.79$, $\eta^2p = 0.002$. There was also no significant interaction between fasting order and fasting state, $F(1,32) = 3.36$, $p=0.07$, $\eta^2p =0.094$. This suggests that performance was similar for those in a fasted and non-fasted state, and that the order in which the tasks were taken had no influence.

Table 1: *Descriptive statistics for psycho-motor speed TMT-A tasks.*

	TMT-A Mean completion time- Fasting		TMT-A Mean completion time- Non-fasting	
	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First
N	25	9	25	9
Mean	23.05s	19.92s	21.02s	21.43s
SD	7.25s	4.61s	5.35s	4.31s

To further investigate psychomotor performance, tapping speed was measured using a two-way ANOVA. Trials one and two were entered as an additional within-subject independent variable to assess any changes in performance between trials (i.e. fatigue effects). The dependent variable was the number of taps within a 15 second time period. Table 2 provides further information regarding descriptive statistics.

There was no significant main effect for fasting state, $F(1,34) = 2.60$, $p=0.11$, $\eta^2p =0.071$ or fasting order, $F(1,34) = 0.24$, $p = 0.62$, $\eta^2p = 0.007$. There were no significant interactions between any of the variables. Additionally, there were no significant changes in performance for participants between first and second tapping trials. The results suggest that performance was similar for those in a fasted and non-fasted state, and that the order in which the tasks were taken had no influence on the outcome.

Table 2: Descriptive statistics for psycho-motor speed tapping tasks

	Tapping speed 1-Fasting		Tapping speed 1-Non-Fasting		Tapping speed 2-Fasting		Tapping speed 2-Non-Fasting	
	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First
N	26	10	26	9	26	10	26	9
Mean	90.80s	87.30	92.73	89.60	88.96	98.00	89.73	89.70
SD	11.76	10.08	11.50	8.82	11.94	10.37	10.05	13.69

Set shifting

Participant's performance on the TMT- B was examined to assess set-shifting abilities using task completion time as the dependent variable. Table 3 lists the mean task completion time (seconds) in the fasting and non-fasting conditions segregated by fasting order. A mixed ANOVA was performed with one within-subjects factor (fasting state) and one between- subjects factor (fasting order). There was no significant main effects of fasting order, $F(1,32) = 0.37$, $p = 0.85$, $\eta^2p = 0.001$ or fasting state, $F(1,32) = 0.02$, $p = 0.69$, $\eta^2p = 0.005$. There was also no significant interaction between fasting state and fasting order, $F(1,32) = 0.04$, $p=0.85$, $\eta^2p = 0.001$. This suggests that performance was similar for those in a fasted and non-fasted state, and that the order in which the tasks were taken had no influence.

Table 3: Descriptive statistics for psycho-motor speed TMT-B tasks.

	TMT-B Mean completion time- Fasting		TMT-B Mean completion time- Non-fasting	
	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First
N	25	9	25	9
Mean	25.20s	25.41s	25.42s	26.03s
SD	5.97s	6.02s	6.01s	7.06s

Rule change

Participant's performance on the Rule Change Task (RC) was examined using a two-way mixed ANOVA to further investigate the impact of fasting on set-shifting performance. Switch and stay trials were additional within-participant variables with reaction time and accuracy (number of correct responses) as the dependent variables.

For accuracy, there was a significant main effect of fasting state, $F(1,33) = 6.01$, $p = 0.02$, $\eta^2p = 0.162$, with those in the non-fasted state (mean=94.58 CI = 93.15 – 96.01) performing better than those in the fasted state (mean=90.51, CI = 87.33 – 93.71). There was no significant main effect of fasting order, $F(1,33) = 0.81$, $p = 0.78$, $\eta^2p = 0.002$.

For reaction time (milliseconds) there was a significant main effect of fasting state, $F(1,33) = 60.73$, $p = <0.01$, $\eta^2p = 0.648$, with those in the non-fasted state (mean=1447ms, CI = 1349 - 1545) performing better than those in the fasted state (Mean=1609ms, CI = 1499 – 1719). There was no significant main effect of fasting order, $F(1,33) = 0.58$, $p = 0.45$, $\eta^2p = 0.017$.

There were no significant interaction effects between any variables on accuracy or reaction time. Unsurprisingly trials with cognitive switching were more challenging than those without. There were significant differences between participants on switch versus stay trials for reaction time, $F(1,33) = 157.77$, $p = <0.01$, $\eta^2p = 0.827$, and accuracy, $F(1,31) = 6.03$, $p = 0.02$, $\eta^2p = 0.163$, with a large effect size for reaction time. See table 4 for information relating to descriptive statistics.

Table 4: Descriptive statistics for Rule Change (RC) Set-Shifting Task

	RC% Correct Switch-Fasting		RC% Correct Stay-Fasting		RC% Correct Switch-Non-Fasting		RC% Correct Stay-Non-Fasting	
	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First
N	24	9	24	9	24	9	24	9
Mean	92.06	91.70	95.37	93.31	93.12	95.80	95.72	97.86
SD	8.39	3.27	3.44	8.04	3.62	4.29	3.34	3.10

	RC Switch Reaction Time-Fasting		RC Stay Reaction Time-Fasting		RC Switch Reaction Time-Non-Fasting		RC Stay Reaction Time-Non-Fasting	
	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First
N	25	10	25	10	25	10	25	10
Mean	1572.95ms	1646.65ms	1261.33ms	1295.31ms	1403.07ms	1492.06ms	1119.65ms	1186.57ms
SD	296.50ms	266.51ms	244.45ms	217.78ms	251.10ms	276.71ms	189.76ms	207.99ms

Working Memory

Participant's performance on the 2n-back task was examined to assess working memory. Table 5 lists the mean accuracy and mean reaction time (milliseconds) in the fasting and non-fasting conditions segregated by fasting order. Mixed ANOVAs were performed with one within-subjects factor (fasting state) and one between- subjects factor (fasting order) using accuracy and reaction time as the two dependent variables.

For accuracy (mean correct trials) there was a significant main effect of fasting state, $F(1,32) = 4.47$, $p = 0.04$, $\eta^2p = 0.123$, with participants performing better in the non-fasted state (mean=87.92, CI = 85.28 – 90.57) than in the fasted state (Mean=85.96, CI = 83.56 – 88.36). There was no significant main effect of fasting order, $F(1,32) = 0.42$, $p = 0.84$, $\eta^2p = 0.001$, and no significant interaction between fasting state and fasting order, $F(1,32) = 2.38$, $p = 0.13$, $\eta^2p = 0.069$.

When examining reaction time there was also a significant main effect of fasting state, $F(1,33) = 7.18$, $p = 0.01$, $\eta^2p = 0.179$, with participants performing better in the non-fasted state (mean=940ms, CI = 871 – 1009) than when fasted (mean=1011ms, CI = 919 – 1102). There was no significant main effect of fasting order, $F(1,33) = 0.59$, $p = 0.81$, $\eta^2p = 0.002$, and no significant interaction between fasting state and fasting order, $F(1,33) = 1.98$, $p = 0.17$, $\eta^2p = 0.056$.

Table 5: Descriptive statistics for Working Memory tasks

	2n back - Mean correct Fasting		2n back - Mean correct Non-Fasting		2n back - Reaction Time Fasting		2n back – Reaction Time Non-Fasting	
	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First
N	24	10	24	10	25	10	25	10
Mean	86.91	85.00	87.44	88.40	1020ms	1011ms	912ms	968ms
SD	5.64	7.60	7.09	6.40	248ms	213ms	117ms	189ms

Prospective Memory

Participants' ability to remember to check the clock timing as well as the accuracy of hits within a specified time frame were examined to assess prospective memory using accuracy and number of hits as the two dependent variables. Table 6 lists the number of clock checks and number of correct clock hits in the fasting and non-fasting conditions segregated by fasting order. Mixed ANOVAs were performed with one within-subjects factor (fasting state) and one between- subjects factor (fasting order).

When examining the number of clock checks there was a significant main effect of fasting order, $F(1,33) = 4.78$, $p = 0.03$, $\eta^2p = 0.127$. Since the fasting order reflects the arbitary allocation of participants by the experimenter to perform their first session in either a fasting or non-fasting state, it is likely that this result reflects a type 1 error rather than a genuine effect. There was no significant main effect of fasting state, $F(1,33) = 2.69$, $p = 0.11$, $\eta^2p = 0.075$, and no significant interaction between fasting state and fasting order, $F(1,33) = 0.02$, $p = 0.89$, $\eta^2p = 0.001$.

For accuracy (clock hits) there was a significant main effect of fasting state, $F(1,34) = 8.14$, $p = <0.01$, $\eta^2p = 0.193$, with performance when participants were in the non-fasted state (mean=7.47, CI = 6.56 – 8.37) better than when in the fasted state (mean=6.30, CI = 5.21 – 7.39). There was no significant main effect of fasting order, $F(1,34) = 0.55$, $p = 0.46$, $\eta^2p = 0.016$, and no significant interaction between fasting state and fasting order, $F(1,34) = 0.10$, $p = 0.75$, $\eta^2p = 0.003$.

Table 6: Descriptive statistics for prospective memory tasks

	Number of clock checks-Fasting		Number of clock checks-Non-Fasting		Clock hits correct - Fasting		Clock hits correct – Non-Fasting	
	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First
N	25	10	25	10	26	10	26	10
Mean	19.80	11.80	22.52	14.10	6.69	5.90	7.73	7.20
SD	12.31	9.34	10.84	7.48	2.96	2.64	2.37	2.39

Reflective Impulsivity

One-way mixed ANOVAs were used to investigate participants performance on the information sampling task. The dependent variables were accuracy (number of correct trials), the extent of information sampling prior to decision making (mean number of boxes opened), mean latency per box (average time elapsed prior to opening the next box) and speed (mean trail completion time). For further information relating to descriptive statistics see table 7.

For accuracy, there were no significant main effects for fasting state, $F(1,34) = 1.07$, $p = 0.30$, $\eta^2p = 0.031$, or fasting order, $F(1,34) = 1.41$, $p = 0.24$, $\eta^2p = 0.040$. Number of boxes sampled prior to decision making did not show significant main effects for fasting state, $F(1,34) = 1.62$, $p = 0.21$, $\eta^2p = 0.046$, or fasting order, ($F(1,34) = 1.30$, $p = 0.26$, $\eta^2p = 0.037$.

Significant main effects for fasting state were found for mean latency per box $F(1,34) = 13.54$, $p = <0.01$, $\eta^2p = 0.285$, and for mean total time, $F(1,34) = 15.69$, $p = <0.001$, $\eta^2p = 0.329$. When in a non-fasted state, participants took less time before opening another box (mean=923ms, CI = 820ms – 1025ms) than in the fasted state (mean=1008ms, CI = 903ms – 1114ms). The mean total time for box opening when participants were non-fasted (mean=11.40s, CI = 9.66s – 13.14s) was also shorter than for when they were fasted (mean=13.26s, CI = 11.22s – 15.29s). There were no significant main effects for fasting order for either latency, $F(1,34) = 0.32$, $p = 0.58$, $\eta^2p = 0.009$, or for mean total time, $F(1,32) = 0.14$, $p = 0.71$, $\eta^2p = 0.004$. There were no significant interaction effects for any aspects of the information sampling trials.

Table 7: Descriptive statistics for Reflective Impulsivity (Information Sampling) tasks.

	IS Correct trials-Fasting		IS Correct trials-Non-Fasting		IS Mean boxes opened-Fasting		IS Mean boxes opened-Non-Fasting	
	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First	Fasting First	Non-Fasting First
N	26	10	26	10	26	10	26	10
Mean	8.26	7.80	8.04	7.40	16.48	13.95	15.68	13.73
SD	11.32	1.68	1.58	1.50	5.53	4.45	5.56	5.24

Overall Cognitive task performance for Reaction Time and Accuracy

Part A

Differences in overall performance in the 5:2 group between fasting and non-fasting states across all tasks were examined. Composite variables for reaction time and accuracy were computed by converting each measure into a Z score by subtracting the population mean (across all participants for both fasting and non-fasting sessions) from each score, then dividing by the population standard deviation. Composite measures were then created by adding z-scores (i.e Composite Reaction Time = IST_ Mean Latency per box + IST_Mean Total Time + 2nBack_Reaction time + RC_Reaction time_Switch + RC_Reaction time_Stay + TMTA + TMTB – Tapping_1 – Tapping_2). Tapping measures were reverse scored as a higher number of taps reflects better performance whereas high scores in other measures reflects the opposite. Composite accuracy was measured in the same way (i.e IS_Number correct + 2nBack_Correct + PM+Correct Hits + RC_Correct_Switch + RC_Correct_Stay). A paired sample t-test was used to compare composite reaction time and composite accuracy for fasting and non-fasting conditions (see table 8 for descriptive statistics).

Overall the fasted condition was associated with slower reaction times. The sample mean difference was 1.73. Regarding the population mean difference, we are 95% confident the value falls between 0.850 and 2.615. The results ($t(28 = 4.02$, $p = <.001$, $d= 0.38$), show that assuming the null hypothesis is true such a value would be highly unlikely to have arisen due to sampling error.

Those in the fasted condition were also less accurate. The sample mean difference is 0.62. Regarding the population mean difference, we are 95% confident the value falls between -1.16 and -.077. The results ($t(30 = -2.37$, $p=0.02$, $d= 0.36$)

show that assuming the null hypothesis is true such a value would be highly unlikely to have arisen due to sampling error.

Table 8:

Descriptive statistics for overall reaction time and accuracy for the 5:2 group segregated by fasting and non-fasting conditions

	Overall Reaction time - Fasting	Overall Reaction time - Non-Fasting	Overall Accuracy - Fasting	Overall Accuracy -Non-Fasting
N	29	29	31	31
Mean	0.598	-1.134	0.4424	1.0622
SD	4.87	4.21	1.73	1.68

Summary of the data for part A.

There were significant differences in task performance for the fasted and non-fasted conditions for several cognitive tasks. A significant main effect was found for accuracy and reaction times for both the rule change task and for the 2nBack working memory task with better performances in the non-fasted condition. Further, when participants were in a fasted state, they performed worse during part of the prospective memory task with a significant main effect of clock checks and clock accuracy. In addition, there was a significant main effect of fasting state on latency per box and mean total time in the reflective impulsivity tasks such that participants were slower when fasted. Finally, composite scores for accuracy and reaction time across all tasks found that when in the fasted state, participants performed significantly worse than when non-fasted.

Results for part B: Comparison between 5:2 and CCR dieters

Participants

For those on the 5:2 diet there were 142 initial responses to the study. Fifty-three completed the cognitive tasks at least once with 36 completing on both a fasting and a non-fasting day. For those on CCR diets 156 responded to the study, 45 of whom completed the cognitive tasks at least once with 30 completing for a second time. Data was analysed by taking the means of the two sessions for each participant who did the tasks twice. The most common length of time for participants in the CCR group was 4-8 weeks (n=14), with the remainder engaged with the diet for longer. Of these, twelve had been using the CCR diet for more than six months (see Table 9 for further information regarding sample demographics).

Table 9:

Descriptive statistics of 5:2 and CCR samples.

	5:2	**CCR**
Gender	F = 34 M = 2	F = 26 M =4
Age	Mean = 44.52 SD = 11.46 Range = 19 - 60	Mean = 42.18 SD = 11.53 Range = 22 - 60
BMI	Mean = 27.30 SD =3.84 Range=21.12-34.16	Mean = 28.08 SD =8.44 Range=20.77-32.01
Country	UK=30, Spain=2, China=2, India=1, Thailand=1,	UK=27, Canada=1, Korea=2,
Education	31 : Primary degree level qualification or above	25: Primary degree level qualification or above

Psychomotor speed

Differences were found in the TMT-A scores measuring psychomotor speed (seconds) between those in the 5:2 group who took longer to complete the tasks, and those in the CCR group. The mean difference between the conditions was 3.63, which corresponds to a large effect size (d=0.81). An independent t-test revealed that, if the null hypothesis were true, such as result would be highly unlikely to have arisen ($t(61) = 3.19$, $p < 0.01$) (See table 10 for descriptive statistics for all tasks).

Set-Shifting

Completion times for the TMT-B tests used to measure set shifting found those in the 5:2 group were slower to complete the tasks compared to those in the CCR group. The mean difference between the conditions was 3.02, which corresponds to a medium effect size (d=0.54). An independent t-test revealed that, if the null hypothesis were true, such as result would be highly unlikely to have arisen (t (62) =2.16, p= 0.03). Examination of the data revealed no further significant differences between the groups for the remaining cognitive tasks

Table 10: Descriptive statistics for cognitive tasks in the 5:2 and CCR diet groups.

	TMT-A		TMT-B		Tapping speed 1		Tapping speed 2	
	5:2	CCR	5:2	CCR	5:2	CCR	5:2	CCR
N	34	29	35	29	36	29	36	29
Mean	21.48s	17.85s	25.68s	22.66s	90.84	96.03	89.19	93.82
SD	4.75s	4.20s	5.61s	5.51s	10.54	13.21	10.68	9.83

	IS Correct trials		IS Mean boxes opened		IS mean latency per box		IS Total time	
	5:2	CCR	5:2	CCR	5:2	CCR	5:2	CCR
N	30	30	36	30	36	29	36	30
Mean	15.42	16.36	15.46	16.34	953ms	855ms	13.55s	12.47s
SD	5.43	6.21	5.30	6.32	265ms	266ms	6.44s	5.69s

	2n-back Mean correct		2n back Reaction time		PM Number of clock checks		PM Correct clock hits	
	5:2	CCR	5:2	CCR	5:2	CCR	5:2	CCR
N	36	29	36	29	36	30	36	30
Mean	85.90	85.86	977ms	901ms	18.81	16.51	7.02	6.08
SD	7.54	7.64	198ms	212ms	10.57	10.42	2.38	3.03

Overall Cognitive task performance for Reaction Time and Accuracy: Part B

Differences in overall performance between the 5:2 and CCR groups across all tasks were examined. Composite variables for reaction time and accuracy were computed by converting each measure into a Z score and composite measures were then created in the same manner as above. Independent t-tests were used to compare both composite reaction time and composite accuracy between 5:2 and CCR conditions. See table 11 for descriptive statistics.

Overall reaction time for those in the 5:2 group was slower compared to those in the CCR group. The sample mean difference is 3.48 which is a difference of medium effect size (d=0.61), and the 95% confidence interval for the estimated population mean difference is between 0.551 and 6.41. An independent t-test revealed that, if the null hypothesis were true, such as result would be highly unlikely to have arisen ($t(58) = 2.38$, $p= 0.02$).

An independent t-test revealed there was no significant difference between the two groups for accuracy ($t(58) = 0.30$, $p= 0.76$

Table 11: Descriptive statistics for overall reaction time and accuracy in the 5:2 and CCR groups

	Overall Reaction Time - 5:2	Overall Reaction Time - CCR	Overall Accuracy – 5:2	Overall Accuracy -CCR
N	34	26	35	25
Mean	1.01	-2.47	0.18	-0.04
SD	5.10	6.24	2.81	2.88

Summary of the data for part B

There were significant differences in cognitive function between those in the 5:2 and CCR groups. As shown in table 10, there were significant differences in the means between the two groups for tasks that measured psychomotor speed and set shifting. Finally, composite scores for reaction time across all tasks were significantly slower for those in the 5:2 group when compared to those in the CCR group.

Discussion

The purpose of this study was to examine the impact of the 5:2 dieting regime on cognitive function. The study was divided into two parts. Part A investigated cognitive performance on fasting and non-fasting days for healthy adult participants who have been following the 5:2 diet for a period greater than 4 weeks. Part B investigated differences in cognitive performance between those following the 5:2 diet and those engaged with CCR diets.

To our knowledge, part A of this study is the first of its kind to investigate the impact to cognitive function of engaging with the 5:2 intermittent fasting diet beyond a period of four weeks. The present study used the same cognitive tasks as that of Mahony (2016) to investigate any differences in cognition between fasting and non-fasting days. Mahony's study recruited participants who were following the 5:2 diet for a period up to four weeks, finding no significant impairments to cognitive function. Our contrasting findings which expanded the design to examine cognitive function beyond a four-week period suggests that a greater length of time spent following the 5:2 diet may contribute to impaired cognitive function. This research tentatively suggests that engaging with the 5:2 diet for more than four weeks may result in slower and less accurate cognitive performance on fasting days.

Furthermore, to our knowledge, part B of the present study was the first to investigate differences in cognitive performance between participants engaged with the 5:2 dieting regime and those engaged with continuous calorie restriction (CCR) regimes. The current findings suggest that following the 5:2 diet for a period greater than four weeks impairs cognitive function with slower overall performance when compared to CCR diets.

Both parts of this study used the same cognitive tasks to measure performance in numerous cognitive domains. The results of these tasks are discussed in further detail below.

Part A

The current study used a variant of the rule-change task employed previously with similar populations to measure cognitive flexibility using a set-shifting paradigm (Bolton et al., 2014; Pender et al., 2014). Our results replicated the findings from these studies that fasting decreased accuracy in set-shifting abilities for participants in a fasted state. However, participants in the current study were not fully fasted as were participants in Bolton and Pender's studies. The present study also found that reaction time was slowed in the fasted state, replicating findings from Bolton and colleagues (2014). Thus, findings from our study and those mentioned above suggest that for healthy individuals some of the difficulties in set-shifting ability may be accounted for by the impact of short-term food restriction.

Where previous studies (Bolton et al., 2014; Pender et al., 2014) have measured cognitive flexibility (CF) in fully-fasted participants, our study is in line with recent research reporting an impairment in set-shifting accuracy following CR of 75% (Solianik et al., 2018). Interestingly, in a separate experiment which measured CF, where calories were reduced by 25%, no set-shifting impairments were found (Makris et al., 2013). This suggests that the degree to which calories are reduced during fasting may influence cognitive performance, at least in respect of cognitive flexibility. Study designs which test cognition while systematically adjusting for the amount of calorie restriction from mild (25%), such as that seen typically in CCR dieting regimes, to absolute fasting may enrich our understanding of the impact of calorie restriction on cognitive performance.

Our study which used a tapping task with nominal loading on processing capacity to measure psycho-motor speed, found no impairment on fasting days. These results are inconsistent with two previous studies investigating psycho-motor speed in fully fasted participants, both of which indicated significant impairments during a 2-finger tapping task (Green et al., 1995; 1997). One possible explanation for this difference may be due to the relationship between glucose levels and cognitive demand. The brain relies on glucose for fuel, much of which comes from carbohydrates in food, and glucose concentration has been shown to alter during brain activation (Haier, Siegel, MacLachlan, Soderling, Lottenberg, & Buchsbaum, 1992). It has been suggested that easier cognitive tasks which require a lower cognitive load, utilise less glucose than tasks which are more demanding (Boyle, Lawton, & Dye, 2018). It may be that unlike Green and colleagues' studies (1995, 1997) where participants were fully fasted, the consumption of food on fasting days in the present study prior to completing the cognitive tasks provided adequate glucose levels to the brain to facilitate a tapping speed task with minimal cognitive load, thus preventing impairment to psycho-motor speed performance.

In the present study impairments to working memory (WM) using a 2n-back task were found in the fasted condition, suggesting that calorie restriction may be partially responsible for slowed and less accurate working memory performance. Our findings compliment recent research investigating brain activation in areas related to cognitive function (Chenko et al., 2015). Their study used fMRI technology to observe brain activation in participants, following a period of overnight fasting (14h). Researchers found that when engaged with the 2n-back task, despite preserved cognitive performance, being in a fasted state was associated with reduced involvement in areas of the brain commonly associated with WM. This suggests that areas linked to WM are affected by calorie restriction.

However, unlike the study by Chenko et al., our study did not involve participants who were in a fully fasted state and the results contrast with previous studies indicating that total food deprivation and continuous calorie restriction has either no effect (Benton & Parker, 1998; Bryan & Tiggemann, 2001; Green et al., 1995; 1997; Harder et al., 2017; Owen et al., 2012; Solianik et al., 2016; Tian, Aziz, Png, Wahid, Yeo, & Png, 2011), or a positive impact on working memory performance. (Brinkworth et al., 2009; Halyburton et al., 2007; Solianik et al., 2018. One possible explanation for the difference in findings could be due to variations in the methods used for measuring WM. Interestingly, apart from Solianik's study (2018), in the studies mentioned above, the digit-span test was used, where participants were required to memorise and repeat back numbers that have been read to them either in the same or reverse order. Although this test is commonly used to measure WM, our study used a 2n-back task which is not well correlated with performance on the digit span test (Miller, Price, Okun, Montijo, & Bowers, 2009). It would be informative if future studies investigating the impact of CR on WM considered using a number of different means of measuring the same construct.

The observation that prospective memory was worse in the fasted condition is intriguing and suggests that fasting may impair ability to accurately remember to perform a future task within a specific time-frame. To our knowledge this is the first study to measure PM following CR. Prospective memory processes are known to use pre-frontal/executive functions (Martin, Kliegel, & McDaniel, 2003). One model that attempts to explain the impact of CR on cognition suggests that raised stress levels and subsequent higher levels of cortisol may impair pre-frontal function (Arnsten, 2009), thus we might expect to see impairments to executive function, including memory processes. However, despite previous studies suggesting a possible link between acute stress and deleterious effects on WM (Arnsten, 2009), for prospective memory (PM) research suggests that in healthy adults, acute stress

improves performance (Piefke & Katharina Glienke, 2017), thus it seems unlikely that higher levels of stress on fasting days may be responsible for the observed results.

Further, if we consider that those on the 5:2 diet vary the content of food consumed on fasting and non-fasting days, then an added consideration for potential differences between the two fasting conditions may be changes in macronutrient content. For instance, rather than exclusively considering the quantity of calories consumed, it may be important to understand the breakdown of simple and complex carbohydrates that are eaten on fasting and non-fasting days. Research suggests that these two types of carbohydrates appear to have different effects on memory processes (Benton et al, 2003). Future research that examines detailed nutritional information during IF would help to disentangle which areas of cognition may be affected.

In line with our prediction, there was a reduction in reflective impulsivity, as measured by the IST, in the fasted condition, when compared with the non-fasted condition. This result corresponds with recent research that used the same cognitive task to measure impulsivity in participants following a 20-hour period of absolute fasting (Howard et al., 2016). In their study, Howard et al. (2016) suggest that rather than viewing this as an indicator that CR leads to less impulsive behaviour, the requirement of the test to shift attention from decision making (deciding on the box majority), to the action of opening boxes, may reflect difficulties in set-shifting. Given that set-shifting was impaired on fasting days in our study, our findings from the IST and Rule Change task lend further support to this theory. Further, given that our findings are inconsistent with that of Mahony (2016), where no differences were found between fasting and non-fasting days, this provides added support for the idea that longer periods of time engaged with the 5:2 diet, where CR is reduced by 75% may impair cognitive performance, at least in respect of set-shifting abilities.

Part B

Performance for participants in the 5:2 group was significantly impaired in the TMT-A task, who took longer to complete the task than those following the CCR diets. TMT-A is widely used as a measure of complex attention and processing speed. The results from the TMT-B task show that participants on the 5:2 diet took significantly longer to move flexibly between different tasks than those following CCR diets. Taken together, the results from the both parts of the TMT test provide strong support for the idea that the 5:2 diet impairs cognitive function when compared to CCR diets.

One hypothesis that might explain these differences relates to a process known as glucoregulation. This refers to the body's need to achieve a balance between glucose in the blood, and glucose that is stored in the form of a complex carbohydrate known as glycogen. As mentioned previously, it is widely accepted that a reduction in blood glucose negatively impairs cognition. The 5:2 diet encourages subscribers to eat more healthily on fasting days (The 5:2 diet, 2016), thus on restricting days we might expect a reduction in added sugars. Combined with a calorie reduction of 75%, this might significantly reduce blood glucose levels.

Glycogen acts as an energy buffer to the brain, with more delivered when glucose levels decrease, and has been linked with improved cognition in animal studies (Waitt, Reed, Ransom, & Brown, 2017). During intermittent fasting it would be logical to assume that glucose levels would be lower on fasting days, thus requiring higher levels of glycogen. Recent research shows that for humans, consuming one low calorie meal in a day is not enough to replenish glycogen levels (Bawden et al., 2014). It may be possible therefore that for those who choose to consume very few calories for two days each week, the combination of low glucose levels and the failure for glycogen reserves to recover to levels that are required for optimum functioning, may contribute to negatively impaired cognitive performance.

Limitations and recommendations

The present study used an online diary that asked participants to record their food and drink intake only on the relevant days leading up to taking part in the cognitive tasks. The diary was used primarily to highlight the ability for researchers to check for differences between fasting and non-fasting days for those on the 5:2 diet, to encourage dietary adherence. This method therefore did not accurately record dietary adherence, and thus the study was overly reliant on participant's honesty. Future studies should seek to accurately record the daily food and drink intake of all participants. However, future studies that use online self-reporting of daily intake would still require the use of self-reporting methods which are not entirely reliable. For instance, a study that examined accuracy of self-reported energy intake examined the food diaries of 266 participants, comparing them to energy requirements for body maintenance. Their study showed 81% under-reported their energy intake compared with 8% who overestimated their intake (Mertz et al.,1991). Moreover, daily food diaries rely largely on retrospective memory to record information, which may be further distorted in accuracy if memory is impacted by intermittent calorie restriction.

It is also worth noting that our study did not tightly control for hydration. Cognitive tasks that depend on speed and accuracy are adversely affected following 3 hours of fluid deprivation (Petri, Dropulić, & Kardum, 2006), with evidence that working memory is impaired by dehydration (Gopinathan, Pichan, & Sharma, 1988). Thus, any replication would benefit from strictly monitoring the consumption of calorie-neutral liquids.

Our design also relied on the remote collection of information, which increases the studies' ecological validity. However, due to the nature of this design we were unable measure blood glucose levels (BGL). An increase in calorie intake increases BGL, and BGL have been shown to facilitate cognitive functioning

(Benton, Parker, & Donohoe, 1996). In part A of our study we attempted to minimise this effect by asking participants to eat something on fasting days prior to completing the cognitive tasks. Considering BGL are affected by calorie consumption and other factors such as exercise, future studies should consider measuring BGL more directly to observe any potential effects on cognition.

A further limitation is the potential influence of specific macronutrients on cognitive performance. Without examining the macronutrient content of foods ingested by participants, we are less informed on the potential impact from specific components, such as simple and complex carbohydrates to cognition. Thus, we cannot conclude that from a dietary perspective the restriction of calories is the only factor that may contribute to changes in cognitive function.

Part B of our study used a between-subjects design, and participant's levels of stress were not monitored. Higher levels of cortisol, linked to an elevation in stress levels have been reported during fasting (Roky et al., 2004). As cortisol is known to affect cognition (Arnsten 2009; Shansky & Lipps, 2013), it would be interesting to investigate any potential differences in stress between participants engaged with CCR diets and those following 5:2 diets. Future studies would benefit from monitoring perceived stress levels and cortisol hormone levels in both diet regimes, in addition to cognitive performance.

Our study has taken a conservative approach where the results from Part-B were taken from averaging out the two cognitive sessions for participants in each group. Thus, by comparing the average scores of fasted/non-fasted 5:2 days with the average scores of the CCR group, this dilutes any effect which would potentially only be seen on fasted 5:2 days. Future research should consider changing the study design whilst controlling for order/learning effects. Moreover, given that participants were not randomised into the CCR and 5:2 groups, any differences

between them could reflect pre-existing differences between individuals who chose either diet, rather than any effects of the diet itself.

Clinical and theoretical implications

Our results provide tentative support for a connection between intermittent calorie restriction and cognitive impairment. Moreover, this study contributes to research that attempts to understand which areas of cognition might be most affected by a short-term reduction in calorie intake. Intermittent fasting regimes such as the 5:2 diet, which reduce calorie intake on fasting days by 75% may have negative consequences for cognitive performance. Furthermore, our results suggest that popular IF diets, such as the 5:2, impair cognition when compared with CCR diets.

With the UK government launching new campaigns through the NHS to encourage adults to consume less calories (NHS, 2018), it is important to provide appropriate health advice about which type of diet is suitable for their needs (i.e. CCR or 5:2). Importantly, in addition to providing education on the physical health benefits of reducing calories, such advice should cover the potential cognitive implications of dieting. This is particularly relevant for adults whose daily roles places them in a position where they are responsible for the safety and wellbeing of others. For instance, given the results of our study, it might be prudent to inform an air traffic controller who is planning to follow a dieting regime, about the potential detrimental impact on cognitive function when engaging with the 5:2 intermittent fasting diet. Such information would allow individuals to decide whether to engage with the 5:2 diet, and if so, to consider scheduling fasting days to coincide with non-working days. Thus, the results of this study are relevant for every healthy adult who is considering losing weight or improving their health by dieting.

Conclusions

The present study demonstrated that short-term intermittent fasting impairs cognition on fasting days, affecting both speed and accuracy of cognitive tasks. Calorie restriction declined performance in psycho-motor speed, memory processes, and cognitive flexibility. In addition, when compared with CCR diets, the present study showed that the 5:2 IF diet impairs cognitive performance, affecting overall speed. Calorie restriction in the 5:2 group declined performance in psycho-motor speed and cognitive flexibility.

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Part 3: The Critical Appraisal

Reflections on the research process

Motivation to study cognitive performance for those following the 5:2 diet

My decision to investigate the impact on cognition for those following intermittent fasting diets, such as the '5:2' diet, was influenced by curiosity and a genuine concern about the potential negative impact of this dieting regime. I had initially considered the 5:2 diet to be a healthy weight loss diet with little or no detrimental impact for those who chose to engage with it. These beliefs were fuelled by the growing popularity of the 5:2 diet, no doubt influenced by a BBC documentary I had seen which reported this form of dieting regime as a potential way to make major improvements to general health (Dart, 2012). The documentary discussed potential physical health benefits and improvements in brain function for rodents during alternate day fasting (ADF). However, there was no mention of any proven benefits to brain function for humans on the 5:2 diet, which differs in its pattern to ADF.

During my clinical work within an eating disorder service I reflected on the connection between the 5:2 diet and some eating disorders (EDs) such as bulimia nervosa and binge eating disorder. Individuals following the 5:2 are encouraged to undertake a pattern of extreme calorie restriction for two days, while for the remaining 5 days they have permission to eat what-ever they wish. This bears resemblance to the pattern of restriction and bingeing seen in some eating disorders. I considered how difficult I had found it to provide CBT to some service-users with an ED who were particularly ridged in their thinking, thus providing anecdotal support of potential cognitive impairment. Considering these reflections, my concern increased for those who had taken onboard the positive health aspects of the 5:2 diet but were, much like myself, in the dark about any potentially negative impact on cognitive function.

Recruitment process

"If history repeats itself, and the unexpected always happens,
How incapable must Man be of learning from experience".
George Bernard Shaw.

Given that a similar joint project had been conducted once before within our research department, both my research partner Freya Donaldson, and myself were confident that recruitment would be straightforward, and move at a rapid pace. The previous UCL joint project (Mahony, 2016; Landon-Daly, 2016) looked at differences in executive function, as well as changes in mood, eating behaviours and eating disorder symptomology, between fasting and non-fasting days in the 5:2 diet for participants who were new to the dieting regime, over a period of four weeks. Their study attracted widespread and rapid interest which allowed them to recruit sufficient numbers at a pace faster than they had anticipated. Given the speed of their recruitment, despite our suspicion that this might still be a substantial obstacle, Freya and I were both confident our recruitment process would follow suit. Further, given that we were recruiting established users of the 5:2 and CCR diets, rather than those new to it, we imagined this would ease the process further. The difficulty and slow speed of recruitment therefore came as an unpleasant surprise.

Despite using similar methods of advertisement that included social media platforms, internet forums, and posters, recruitment was painfully slow. Any efforts to join online intermittent fasting or CCR platforms were often met with suspicion about the purpose of the research, and subsequently many efforts to advertise were met with rejection. When using social media platforms, the process necessitated a request to join numerous groups which were tightly controlled by online administrators. Often, the administrators would not answer requests to join their group, and on the occasions where our presence was accepted, posting information

without their strict consent would result in being barred from the ability to post further. I realised that to gain access to some of these groups I would need follow the advice of Barker, Pistrang, and Elliot (2002), who suggest that during the groundwork stage of research one should employ political savvy, be flexible and practice good interpersonal skills. Taylor & Bogdan (1998) discuss the importance of identifying and approaching *gatekeepers*, whose role it is to protect and control access to your area of interest. One way of doing this is to gain a thorough working knowledge of the system (Barker, Pistrang, & Elliot, 2002). I therefore changed my approach by only discussing the project with those who owned the online group pages. In addition, I agreed to become a moderator for some of the 87 groups I had eventually joined, to win trust and bolster the recruitment process. As a moderator I became responsible for allowing access to others who were interested in joining the groups, and for controlling unsolicited posts. The extra time required for this was unwelcome but necessary as it ultimately proved fruitful.

In addition, I attempted to boost recruitment by privately paying a well-known social media website to place my advert strategically onto a variety of unrelated web pages where targeted individuals had previously visited websites that relate to dieting. This proved to be unsuccessful as despite my payment, the same site then barred me from using the service for breaching rules on advertisement. Their reason was their belief that the advert promoted dieting, which in fact my poster was careful to avoid. Remaining flexible, I employed another online participant recruitment website (callforpartipants.com) which was initially encouraging. However, despite a steady stream of interest in the study, it soon became apparent that the primary motivation for those interested in my study was the opportunity to acquire financial incentives in exchange for participation. Eager to ensure that the study was not corrupted by those pretending to be on a diet for personal gain, the decision was taken to discount any interested parties from this website.

Further, unlike Mahony and Langdon-Daly's project, our research also involved recruiting participants who were following continuous calorie restricted diets (CCR), thus doubling the time and effort required. Recruiting the CCR group proved to be most challenging. I soon discovered that people following CCR diets appeared to be less committed to remaining on any particular dieting regime, thus prone to switching between periods of dieting and non-dieting. Additionally, many on CCR diets were inclined to frequently switch between CCR and intermittent dieting within the space of one month. Considering the need to recruit participants who were continuously engaged with their chosen diet for a minimum of four weeks, this proved an unexpected challenge, resulting in the rejection of many individuals who had initially expressed interest.

Whilst this began as a joint study with Freya, it soon became apparent to us both that, apart from the initial stages of planning and applying for ethics, we were both conducting very separate studies using separate methodologies and different participants. Originally, we had planned for those who completed Freya's study to be offered an opportunity to join my study. However, with only three people joining from Freya's study, this idea was soon abandoned. It is unclear if this was due to differences in interest from Freya's sample (i.e. having more interest in the impact of the 5:2 on mood and less so on its impact on cognition), or perhaps due to boredom or fatigue effects whereby participants in Freya's study who were required to complete weekly questionnaires over a four week period, as well as a food diary, no longer had the enthusiasm to continue.

Problems also arose with the technology when it became evident that many people did not thoroughly read the participant information sheet, attempting to use iPads and smart-phones when our cognitive testing system was only compatible with laptops and home PC's. This meant that many interested parties were not able to take part, despite their initial interest.

Ultimately, the slow recruitment process heavily delayed data collection and analyses. Any future replication of this study would need to consider the potential difficulties relating to recruitment, contacting gatekeepers early, allowing more time than predicted to gain the trust of dieters, being flexible and adaptive to change, and ensuring the software used to measure cognitive function is widely compatible with modern portable devices.

Reflections during recruitment

I noted that when compared with the CCR group, those who signed up to online 5:2 social media groups, which are designed to provide support, posted less '*before and after'* photos of themselves regarding personal weight loss, and viewed the diet as a lifestyle rather than a means to lose weight. They appeared less worried than the those who had joined online CCR groups about weight loss and body shape, and more interested in the positive health benefits associated with intermittent fasting (IF). Weight and shape are often primary concerns for those with an eating disorder (i.e. checking and/or avoidance), and I wondered if those following CCR diets might display symptoms similar to those with an ED. Interestingly, my colleague Freya, who investigated differences between the CCR and 5:2 diets on mood, eating behaviours and eating disorder symptomology found that global eating disorder symptoms did increase in CCR, when compared to the 5:2 diet (Donaldson, 2019), suggesting a link between continuous dieting and unhelpful behaviours and attitudes around eating.

The 5:2 diet is designed to be flexible allowing those who follow the regime to eat what-ever they like on non-fasting days. They are also free to vary their fasting days. This flexible approach however may not reflect reality. Many of the 5:2 dieters I had contact with were ritualistic, informing me that their fasting days were

fixed each week, and that during these periods they would stay at home. This concrete approach to a diet that was designed to be flexible mirrors the impairment in cognitive flexibility reported in our results, and I considered the possibility that for many individuals on the 5:2 diet, a reduction in cognitive flexibility resulting from intermittent calorie restriction may lead to ridged and habitual social and eating behaviours which reinforce concrete thinking styles.

Improved understanding

"The noblest pleasure is the joy of understanding".

Leonardo da Vinci.

Undertaking this research changed my understanding about the role played by continuous calorie restriction (CCR) in cognitive function. At the beginning of this project my goal was to investigate any potential changes in cognitive performance for those who follow intermittent fasting diets and viewed those in the CCR group simply as a potential control group for my study. What I discovered was a vast amount of research supporting the idea that CCR can increase longevity and health-span and improve cognition. Given that our results showed that those on CCR diets performed better than those following the 5:2, our study supports the idea that continuous, rather than intermittent fasting may be a safe and effective method to lose weight, whilst maintaining cognitive function.

Further, I realised that energy restriction in both IF and CCR regimes cannot viewed in isolation as the only potential influence for cognitive impairment. My research took me along other interesting paths, expanding my knowledge beyond energy reduction. I found myself becoming further interested in other important factors such as the impact of macronutrients on cognition. In humans, correlational studies have indicated that diets high in saturated fats may be a risk factor that

impairs working memory (Devore, et al., 2009), and cognitive flexibility (Kalmijn, Van Boxtel, Ocke, Verschuren, Kromhout, & Launer, 2004), whilst Mediterranean style diets, typically lower in saturated fats have been shown to improve cognition (McMillan, Owen, & Scholey, 2011). Thus, macronutrient content could be one of numerous factors that explain a potential connection between the higher levels of obesity found particularly in western societies, and impaired cognition.

Moreover, for clinicians working in eating disorder services, this highlights the need for qualified nutritionists and psychologists to work closely together to ensure that those with an eating disorder are receiving a focussed package of care that accounts for calorie restriction, nutritional content and psychological intervention.

Ethics

"Ethics cannot function if it does not take account of the human values of reciprocal responsibility".

Pope Benedict XVI

The decision to recruit participants worldwide provided greater ecological validity for the study. However, this design also relied almost entirely on recruiting from social-media groups. What I quickly realised when joining online groups for CCR and IF, is that whilst the groups provided encouragement and support, photos that were posted online which are designed to demonstrate to others how dieting can change one's appearance often encouraged unhelpful comparisons between dieters, and fuelled anxiety about the which process and methods should be used whilst dieting. This observed drive for emotional support from others left me concerned about the motives for participants volunteering to take part in my study. I had not hidden my role as a trainee psychologist and I was aware that taking part in

my study may offer the opportunity to have contact with and confide in someone who is receiving psychological training.

Further, I was concerned that those taking part in my study were potentially being subjected to additional anxiety. Following completion of the study, numerous participants voiced their concern about their perceived performance in the cognitive tasks, typically worrying that they had performed badly, and that the cause of their poor performance was their chosen diet regime. Their anxiety may have arisen from their realisation that the cognitive tasks were more challenging than they had anticipated, as well as the process of completing them. Therefore, ensuring that participants are fully informed is vital, not only because we have a duty of ethical care to participants, but also because we need to nurture the public image of psychology as a profession.

Being unable to offer immediate reassurance was uncomfortable but given that I had provided participants with full information about the study prior to their decision to take part, gained informed consent, and that no one reported distress during the process of completing the online tasks, this helped to ease my dilemma. In addition, all participants accepted for the study had already chosen to follow their diets, thus I had not encouraged them to begin any dieting regime. I therefore validated and normalised their anxiety whilst reminding them that the results would be provided upon completion of the research, thus helping them to make informed changes.

Reflections on the use of neurocognitive testing.

"You don't understand anything until you learn it more than one way".

Marvin Minsky.

During the writing of this project I became aware that many different types of cognitive tests were being used to measure areas of cognitive function. Often, cognitive performance in one area has been measured with multiple tests. The use of multiple research designs contribute to a broader understanding of a chosen topic, but this makes it difficult to compare results, which is why I decided that despite the results from my conceptual introduction (CI) indicating changes following calorie restriction and fasting to inhibition and specific psycho-motor abilities, I would not add these to my empirical study, but would instead use the same tasks as that of Mahony (2016). I also realised that adding further tasks to the cognitive battery may lead to participants feeling fatigued and demotivated.

The use of online testing in the study improved its ecological validity and increased accessibility to the target sample, but this method of testing is also problematic. Firstly, it requires trust that the participant is following the correct procedures. It is also entirely possible that the person sitting the test is not the individual recruited, as there is no guaranteed method to verify their identity. Second, environmental factors may influence the results. No matter how prepared one might be to sit a test, there is less control over outside distractions such as the telephone, noisy neighbours, or dependent children. Supervised tests would ensure the results are genuine, whilst providing a personalised experience that may help the participant feel valued, though at a cost to ecological validly. Ideally, future replications of this study might benefit from an equal mix of online and laboratory-based testing to balance the costs and benefits of each approach.

Reflections on findings

"Das Kind mit dem Bade ausschütten" (Don't throw the baby out with the bathwater).

Thomas Murner

The results of this study indicated that following the 5:2 diet may be linked with cognitive impairments. This suggests that on a wider scale, other intermittent fasting diets might also be detrimental to some areas of cognitive function. For me these findings were bittersweet. On the one hand I was pleased to discover a variety of significant findings, since the purpose of research is to add something to knowledge in the hope that it might make a valuable contribution to science, and perhaps lead to a change in professional practice. However, had I found the same pattern of non-significant results as Mahony's study (2016), then together our studies would have provided considerable evidence that the 5:2 diet has no negative impact on cognitive function in healthy adults. Instead, whilst my findings will inform interested parties about the potential link between the 5:2 diet and cognitive impairments, it may also discourage the use of a dieting regime that claims to have many proven physical health benefits. It is important therefore not to completely discard the 5:2 diet, but further research will help to provide clarity on the advantages and disadvantage of its use.

Conclusions

This project has taught me that despite having preconceived ideas and expectations regarding my topic of research and my methodology, both the beginning and the end of the research process are gateways to further information and knowledge. Flexibility, openness, determination and contingency planning are fundamental components of the recruitment process. My research journey provided me with an opportunity to reflect on the debt we have as researchers towards our participants who view our intentions with an element of trust, and the responsibility we have as scientist-practitioners of modelling ethical and considerate psychological research practices.

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Appendices

Appendix I

Details of collaboration in joint thesis

The empirical research outlined in this thesis was undertaken as part of joint project with Freya Donaldson, a trainee clinical psychologist in the same cohort at UCL. Her research investigated participants' mood, eating behaviours and eating disorder symptomology before beginning the 5:2 diet and after 4 weeks of dieting, using a repeated measures design and a between-subjects design. Please refer to her thesis submission for further details.

Aspects of research undertaken independently*:*

- Review of relevant literature
- Research proposal
- Selection of outcome measures
- Study design for individual project
- Recruitment and screening of participants
- Correspondence with participants
- Data collection, extraction and processing
- Data analysis
- Write up of empirical paper

Aspects of research undertaken jointly:

- Planning procedure of overall study
- Research governance tasks (application for ethical approval, funding, risk assessment, data protection)

Appendix II

Advertisement used for Recruitment

Have you been following the
5:2 diet or a low calorie diet
(15-25% calorie restriction per day)
for at least 4 weeks??

We are exploring the effect that the 5:2 diet and low calorie diets have on our thinking abilities. We will compare the results of cognitive tasks between the two groups. Participation will involve completing some short online tasks from the comfort of your own home.

For more information or to sign up, please email us at:
[redacted]

Want to know if dieting changes your thought processes?

Perhaps you have noticed differences in your abilty to concentrate, or remember things?

Are you aged between 18-60?

Win a range of Amazon Vouchers

(£20, £50, £100)

UCL
Research Department of Clinical Educational and Health Psychology

All data will be collected and stored in accordance with the Data Protection Act 1998
This study has been approved by the UCL Ethics Committee: 12965/001

Appendix III

Screening form

Thank you so much for contacting me to let me know that you are interested in taking part in our intermittent fasting study at University College London (UCL Project ID 12695/001). The study will involve some online tasks that will take up around 15-20 minutes of your time and can be done from anywhere. We ask these are completed two times within 7 days.

Please find attached an information sheet that explains more about the study and a consent form. The consent form can be completed by electronically entering your initials or a tick on Microsoft Word or printing it off, completing it and scanning it in.

To begin with, please note our inclusion and exclusion criteria for participation below:

- Aged between 18 and 60 years old
- Sufficient level of English language and computer literacy to complete the study
- Normal or corrected to normal visual acuity
- No current or past history of eating disorders (In line with NHS advice).
- No current diagnosed mental health problem
- No diagnosis of a moderate-severe intellectual disability
- No specific learning difficulty (such as dyslexia or dyscalculia)
- Not currently pregnant, or with health conditions such as diabetes where medical advice indicates that fasting would potentially endanger your health
- You should have been following either the 5:2 intermittent fasting diet or your chosen calorie controlled diet for at least 4 weeks by now.

If you are eligible to take part in this study and If you are happy to participate, please complete the following and **return it to us via email along with the consent form** mentioned above. **You will then be sent a unique weblink to begin the online puzzles**. Thank you !

The information you provide below will be stored anonymously and securely in accordance with the Data Protection Act 1998.

What is your age?

What is your Gender? (delete as appropriate) Male/Female/Other

What is your ethnicity?

What country do you currently live in?

Please tell us your highest qualification (i.e. A-Level/BA/PHD) …….

What is your current height? _____(please state centimetres, metres or feet/inches)

What is your current weight? _____(please state Kg, Lb or Stones/pounds)

What is your ideal weight? _____(please state Kg Lb or Stones/pounds)

How long have you been on your chosen current diet? (place X by answer)

Between 4-8 weeks

Between 2-4 months

Between 4-6 months

Between 6 months to 1 year

Between 1-2 years

More than 2 years

Please briefly list your previous diet history beginning with the one you are on now.

Please include the type of diet and an estimate of how long you were dieting for.

Here is an example of the correct format:

5:2 diet for 6 months

Weight watchers for 4 months

If you have any questions or concerns you can either email us or we can arrange a time to discuss this information over the phone and help you to decide whether you want to take part. If you would like to speak over the phone, please send us a range of suitable times to call you, along with your phone number (or Skype details if you live outside of the UK). We will get back to you as soon as possible to confirm a time.

Please note that you do not have to decide straight away whether you want to take part.

Best wishes,

John O'Leary

Trainee Clinical Psychologist

UCL DClinPsy Programme

1-19 Torrington Place London

WC1E 7HB

Tel: [redacted] (Please leave a message and I will call you back)

Appendix IV

Letter of ethical approval

UCL RESEARCH ETHICS COMMITTEE
OFFICE FOR THE VICE PROVOST RESEARCH

5th March 2018

Dr Lucy Serpell
Department of Clinical, Educational and Health Psychology
UCL

Dear Dr Serpell

Notification of Ethics Approval with Provisos
Project ID/Title: 12695/001: Investigating the impact of intermittent fasting diets on cognition, behaviour and emotional wellbeing

Further to your satisfactory responses to my comments, I am pleased to confirm in my capacity as Joint Chair of the UCL Research Ethics Committee (REC) that I have ethically approved the data collection element of your study until **1st June 2019.**

Ethical approval is subject to the following conditions.

Notification of Amendments to the Research
You must seek Chair's approval for proposed amendments (to include extensions to the duration of the project) to the research for which this approval has been given. Ethical approval is specific to this project and must not be treated as applicable to research of a similar nature. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing an 'Amendment Approval Request Form'
http://ethics.grad.ucl.ac.uk/responsibilities.php

Adverse Event Reporting – Serious and Non-Serious
It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator [redacted] immediately the incident occurs. Where the adverse incident is unexpected and serious, the Joint Chairs will decide whether the study should be terminated pending the opinion of an independent expert. For non-serious adverse events the Joint Chairs of the Ethics Committee should again be notified via the Ethics Committee Administrator within ten days of the incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol. The Joint Chairs will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

Final Report
At the end of the data collection element of your research we ask that you submit a very brief report (1-2 paragraphs will suffice) which includes in particular issues relating to the ethical implications of the research i.e. issues obtaining consent, participants withdrawing from the research, confidentiality, protection of participants from physical and mental harm etc.

1

Appendix V

Participant information sheet

Participant Information Sheet:
For individuals who are considering, or who have already begun the 5:2 or a calorie restricted diet.

UCL Research Ethics Committee Approval ID Number: **12695/001**

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of Study: The impact of fasting on thinking, behaviours and mood

Department: Research Department of Clinical Educational and Health Psychology

Name and Contact Details of the Researcher(s):
John O'Leary [redacted]
Freya Donaldson [redacted]

Name and Contact Details of the Principal Researcher: Dr Lucy Serpell
[redacted]

You are being invited to take part in a research project. Before you decide it is important for you to understand why the research us being done and what participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

1. **What is the project's purpose?**
   The aim of this study is to find out about the impact of starting or remaining on the 5:2 diet on mood, eating behaviour and ability to do certain mental tasks and to explore whether there are any differences between the impact of this diet compared to a continuous calorie restriction diet. The project will run for 1 year.

2. **Why have I been chosen?**
   You have been chosen to take part in this study because you are a healthy adult (18-60 yrs) who is planning to start or who has already begun either the 5:2 diet or a continuous calorie restriction (daily calorie restriction of between 15-25%) diet. Any individuals who may be putting their health at risk, such as those with diabetes, those who are pregnant or have other health conditions for whom medical advice indicates that fasting would potentially endanger their health will not be able to take part in this study. As dieting is a known risk factor for the development of eating disorders, individuals with any past or current history of an eating disorder will also be excluded from the study.

3. **Do I have to take part?**

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep (and be asked to sign a consent form). You can withdraw at any time without giving a reason and without it affecting any benefits that you are entitled to. If you decide to withdraw you will be asked what you wish to happen to the data you have provided up that point.

4. What will happen to me if I take part?

If you decide to participate and haven't already started the diet, we will ask you to complete a food diary for one week and fill out a series of questionnaires online which will ask about your mood, eating behaviours, self-esteem and thinking about food, shape and weight (around 15 minutes). You will then be asked to begin dieting. We will then ask you to complete some of the questionnaires again on a weekly basis (5 minute), and also some online tasks (lasting about 20 minutes) twice, on different days. After one month of dieting, you will be asked to complete the same food diary again and the questionnaires for the last time (5 times in total).

However, if you have already begun your diet for a period of 4 weeks or more, we will only ask you to complete complete a food diary once, and some online tasks (lasting about 20 minutes) twice, on different days. We will use the data to compare how people answer certain questions before, during and after starting the diet, and how they perform on certain online tasks on fasting and non-fasting days

5. What are the possible disadvantages and risks of taking part?

Some questions will ask you about body image, eating behaviour, mood and self-esteem so it is possible that you may find them upsetting. It is also possible that the process of following the diet may lead to changes in mood or you may experience symptoms that are more common in eating disorders. Should you experience distress or changes in eating behaviour, then please withdraw from the study and contact us immediately using the contact details at the top of this information sheet. We will then discuss your difficulties and your options for further support.

6. What are the possible benefits of taking part?

Whilst there are no immediate benefits for those people participating in the project, some participants may find it useful to track their mood, behaviours and other psychological variables during the initial stages of following their chosen calorie restricted diet, and may find the cognitive tasks interesting to complete. In addition, participants may find it interesting to learn of the findings of this study in terms of how this diet impacted on them as a group.

Participants will be entered into a prize draw to win Amazon vouchers. Student participants recruited through the Sona system also receive course credits for participation.

7. What if something goes wrong?

If you feel that you have been treated unfairly or incorrectly by our research team, then you can make a formal complaint by using the contact details below.

Dr Lucy Serpell

Research Department of Clinical, Educational and Health Psychology
University College London
Gower Street
London WC1E 6BT . Tel: [redacted]

Should you feel your complaint has not been handled to your satisfaction then you can contact the Chair of the UCL Research Ethics Committee – [redacted]

If you feel that you are becoming distressed during or directly following your participation in the research study, then please do not hesitate to contact Dr Lucy Serpell directly, using the details above. If you feel that taking part in this study has contributed to changes in your diet or eating habits, which are causing you to feel distressed, then please contact your General Practitioner.

8. Will my taking part in this project be kept confidential?

All information provided (along with your personal details) will be kept confidential, anonymized and stored on a secure database. Your personally identifiable details will not be linked to your individual responses. No information about you will be disclosed to a third party and you will not be able to be identified in any ensuing reports or publications.

9. Limits to confidentiality

Please note that assurances on confidentiality will be strictly adhered to unless evidence of potential harm to yourself during the research process is uncovered. In such cases the University may be obliged to contact relevant statutory bodies/agencies.

10. What will happen to the results of the research project?

The results of the study will be written up into two theses for submission for the Doctorate in Clinical Psychology and submitted to the Department of Clinical, Health and Educational Psychology in June 2019. Interested participants will be provided with a summary sheet of the overall study's results. We will aim to provide this in a timely manner so that those who are still following the diet will be able to make an informed decision about whether or not to continue.
The study will aim to be published in peer-reviewed journals following the completion of the Doctorate.

11. Data Protection Privacy Notice

Notice:
The data controller for this project will be University College London (UCL). The UCL Data Protection Office provides oversight of UCL activities involving the processing of personal data and can be contacted at data-protection@ucl.ac.uk. UCL's Data Protection Officer is [redacted] and he can also be contacted at data-[redacted]

Your personal data will be processed for the purposes outlined in this notice. The legal basis that would be used to process your personal data will be the provision of your consent. You can provide your consent for the use of your personal data in this project by completing the consent form that has been provided to you.

Your personal data will be processed so long as it is required for the research project. We will anonymise the personal data you provide, and will endeavour to minimise the processing of personal data wherever possible.

If you are concerned about how your personal data is being processed, please contact UCL in the first instance at data-protection@ucl.ac.uk. If you remain unsatisfied, you may wish to contact the Information Commissioner's Office (ICO). Contact details, and details of data subject rights, are available on the ICO website at: https://ico.org.uk/for-organisations/data-protection-reform/overview-of-the-gdpr/individuals-rights/

Given the nature of this information we will be storing your personal details in a secure, password-protected database and assigning each participant an ID code so that your personal details remain anonymous and separate from the other variables collected during the research. Only the two main researchers (John and Freya) will have access to this database. Your personal details will remain anonymous and confidential on the study information sheet provided to all interested individuals, and you will be provided with an opportunity to ask the researchers any questions you have about anonymity prior to consenting to participate.

12. Who is organising and funding the research?

This research is being undertaken in collaboration with University College London,
Gower Street
London WC1E 6BT

16. Contact for further information

For further information relating to this study, please contact;
Dr Lucy Serpell
University College London
Gower Street
London WC1E 6BT

Tel: [redacted]

You will be provided with a copy of this information sheet, and a signed consent form for your reference.

Thank you for reading this information sheet and for considering taking part in this research study.

Appendix VI

Informed consent form

Informed consent form for adult participants in research studies

Please complete this form after you have read the information sheet and/ or listened to an explanation about the research.

Project Title: The impact of fasting on thinking.
Department: Department of Clinical, Educational and Health Psychology
Name and contact details of the researcher: John O'Leary, [redacted]
Name and Contact Details of the Principal Researcher: Lucy Serpell, l[redacted]

Name and Contact Details of the UCL Data Protection Officer: Lee Shailer l[redacted]

This study has been approved by the UCL Research Ethics Committee: Project ID number: 12695/001

Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.

I confirm that I understand that by electronically ticking/initialing each box below I am consenting to this element of the study. I understand that it will be assumed that unticked/initialled boxes means that I DO NOT consent to that part of the study. I understand that by not giving consent for any one element that I may be deemed ineligible for the study.

		Tick or initial
1	I confirm that I have read and understood the Information Sheet for the above study. I have had an opportunity to consider the information and what will be expected of me. I have also had the opportunity to ask questions which have been answered to my satisfaction. I would like to take part in (please tick one or more of the following): - *The online cognitive testing*	

2	I consent to the processing of my personal information *(demographics, food diary, online cognitive test results)* for the purposes explained to me. I understand that such information will be handled in accordance with all applicable data protection legislation.	
3	**Use of the information for this project only**: I understand that all personal information will remain confidential. I understand that my data gathered in this study will be stored anonymously and securely. It will not be possible to identify me in any publications. I understand that I will be given a unique ID code, which will be used when completing questionnaires and the online cognitive test. Personal details will be saved on a secure, password-protected database, stored on the UCL network. Only researchers will have access to this database. All efforts will be made to ensure I cannot be identified.	
4	I understand that my anonymous information may be subject to review by responsible individuals from the University for monitoring and audit purposes.	
5	I understand the potential risks of participating and the support that will be available to me (to contact the researchers, advice to contact GP or eating disorder charity contact details) should I become distressed during the course of the research.	
6	I understand that no promise or guarantee of benefits have been made to encourage me to participate. However, I understand that I will be entered in to a prize draw with the possibility of winning Amazon vouchers.	
7	I understand that the data will not be made available to any commercial organisations but is solely the responsibility of the researchers undertaking this study.	
8	I understand that I will not benefit financially from this study or from any possible outcome it may result in in the future.	
9	I agree that my anonymized research data may be used by others for future research. No one will be able to identify you when this data is shared.	
10	I understand that the information I have submitted will be published as a report and I wish to receive a copy of it. - *Yes* - *No*	
11	I hereby confirm that I understand the inclusion criteria as detailed in the Information Sheet and explained to me by the researcher.	
12	I hereby confirm that: (a) I understand the exclusion criteria as detailed in the Information Sheet and explained to me by the researcher; and (b) I do not fall under the exclusion criteria.	
13	I agree that my GP may be contacted if any unexpected results are found in relation to my health.	
14	I have informed the researcher of any other research in which I am currently involved or have been involved in during the past 12 months.	
15	I am aware of who I should contact if I wish to lodge a complaint.	
16	Use of information for this project and beyond	

	I would be happy for the anonymous data I provide to be archived at UCL. Personal identifiable information (name linked to ID code) will be kept for 1 year. Anonymised research data will be kept for 10 years.	

Appendix VII

Study instructions for participants

Many thanks for returning your consent form, and my thanks again for participating in our study. You should have been following the 5:2 intermittent fasting diet or your chosen low calorie diet for at least 4 weeks by now.

It is now time for you to complete the cognitive tasks online as part of our study. These should take you between 15-20 minutes to complete online using a PC or Laptop. Please make sure that you enter your participant ID number, which is **1264**.

Remember, we want you to do these tasks on two occasions over the next 7 days. If you are on the 5:2 diet you must do the first set of tasks on a **FASTING** day, and the second set of tasks on a **NON-FASTING** day. **If you are on any other diet**, please pick any 2 days within a seven-day period.

Please follow these instructions when completing the tasks: • Do these tasks in the evening time between 6-10pm (your own time-zone) and at approximately the same time of day each testing session (give or take about 30 minutes). • Do these tasks in a quiet area, free of potential distractions/interruptions, and complete them in one sitting. • Please eat something 30 minutes before starting the tasks each time. For those who are completing the tasks on a fasting day, please consume at least half of your restricted calorie intake before starting the tasks. • Do not eat any food or consume any calorific drinks during task completion (drinking water is fine). • Use the same computer and internet browser each time you do the tasks. Please ensure your internet connection is working. • Do not refresh the webpage once you have begun the tasks as this will bring you back to the opening page.

Please read the online instructions carefully for each of the tasks, as you will not be able to return to them once you have started the task. There will be an opportunity to practise most tasks before doing the real thing.

Click the link below (or paste into your internet browser) to begin.

http://www.ucl.ac.uk/sam-gilbert/IFS2018/IntermittentFastingStudy.html?id=1264

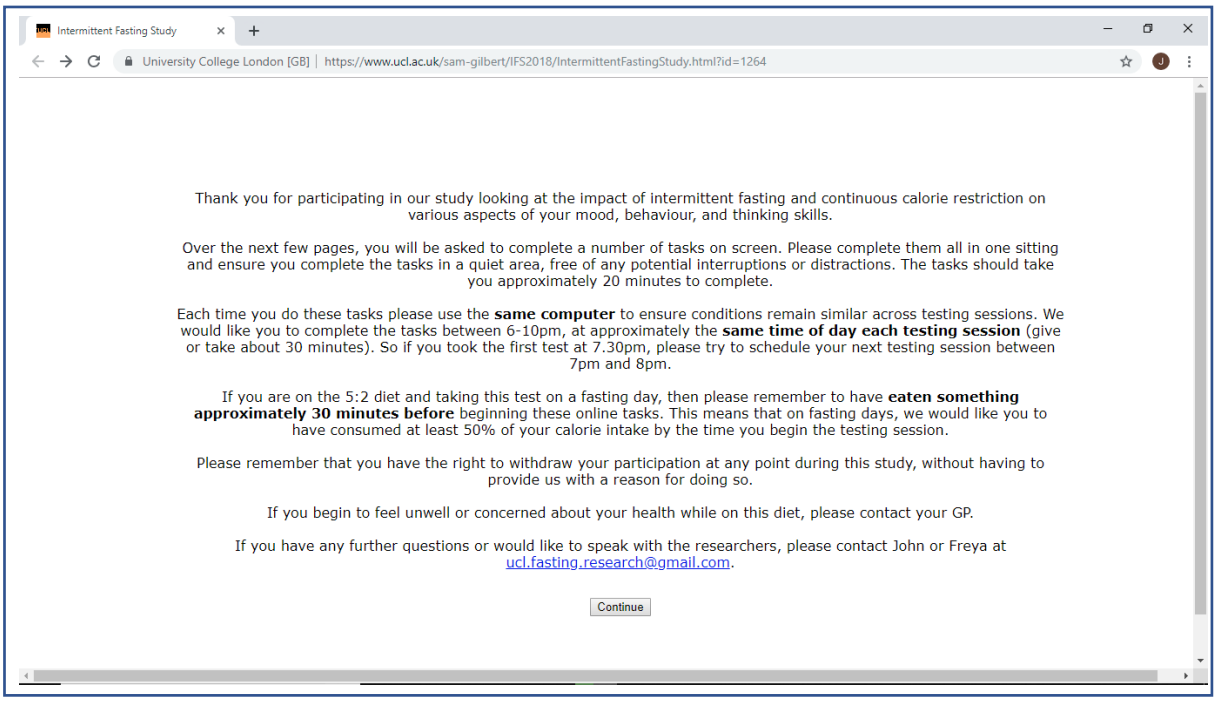
If there are any further questions, please email us and we will get back to you as soon as possible.

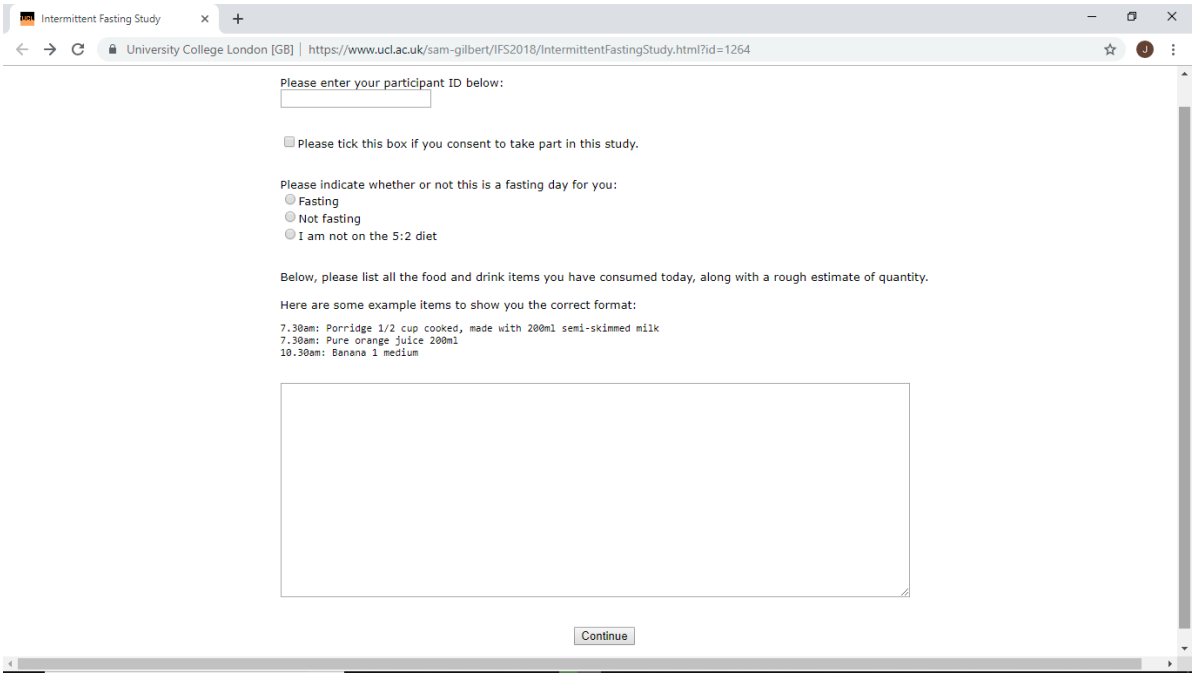
Many thanks, John and Freya

Appendix VIII

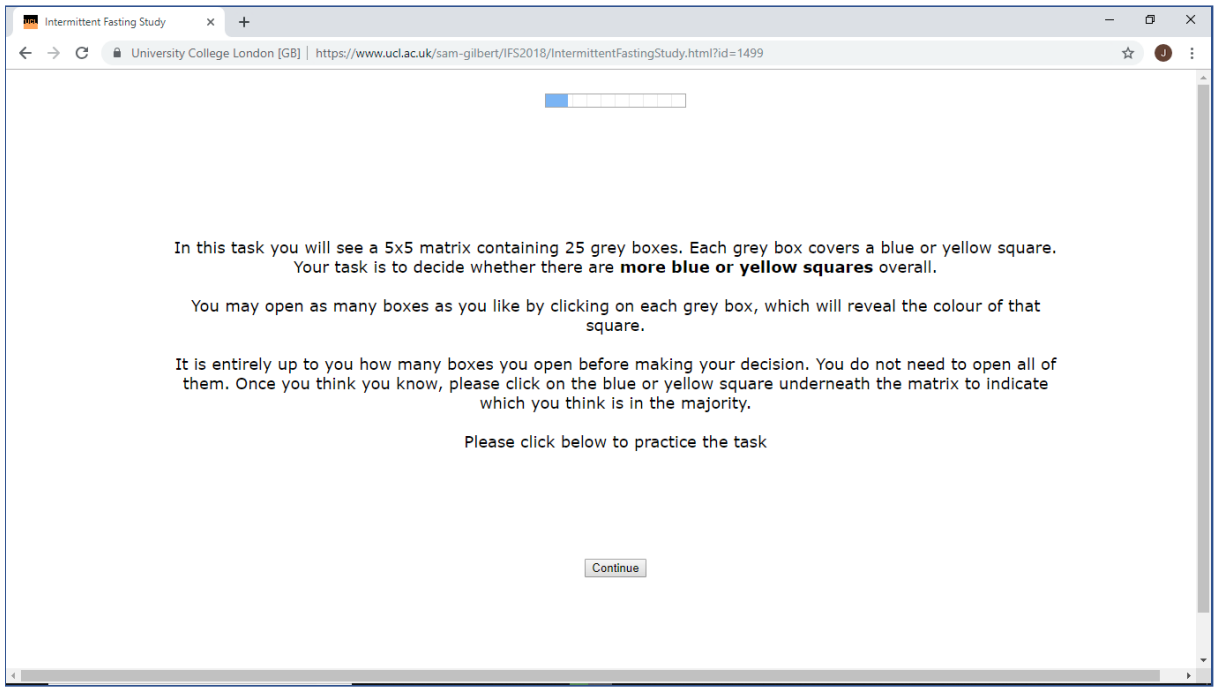
Online Tasks

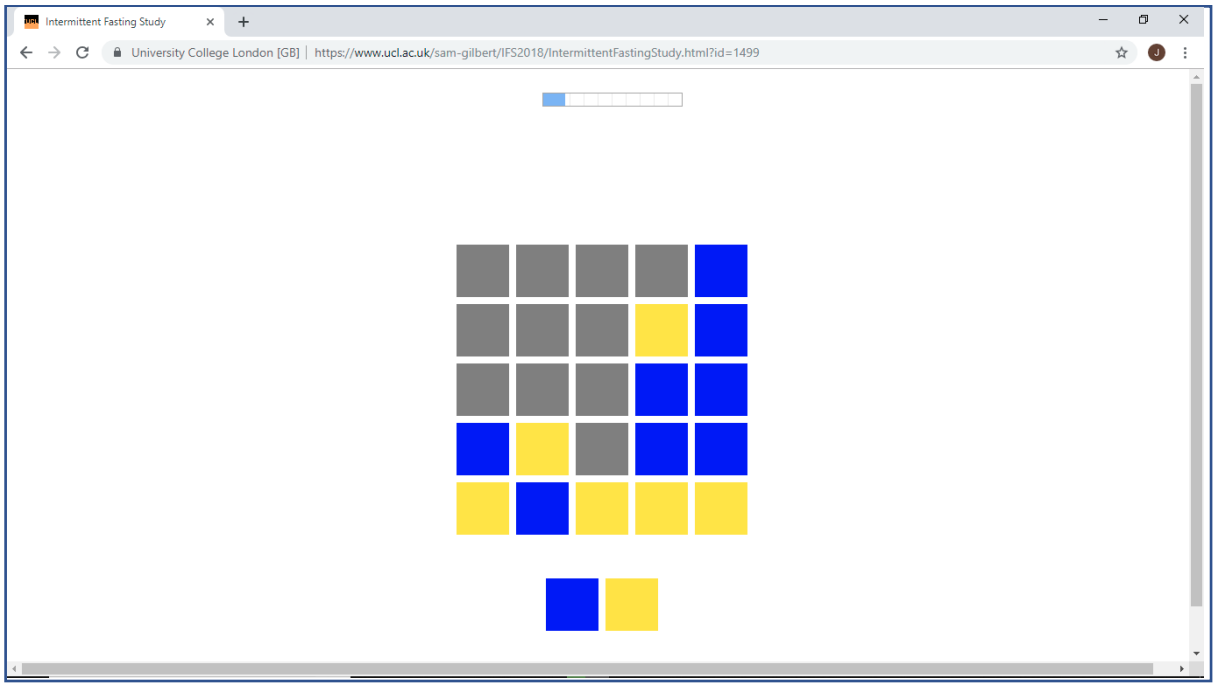
Opening Webpages



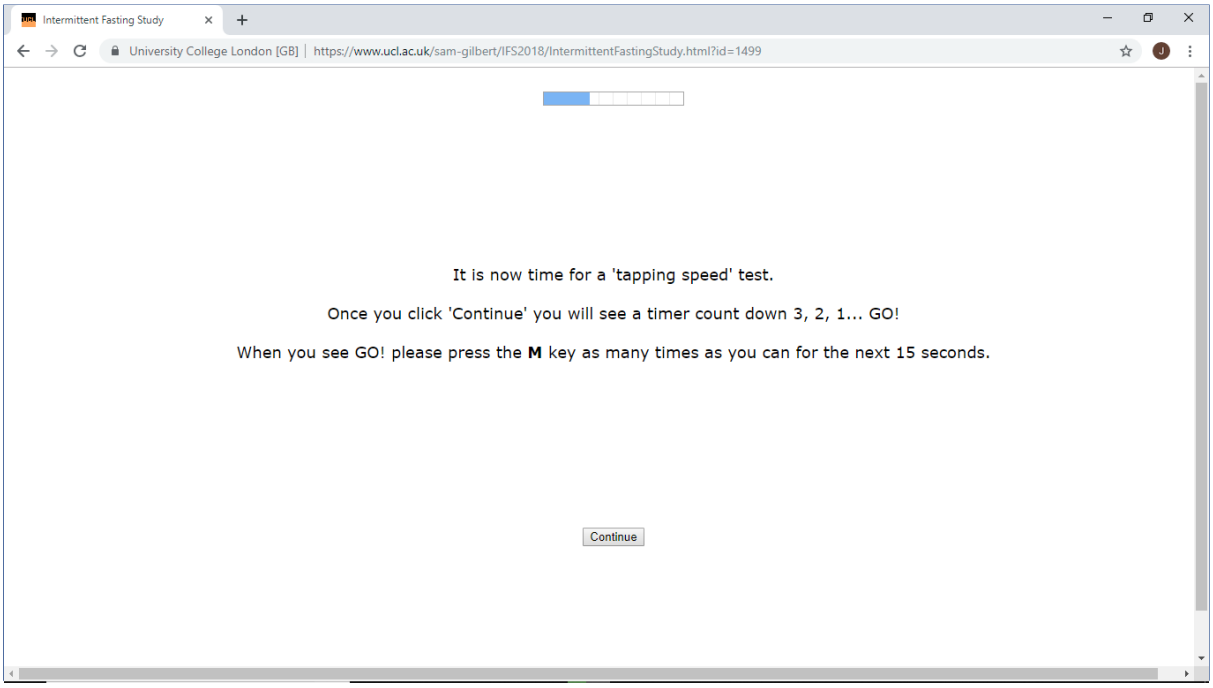


Information Sampling Task

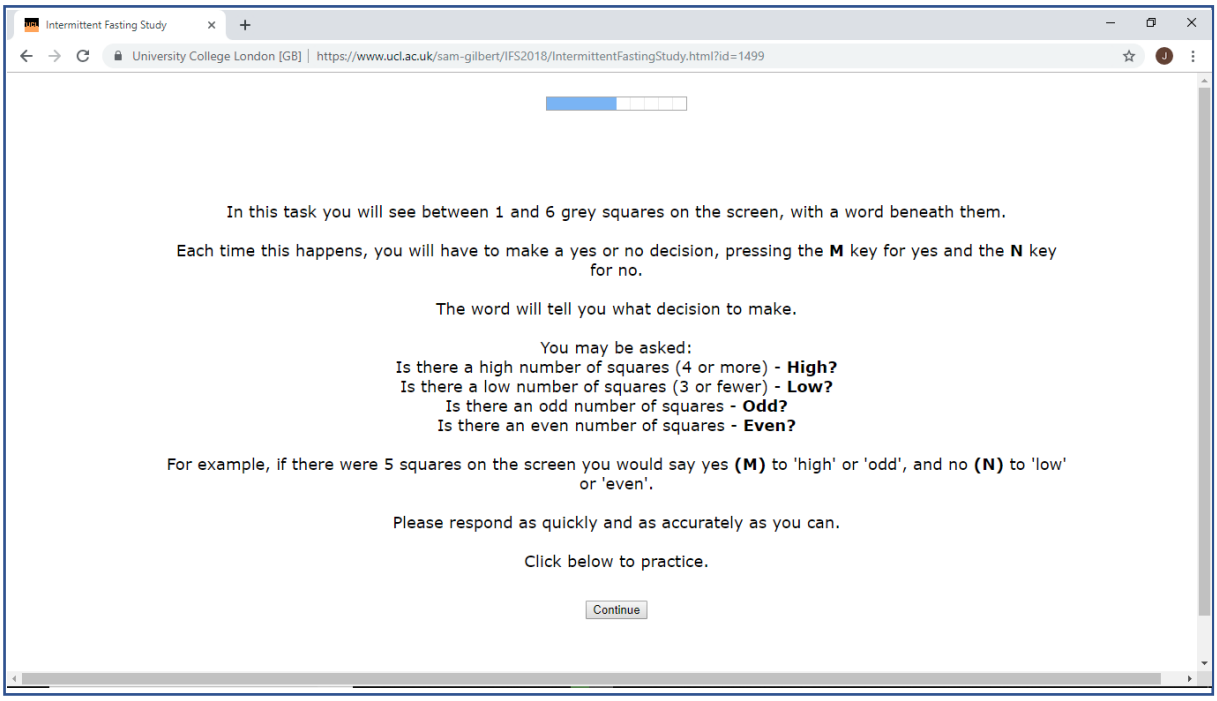


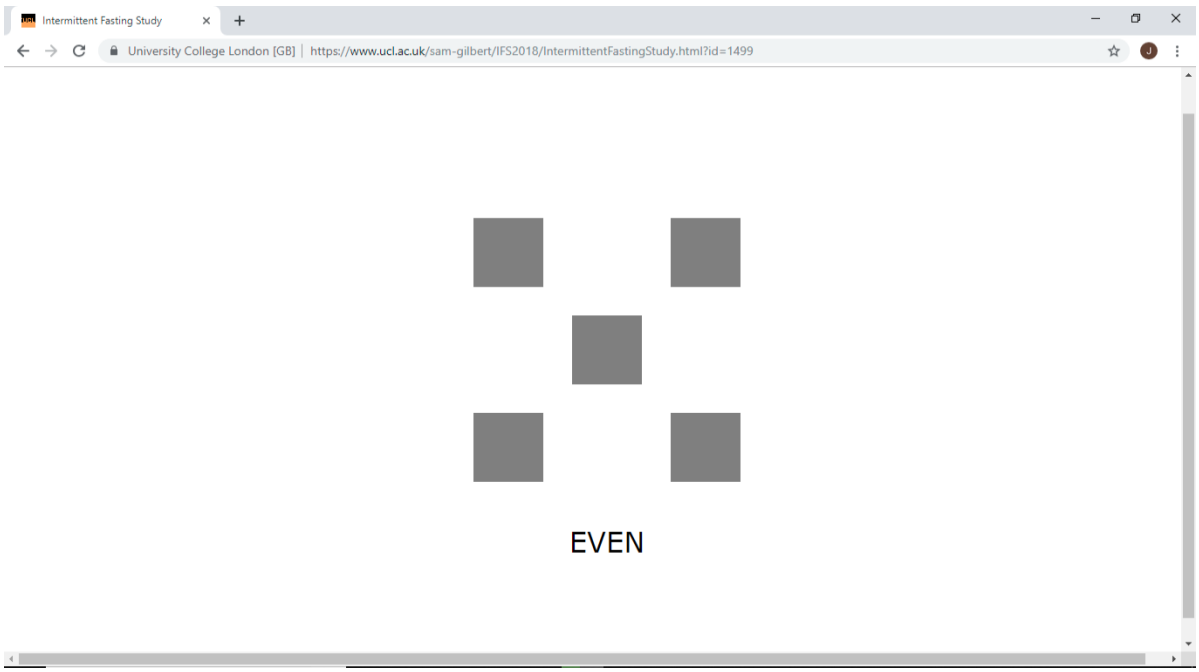


Tapping Speed task



Rule Change Task

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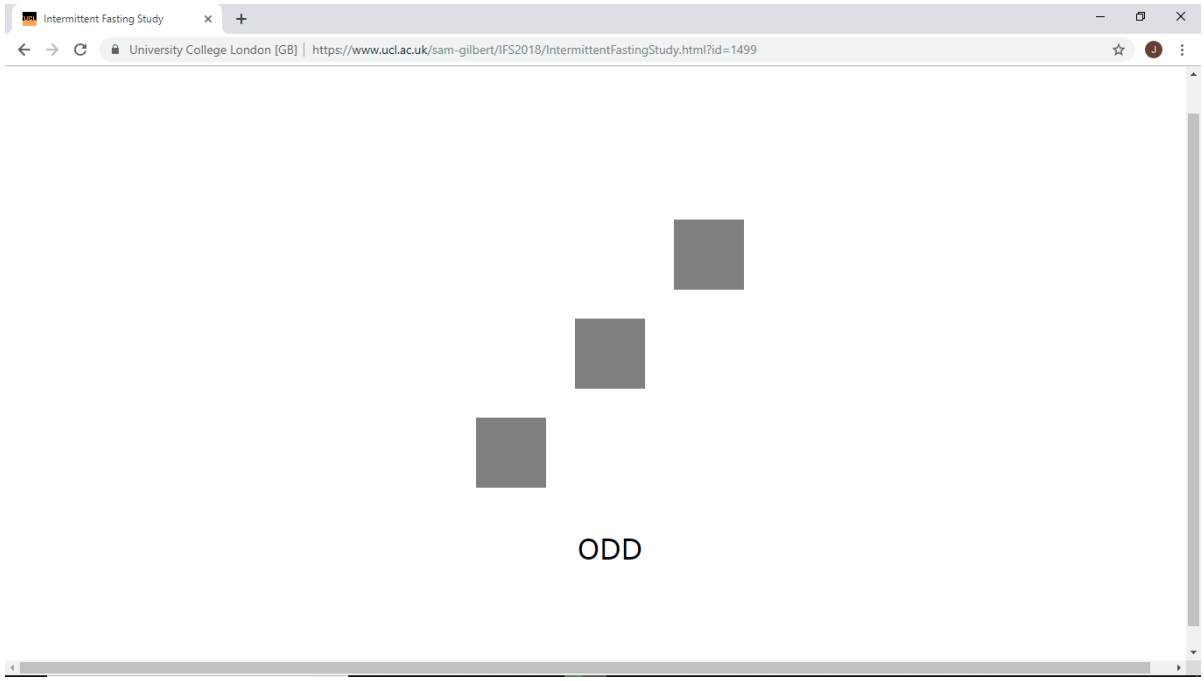
EVEN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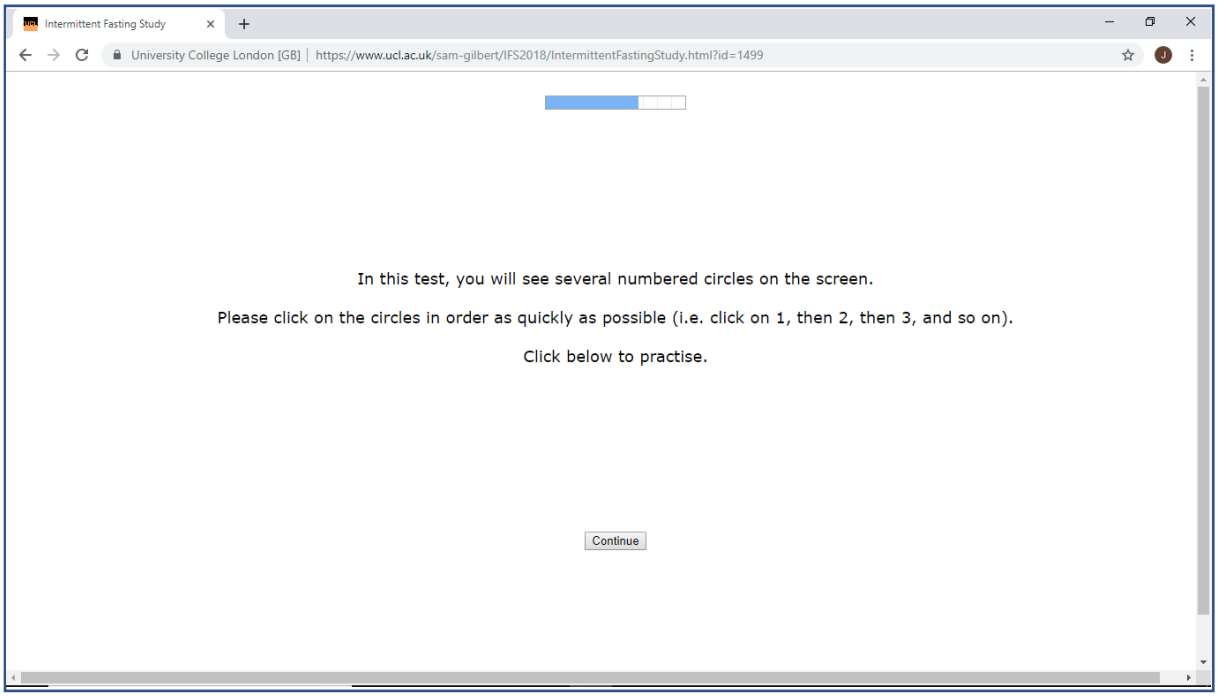
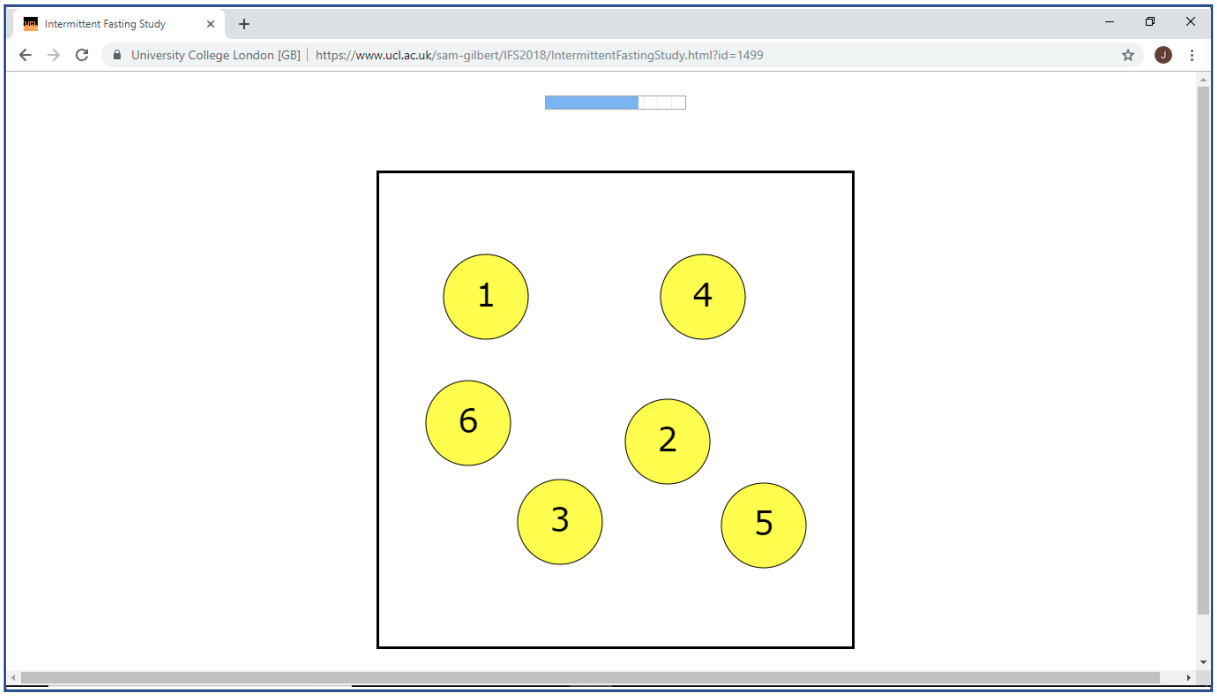
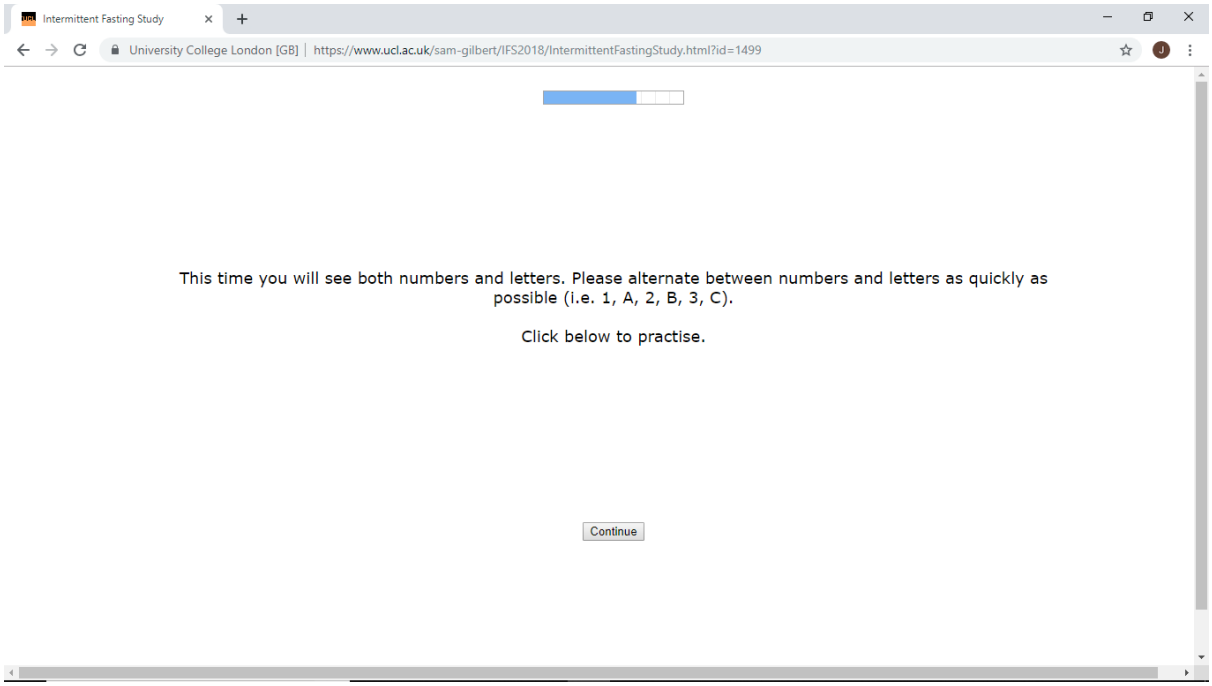
ODD

Trail Making Task-Part A



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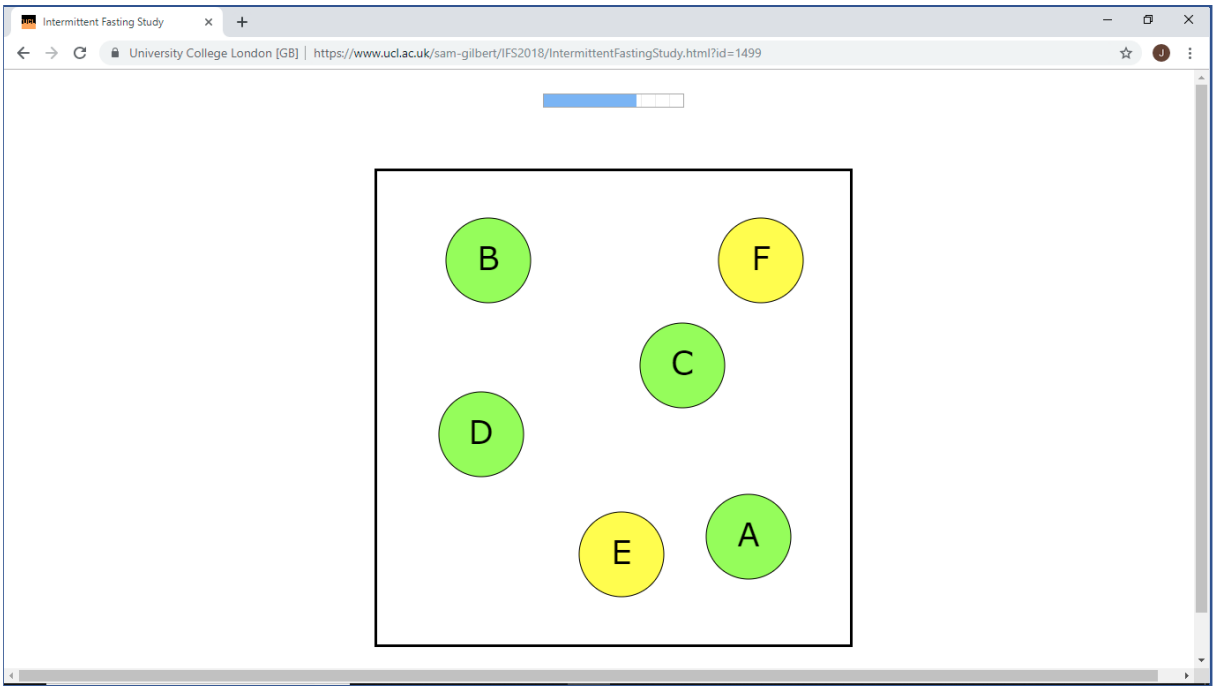
This time you will see both numbers and letters. Please alternate between numbers and letters as quickly as possible (i.e. 1, A, 2, B, 3, C).
Click below to practise.
Continue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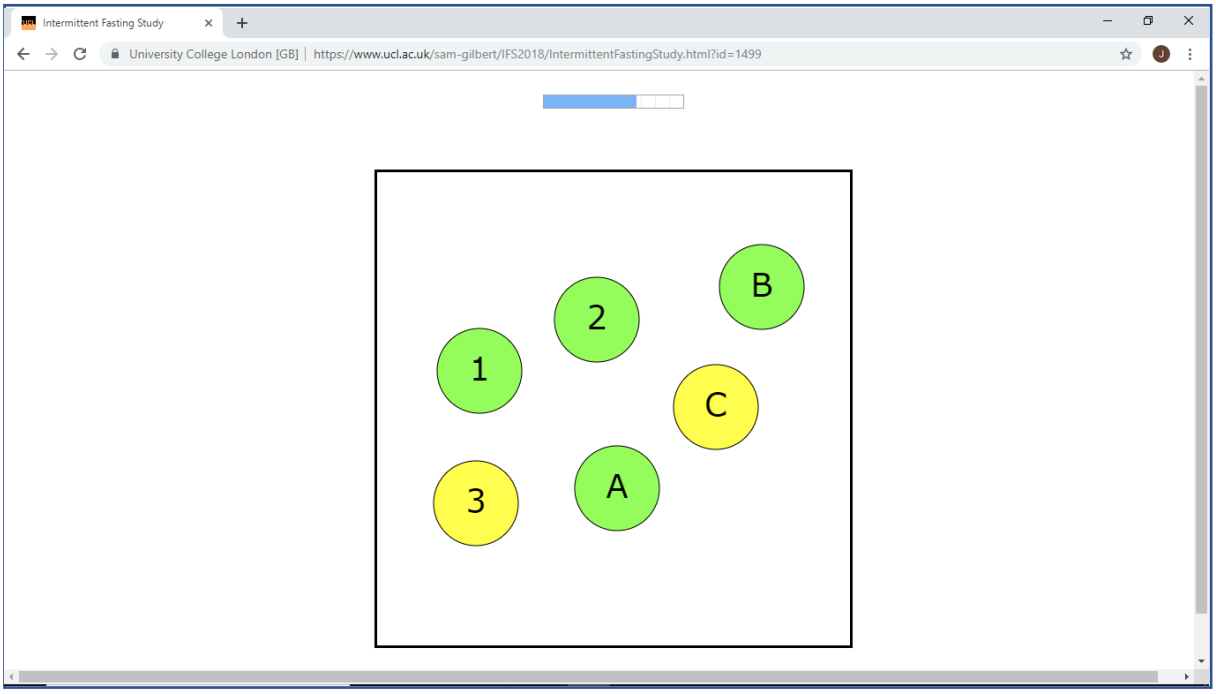
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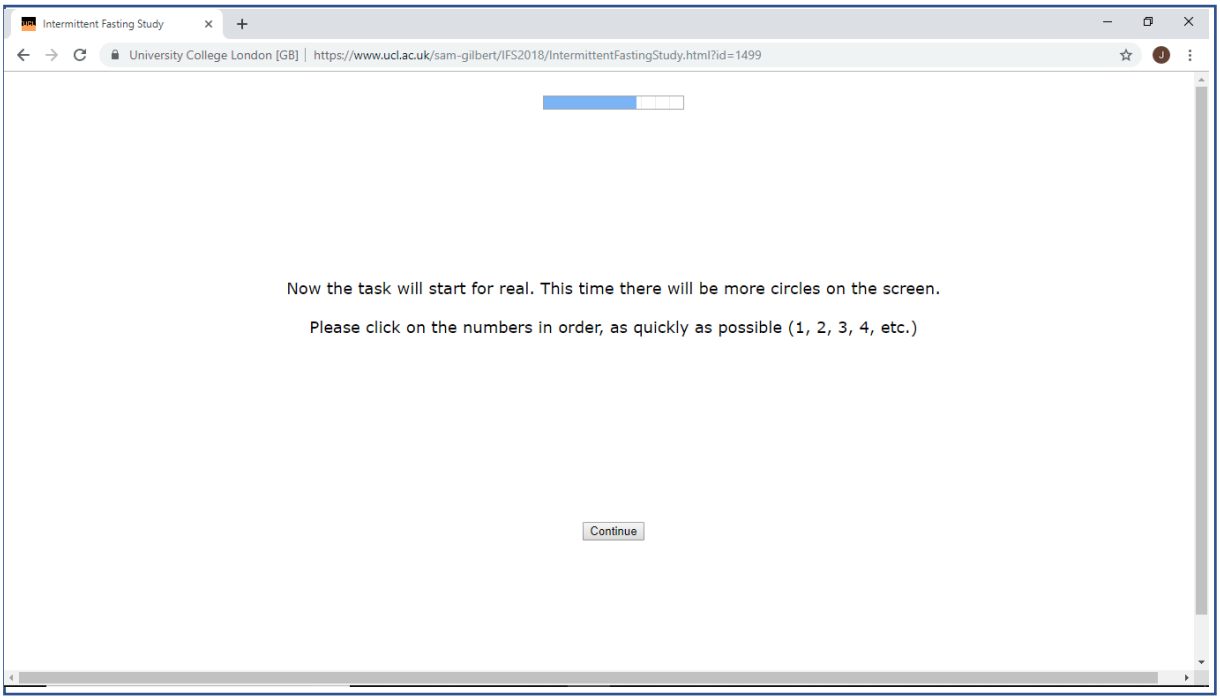
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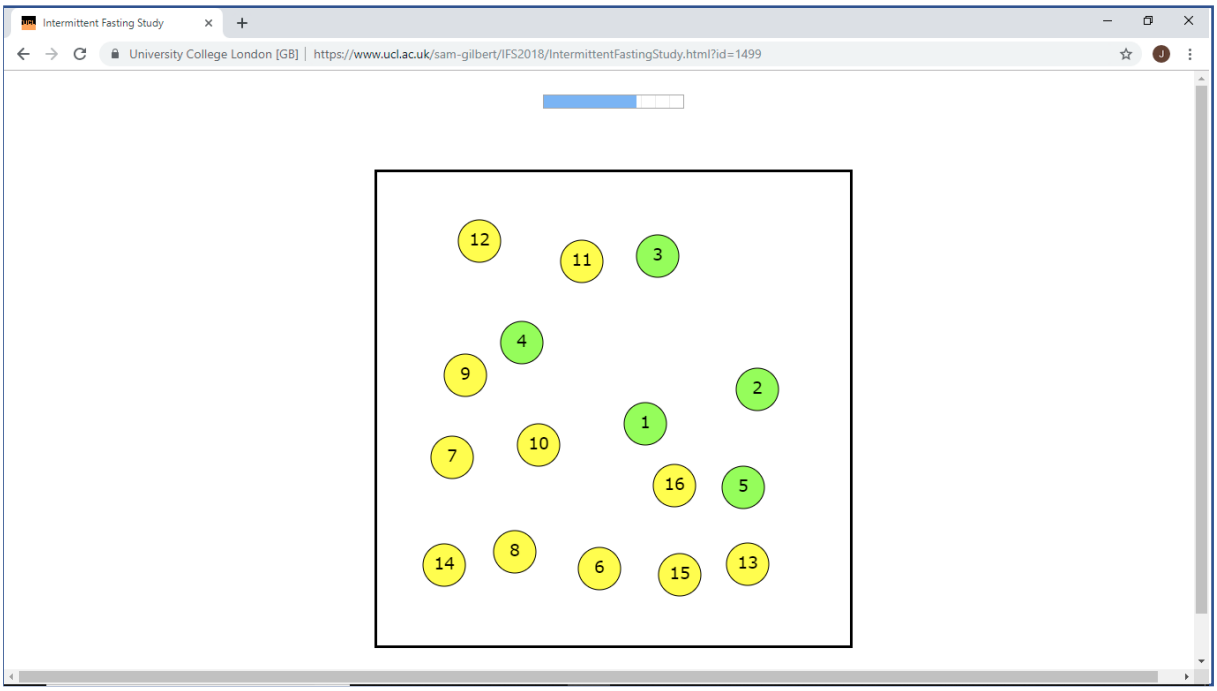
Now the task will start for real. This time there will be more circles on the screen.
Please click on the numbers in order, as quickly as possible (1, 2, 3, 4, etc.)
Continue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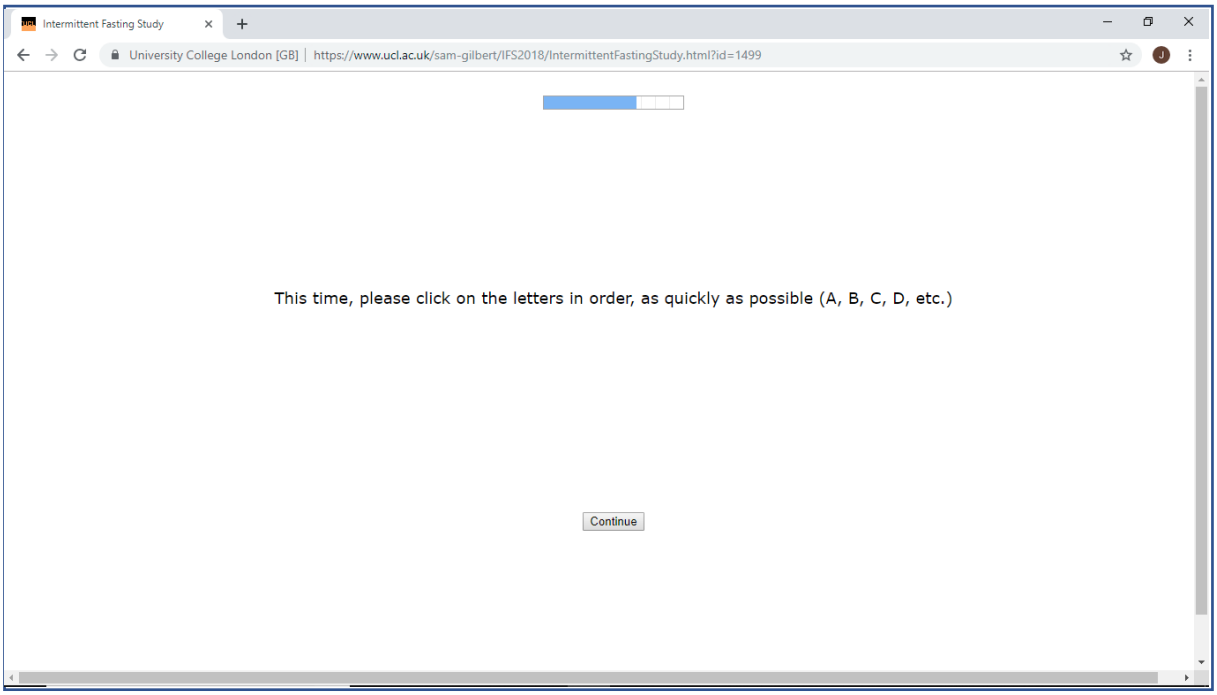
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This time, please click on the letters in order, as quickly as possible (A, B, C, D, etc.)
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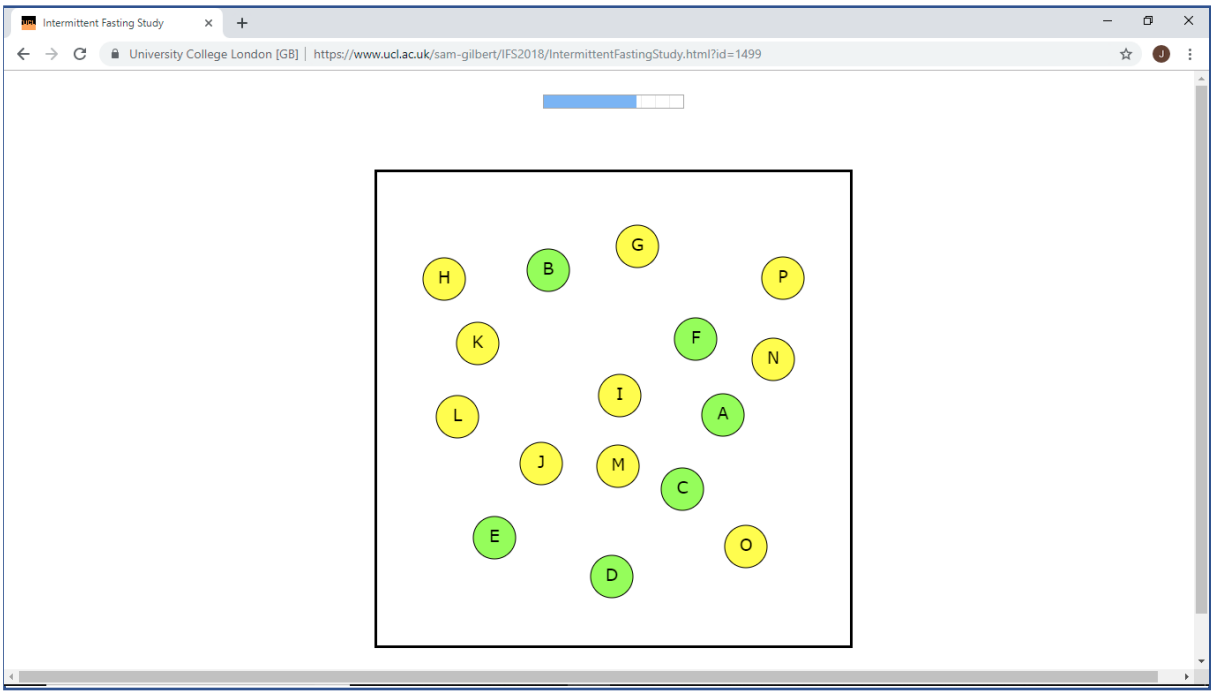
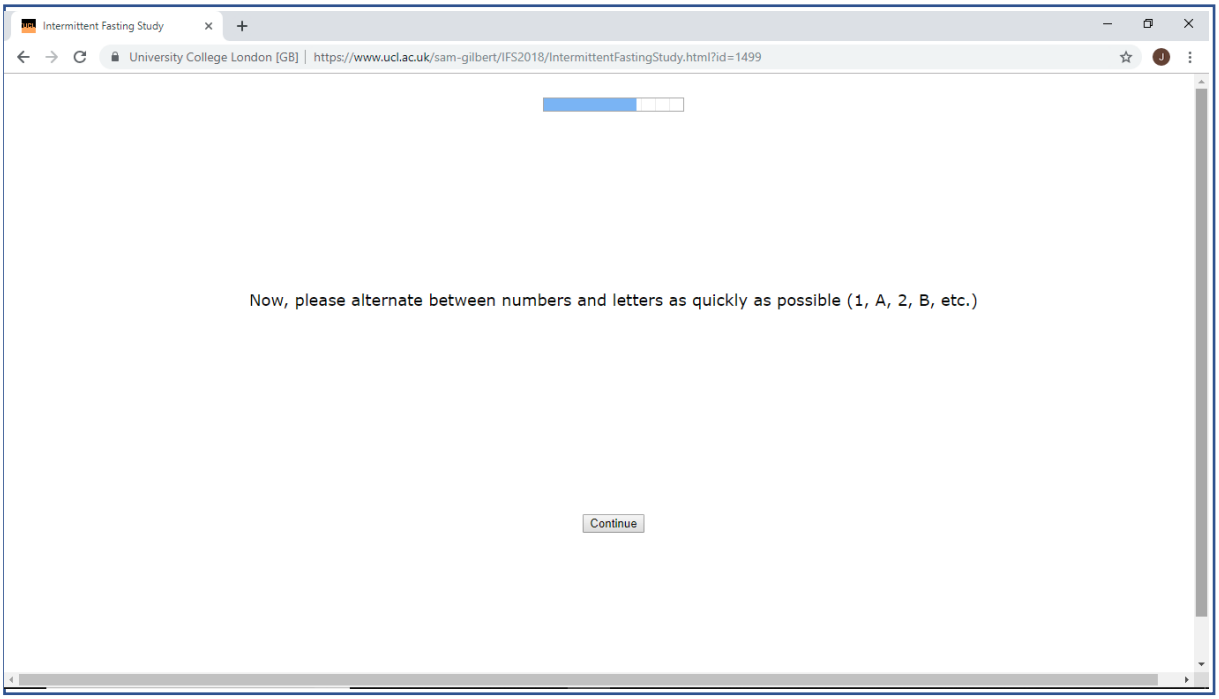
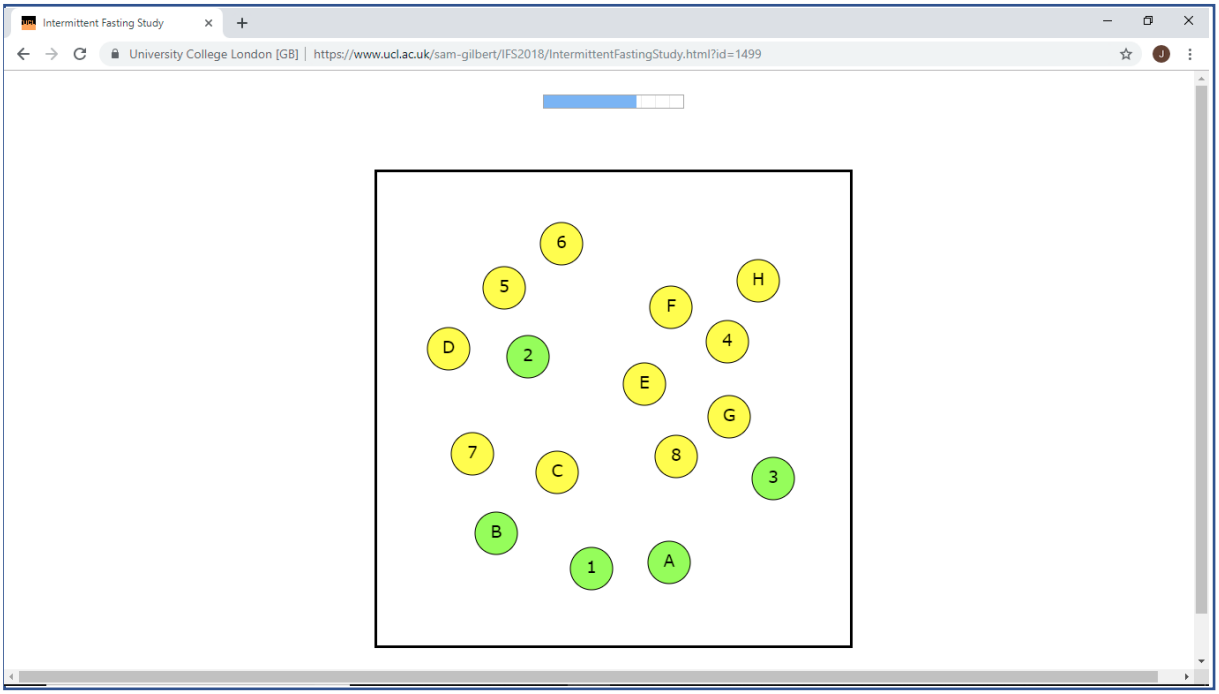
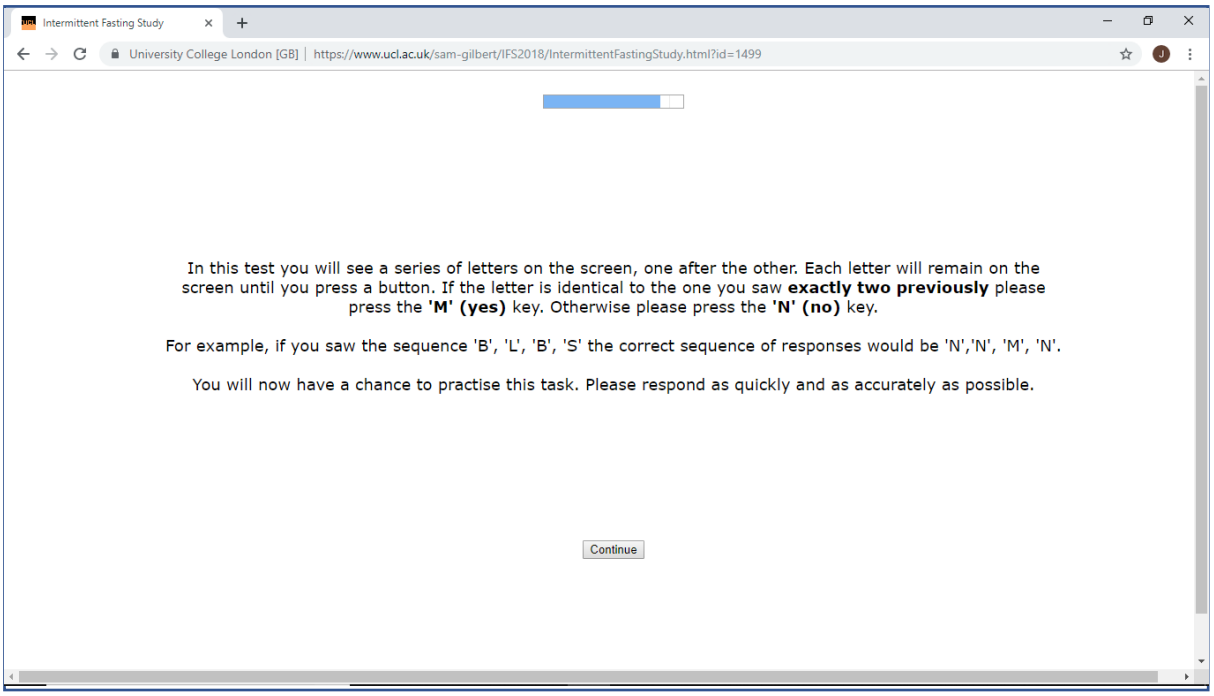


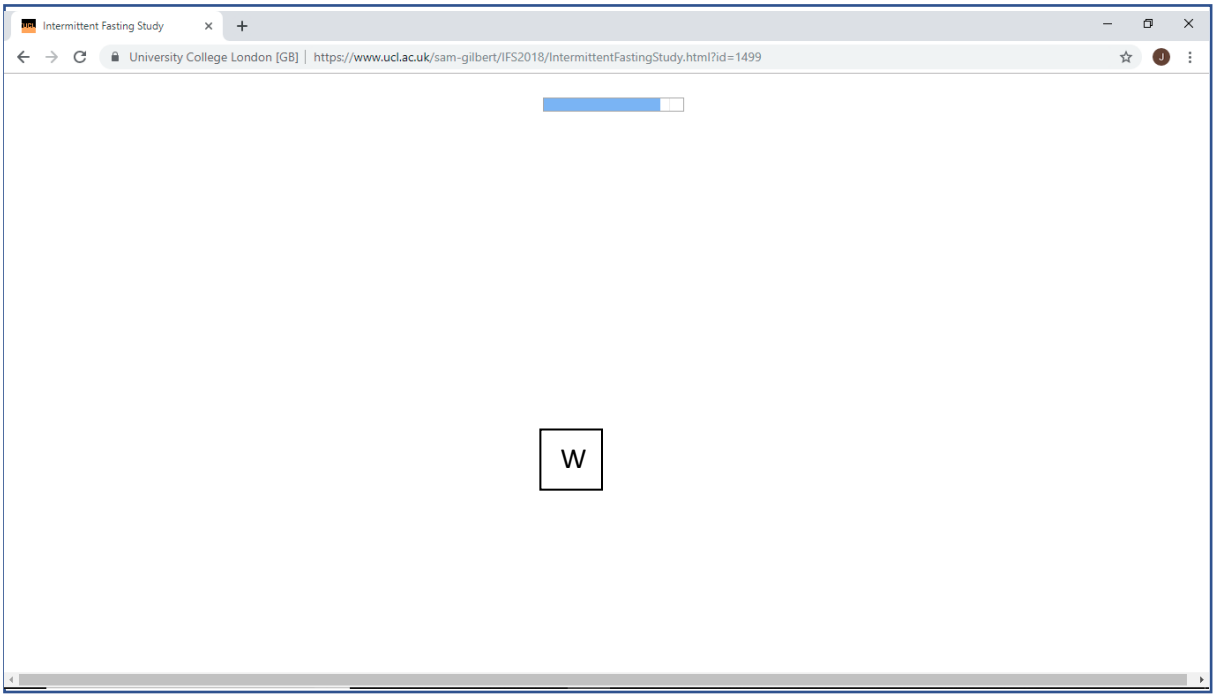
Trail Making Task- Part B





2n-back Task with inbuilt clock watching

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University College London [GB] | https://www.ucl.ac.uk/sam-gilbert/IFS2018/IntermittentFastingStudy.html?id=1499
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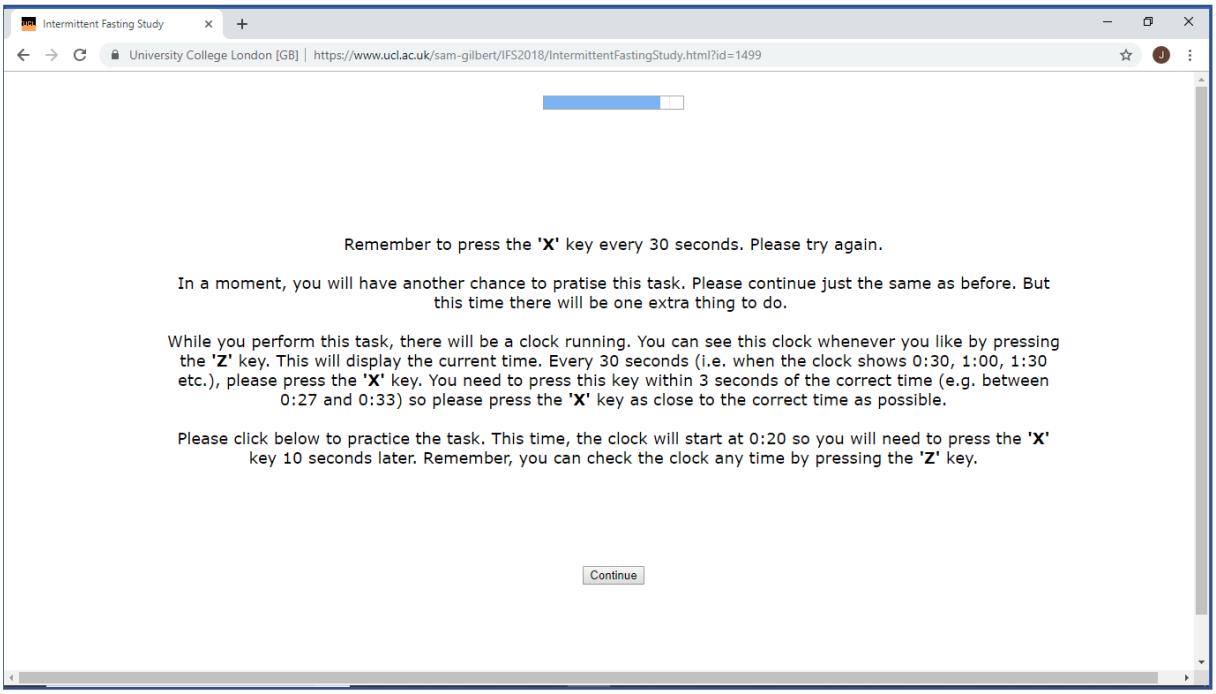
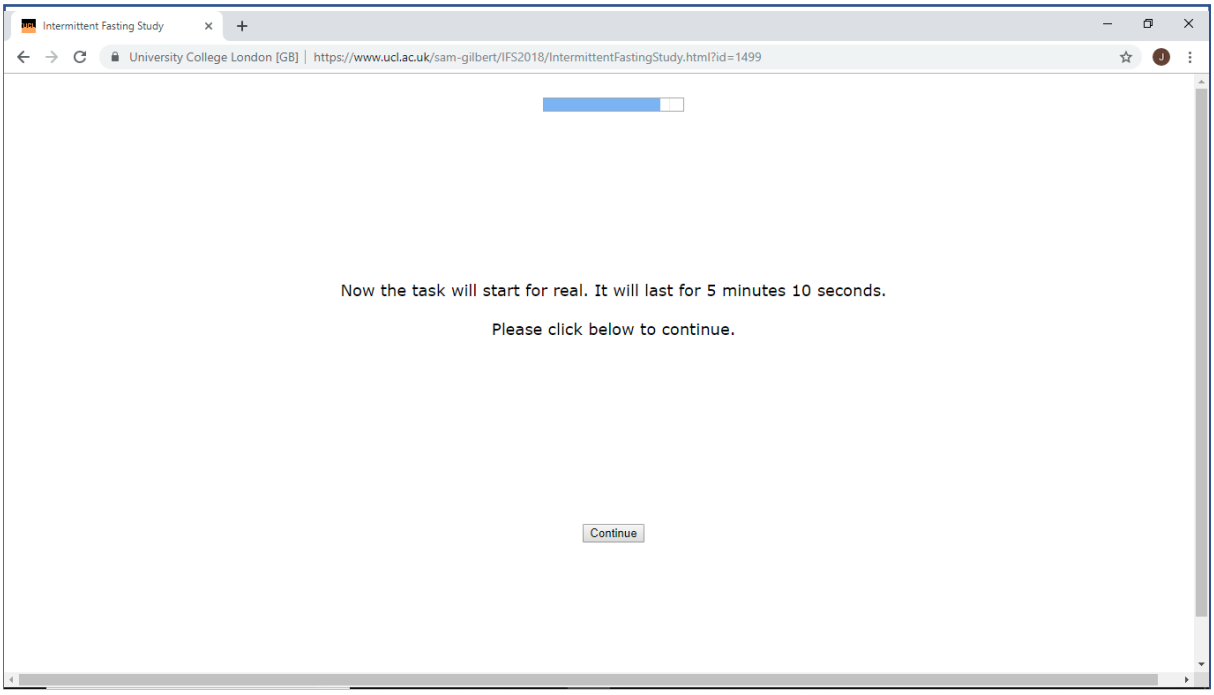

Intermittent Fasting Study
University College London [GB] | https://www.ucl.ac.uk/sam-gilbert/IFS2018/IntermittentFastingStudy.html?id=1499
Remember to press the 'X' key every 30 seconds. Please try again.
In a moment, you will have another chance to pratise this task. Please continue just the same as before. But this time there will be one extra thing to do.
While you perform this task, there will be a clock running. You can see this clock whenever you like by pressing the 'Z' key. This will display the current time. Every 30 seconds (i.e. when the clock shows 0:30, 1:00, 1:30 etc.), please press the 'X' key. You need to press this key within 3 seconds of the correct time (e.g. between 0:27 and 0:33) so please press the 'X' key as close to the correct time as possible.
Please click below to practice the task. This time, the clock will start at 0:20 so you will need to press the 'X' key 10 seconds later. Remember, you can check the clock any time by pressing the 'Z' key.
Continue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Now the task will start for real. It will last for 5 minutes 10 seconds.
Please click below to continue.
Continue