Caffeine: Evidence-based guidance for use during upper-body exercise and for individuals with a spinal cord injury.

By
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Abstract

The use of nutritional supplements (NS) is common in able-bodied (AB) athletic populations and good evidence exists for a number of NS such as sports drinks, protein powder, creatine, caffeine and buffering agents. However, little evidence is available regarding the popularity and efficacy of NS in a population of athletes with physical impairments.

Fifty-eight percent of athletes with a physical or visual impairment reported the use of one or more NS in the previous six months (Chapter three). The types of NS used were similar to AB athletes (most commonly protein, carbohydrate-electrolyte sports drinks, carbohydrate supplements and multivitamins) and were used for similar reasons (energy, recovery and immunity). A concerning finding was that 9% of athletes surveyed reported experiencing negative side-effects for the use of NS, which may in part be due to following AB dosage and timing guidelines. Approximately half the athletes wanted more information and education regarding anti-doping, NS and their efficacy. Further research on the effectiveness of different NS in a population of athletes with physical impairments is therefore warranted. The results indicated that caffeine was the most popular NS beyond any that provided only macronutrients. There is a large body of literature exploring its use as an ergogenic aid in AB athletes and yet the small amount of evidence remains equivocal in a population of athletes with physical impairments.

Chapter four found that caffeine (4 mg·kg$^{-1}$) significantly improved cycling (2.0(2.0)%; 16:35 vs 16:56 min; $p=0.033$) but not handcycling (1.8(3.0)%; 24:10 vs 24:36 min; $p=0.153$) 10 km time trial (TT) performance compared to placebo (PLA) in recreationally active AB participants. The improvement during cycling can be attributed to the increased power output (PO) during the first and last 2 km following caffeine. An increased PO for a given rating of perceived exertion (RPE) was also apparent during cycling. Participants with a handcycling peak oxygen uptake ($\dot{V}O_2$ peak) above the mean improved their handcycling TT performance by 3.2% whereas those below the mean had a 0.3% reduction, which suggests training status may have an influence on caffeine’s ability to improve upper-body exercise (UBE) performance. An individual’s training status may increase the amount of recruitable muscle mass during maximal exercise, improve consistency of performance and increase maximal effort due to motivation.
Further support for the influence of UBE-specific training status was provided in the form of 20 km TT performance improvements in an elite Paralympic triathlete following caffeine (2, 4 and 6 mg·kg⁻¹) (Chapter seven). Performance improvements were seen alongside increased PO and arousal scores, but not RPE. The athlete experienced spasticity during two trials but attributed this to the maximal effort delivered not necessarily the ingestion of caffeine and he did not believe it influenced his performance.

Caffeine has previously been shown as ergogenic during short-term, high-intensity exercise in AB athletes during lower- or whole-body exercise and now during UBE (Chapter five). Caffeine (4 mg·kg⁻¹) improved both 20 m sprint and a one-off bout of 4 min maximal push performance in club-level wheelchair sportsmen. Caffeine did however fail to improve repeated bouts of 4 min push. There were no apparent changes in arousal or RPE, but Feeling scores (a measure of the affective dimension of pleasure-displeasure) increased following caffeine. Salivary caffeine concentration results raised concerns over the absorption time in individuals with a physical impairment. Measurements of plasma caffeine concentration ([CAF]) at rest (150 min) however, showed that the NS peaked at similar times in AB participants and participants with paraplegia and tetraplegia (80, 80 and 70 min, respectively) (Chapter six). The pattern of caffeine absorption did however differ. Peak [CAF] were higher in participants with tetraplegia, followed by a gradual decline. Caffeine curves did not significantly differ between AB participants and participants with paraplegia yet there was large inter-individual variance in both SCI groups.

Findings suggest that caffeine does appear to positively influence UBE performance during short-term, high-intensity and endurance tests in certain individuals with and without physical impairments. Based on the data, the magnitude of caffeine’s ergogenic effects are likely to be influenced by training status and SCI level.

Keywords: Wheelchair sport, ergogenic, supplement, exercise, performance, handcycling
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Preface

Peer-reviewed publications


Conference presentations and published abstracts


**Graham-Paulson, T.S.,** Perret, C., Watson, P. & Goosey-Tolfrey, V.L. Effects of caffeine supplementation on sprint, 4-min push & cognitive performance in wheelchair


Other relevant publications

Contribution to BASES workshop
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<tr>
<td>A = adrenaline (nmol·L⁻¹)</td>
<td>HR = heart rate (beats·min⁻¹)</td>
</tr>
<tr>
<td>AB = able-bodied</td>
<td>FM = fat mass (kg)</td>
</tr>
<tr>
<td>ACE = arm crank ergometry</td>
<td>LBE = lower-body exercise</td>
</tr>
<tr>
<td>ANOVA = analysis of variance</td>
<td>LBM = lean body mass (kg)</td>
</tr>
<tr>
<td>ANCOVA = analysis of covariance</td>
<td>NA = noradrenaline (nmol·L⁻¹)</td>
</tr>
<tr>
<td>ASIA = American spinal injury association</td>
<td>NS = nutritional supplements</td>
</tr>
<tr>
<td>ATP = adenosine triphosphate</td>
<td>OH = orthostatic hypotension</td>
</tr>
<tr>
<td>AUC = area under the curve</td>
<td>PARA = groups of individuals with paraplegia</td>
</tr>
<tr>
<td>[Bla] = blood lactate concentration (mmol·L⁻¹)</td>
<td>PLA = placebo</td>
</tr>
<tr>
<td>BM = body mass (kg)</td>
<td>PO = power output</td>
</tr>
<tr>
<td>CAF = caffeine supplementation</td>
<td>PUSH = 4 minute maximal push test (m)</td>
</tr>
<tr>
<td>[CAF] = plasma caffeine concentration (µM)</td>
<td>QC = quality controls</td>
</tr>
<tr>
<td>CI = confidence interval</td>
<td>RER = respiratory exchange ratio</td>
</tr>
<tr>
<td>C_max = peak plasma caffeine concentration (µM)</td>
<td>RPE = ratings of perceived exertion</td>
</tr>
<tr>
<td>CNS = central nervous system</td>
<td>RPE_c = central ratings of perceived exertion</td>
</tr>
<tr>
<td>CV = coefficient of variation</td>
<td>RPE_o = overall ratings of perceived exertion</td>
</tr>
<tr>
<td>DXA = dual-energy x-ray absorptiometry</td>
<td>RPE_p = peripheral ratings of perceived exertion</td>
</tr>
<tr>
<td>EE = energy expenditure (kcal·min⁻¹ / kcal·h⁻¹)</td>
<td>SCI = spinal cord injury</td>
</tr>
<tr>
<td>ELISA = Enzyme-linked immunosorbent assay</td>
<td>SD = standard deviation</td>
</tr>
<tr>
<td>ES = effect size</td>
<td>SPR = 20 m sprint (m)</td>
</tr>
<tr>
<td>FFA = Free fatty acids (nmol·L⁻¹)</td>
<td>TETRA = group of individuals with tetraplegia</td>
</tr>
<tr>
<td>FFM = fat-free mass (kg)</td>
<td>TSI = time since injury (y)</td>
</tr>
<tr>
<td>GE = gastric emptying</td>
<td>TT = time trial (min:sec)</td>
</tr>
<tr>
<td>GME = gross mechanical efficiency</td>
<td>UBE = upper-body exercise</td>
</tr>
<tr>
<td>GI = gastrointestinal</td>
<td>VO₂ = oxygen uptake (l·min⁻¹ / ml·kg·min⁻¹)</td>
</tr>
<tr>
<td>[GLU] = blood glucose concentration (mmol·L⁻¹)</td>
<td>VO₂max/peak = maximal/peak oxygen uptake (l·min⁻¹ / ml·kg·min⁻¹)</td>
</tr>
<tr>
<td>HPLC = High performance liquid chromatography</td>
<td>WADA = World Anti-Doping Agency</td>
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General introduction

The use of nutritional supplements (NS) is common among able-bodied (AB) athletes (Braun et al., 2009; Dascombe et al., 2010; Erdman et al., 2006; Heikkinen et al., 2011; Sundgot-Borgen et al., 2003) and there is a large body of evidence which has accumulated over recent years regarding the safety and effectiveness of many (Maughan et al., 2011). Elite athletes with a physical impairment experience the same pressure to succeed and improve their exercise performance as AB athletes. One may therefore predict that NS are also commonplace in the world of Paralympic and disability sport yet there is very little evidence to support this. There are currently 10 eligible impairment types for Paralympic athletes including impaired muscle power/range of movement, limb deficiency, short stature, ataxia, athetosis and visual impairment. Common physical impairments therefore include spinal cord injury (SCI), cerebral palsy, amputation and visual impairment. A SCI has major physiological consequences that can significantly impact upon sporting performance. Hence this area of research has received a great deal of interest in recent years. A SCI can also influence an individual’s nutritional requirements and the potential ergogenic effect of NS, which has received less attention in the literature. Tsitsimpikou et al. (2009) investigated the NS habits of Paralympic athletes (Athens 2004 Paralympic Games) and revealed that vitamins (43.5%), minerals/electrolytes (16.1%) and proteins/amino acids (10.5%) were most commonly consumed. This study was purely descriptive and therefore did not report the athletes’ reasons for NS use or the sources of information they consulted.

There is growing evidence to suggest that certain NS such as caffeine, creatine and buffering agents are effective in the correct exercise setting in an AB population (Close et al., 2016). On the other hand there is limited evidence that the reported ergogenic benefits can be translated to athletes with a physical impairment. Only a handful of studies have investigated
the use of NS in individuals with a physical impairment exploring the effects of caffeine (Flueck et al., 2014; 2015), carbohydrate sports drinks (Spendiff & Campbell, 2005), creatine (Jacobs et al., 2002; Perret et al., 2006) and sodium citrate (Flueck et al., 2014) (Table 2.1). Hence, it remains hard to make evidence-based recommendations for NS use in this population. The sports practitioner must currently rely on interpreting AB findings and athletes will often apply an element of trial and error.

Inaccurate labelling of NS or insufficient knowledge regarding NS dosage may have more serious consequences on the health of individuals with a physical impairment due to unknown effects on their impairment. Furthermore, NS could have the potential to interact negatively with medication use for general health. Some athletes remain uneducated regarding their individual needs and the use of NS to complement their daily diet (Dascombe et al., 2010; Rastmanesh et al., 2007). A lack of evidence and knowledge in physically impaired populations raises concern given the potential for, or more acute sensitivity to side-effects in some sportspeople with a physical impairment (Van de Vliet et al., 2011).

Caffeine is a NS that has received a lot of attention in recent years since its removal from the World Anti-Doping Agency (WADA) prohibited list in 2004. There is evidence for caffeine’s positive impact on endurance exercise, intermittent sports and events involving sustained efforts lasting 1-60 min (for reviews see Burke, 2008; Graham, 2001). The evidence of a positive impact on single short-term events, strength and repeated high intensity efforts is less clear (for reviews see Astorino & Roberson, 2010; Burke, 2008; Keisler & Armsey, 2006). The majority of research in AB individuals has employed whole- or lower-body exercise (LBE) testing protocols such as cycling or running. In contrast, very few have assessed the impact of caffeine on upper-body exercise (UBE) performance and previous findings remain equivocal (Aedma et al., 2013, Black et al., 2015; Stadheim et al., 2013). There are a number of reasons why the results from UBE performance trials following the consumption of caffeine may differ to those from whole- or LBE. The arms possess a smaller active muscle mass and may display a different muscle fibre type distribution (Mizuno et al., 1990; Mygind, 1995). The arms also appear to have a lower capillarisation and oxygen extraction capacity (Calbet et al., 2005; Pendergast, 1989) resulting in the earlier onset of anaerobic metabolism compared to LBE (Pimental et al., 1984).

When discussing the use of caffeine by individuals with a physical impairment during UBE, one must consider the impact of the impairment. The impact of a SCI for example, on caffeine’s ergogenic potential may be related to autonomic dysfunction (Krassioukov, 2009), slowed gastrointestinal (GI) transit times (Fynne et al., 2012; Krogh et al., 2000) and changes
in muscle fibre type distribution (Castro et al., 1999; Schantz et al., 1997). It would therefore be unreasonable to directly translate the results from LBE studies to UBE scenarios and furthermore, AB findings to individuals with a physical impairment such as a SCI.

1.1. Thesis aims and outline

This thesis has two main aims: firstly to understand the habits and perceptions of athletes with a physical impairment towards nutritional supplements (NS), and secondly to provide evidence and practical recommendations for the use of caffeine during UBE, especially by individuals with a SCI.

The main objectives were as follows:

- To determine the NS habits and perceptions of athletes with a physical or visual impairment, and to establish whether caffeine is a popular NS in this population (Chapter three)
- To examine the influence of caffeine on upper-body i) sprint, ii) short-term, high-intensity and iii) endurance performance (Chapters four, five and seven)
- To explore the acute effects of caffeine in individuals with a SCI to help determine the appropriate dose and timing recommendations for its use (Chapter six)

A brief introduction to the chapters contained within this thesis is presented below and the thesis design can be seen in Figure 1.1.

The following chapter (Chapter two) provides an overview of the current evidence relating to the use of NS by AB athletes and athletes with a physical impairment. The chapter also discusses the use of caffeine as a NS, the physiological consequences of a SCI and compares different modes of UBE.

The first experimental chapter (Chapter three) investigates the NS habits and perceptions of athletes with a physical or visual impairment using an online questionnaire and establishes whether caffeine is a popular ergogenic aid in this population. Chapter four assesses the effects of caffeine (4 mg·kg⁻¹) on preloaded 10 km time trial (TT) cycling and handcycling performance in the same AB participants. Chapter five investigates the effects of caffeine (4 mg·kg⁻¹) on wheelchair propulsive exercise performance (4 min maximal push (PUSH) and 20 m sprint (SPR)) and subjective feelings in club level wheelchair sportsmen. Chapter six explores the caffeine absorption curves of AB individuals and individuals with
paraplegia and tetraplegia following the consumption of caffeine (3 mg·kg$^{-1}$) to assess the impact of SCI lesion level. Finally, *Chapter seven* investigates a real world scenario for an elite Paralympic triathlete whereby the effects of three different doses of caffeine (placebo, 2, 4 and 6 mg·kg$^{-1}$) prior to a 20 km handcycling TT are assessed.
Figure 1.1. Schematic of thesis. AB=able-bodied, SCI=spinal cord injury and TT=time trial.
Literature review

2.1. The rise of disability sport

The popularity of disability sport from grassroots up to elite level has been on the rise over recent years. This is evidenced by the increasing number of sports and nations competing at the Games since its first introduction at the Stoke Mandeville Games in 1948. The number of summer Paralympic sports for which medals are awarded has increased from six in 1952 to the 23 in Rio in 2016. The number of winter sports has also increased from two in 1976 to the five which were at the 2014 Sochi Paralympic Games. Since the 1988 Paralympic Games it is notable that the Games have been hosted by the same city, in the same year and at the same venues as the Olympic competitions and hence a similar level of professionalism is expected.

To match the rise of professionalism in disability and Paralympic sport, many Paralympians now train and access sport science and medicine services in the same manner as their AB and Olympic counterparts. This newfound professionalism and desire for optimising performance has seen an upsurge in research examining the physiological and biomechanical aspects of Paralympic sports that involve athletes with an impairment. However, given the heterogeneity of athletes’ impairments, impairment-specific information and research within sports nutrition is unknown. For this reason, disability sport practitioners often look to adapt findings from the AB literature to apply to their athletes, which is far from ideal when the majority of practitioners aim to deliver evidence-based practice.

2.2. Nutritional supplements

2.2.1. Dietary practices of individuals with a physical impairment

The evaluation of nutritional intakes and requirements of healthy AB athletes are well versed in the scientific literature. The 2009 American College of Sports Medicine position stand on ‘Nutrition and Athletic Performance’ highlighted topics such as nutrient intake
recommendations, hydration and NS but impairment-specific guidelines are notable for their absence (Rodriguez et al., 2009). Numerous studies have documented the nutritional knowledge and practices of AB athletes (Dunn et al., 2007; Economos et al., 1993; Zawila et al., 2003). However, few have focused on athletes with a physical impairment reporting inadequate nutritional knowledge (Rastmanesh et al., 2007) and varying degrees of micronutrient adequacy (Goosey-Tolfrey & Crosland, 2010; Grams et al., 2016). The nature of a physical impairment may result in the individual having to face any number of practical issues regarding their dietary habits such as the sourcing and preparation of fresh meals due to accessibility, dexterity or visual impairment. The use of some macronutrient providing NS may therefore be increased to help meet nutritional needs due to their convenience. Moreover, the specific needs of different impairments could result in a greater prevalence of supplement use in this population such as the use of meal replacement or protein drinks in those with severe cerebral palsy to help prevent the risk of malnutrition (Dahl et al., 1996). Athletes’ perceptions regarding their use of NS may therefore differ from those of the AB athlete population, viewing them as essential for health and maintenance of their daily diet, rather than optional. Hence, there is a need for a greater understanding of the dietary practices of athletes with a physical impairment to provide evidence-based nutritional recommendations based on their impairment and exercise modality.

It is widely accepted that diet can significantly influence both health and sporting performance and that many athletes adopt individualised nutrition strategies. However, even in the most popular AB sports such as football, some athletes have poor nutritional knowledge and do not meet the training and/or daily nutrition and hydration recommendations for their sport (Ruiz et al., 2005; Shirreffs et al., 2005). For example, Ruiz et al. (2005) reported lower than recommended carbohydrate intakes in adult club footballers and Shirreffs et al. (2005) highlighted inadequate rehydration strategies in elite professional footballers. An athlete’s nutritional needs are largely determined by daily energy expenditure (EE) (Rodriguez et al., 2009), which is influenced by two main factors; i) training load (intensity × frequency × duration of training sessions), and ii) body mass (Maughan & Burke, 2002). These two factors will be considered in relation to athletes with a physical impairment in the following paragraphs.

Athletes with a physical impairment often undertake similar training schedules to their AB counterparts, especially at an elite level, (Krempien & Barr, 2011) and should therefore also adopt specific nutritional strategies for their sport. It is often assumed that the EE of disability sports is lower than AB versions. Research to determine the energy demand
of such sports is scarce (for review see Price, 2010) yet necessary to help practitioners calculate athletes’ nutritional requirements. For select sports and impairment categories, the EE of training may not greatly differ (e.g. a visually impaired cyclist who trains with an AB guide). On the other hand, modes of exercise involving the upper-limbs result in much lower absolute EE than LBE. For example, the EE during wheelchair treadmill exercise was 43 and 62.5% in individuals with tetraplegic and paraplegia compared to that of AB runners during a 5 km TT (Lakomy et al., 1987; Ramsbottom et al., 1987). Abel et al. (2008) investigated the demands of the wheelchair court sports in training. The average exercise EE of the wheelchair athletes studied was 313.6(101.1) kcal·h⁻¹ but the values from wheelchair rugby (249(70) kcal·h⁻¹) were significantly lower than basketball and tennis (Abel et al., 2008). Data from AB rugby league match-play estimates EEs of ~876 kcal·h⁻¹ (Cummins et al., 2016), more than three times the wheelchair rugby training values. There remains limited EE data for the majority of disability sports and the aforementioned research shows that AB data is not transferable even when there appears to be a similar sport. The availability of this type of data would help to determine daily energy intake needs and which (if any) NS would aid performance in such sports.

An athlete with a physical impairment may need to adapt their diet to suit a reduced active muscle mass due to their impairment. For example, an individual with a SCI who has full use of their trunk may use only 60-70% of their muscle mass during wheelchair propulsion (Goosey-Tolfrey & Crosland, 2010). This smaller active muscle mass will reduce the individual’s energy requirements and hence they will often reduce the total volume of food they consume to help prevent a concomitant increase in body mass. This reduced energy intake may result in an athlete not meeting nutritional recommendations, which may not be optimal for sporting performance (Goosey-Tolfrey & Crosland, 2010). This can also result in individuals not meeting their perceived macro- and micronutrient recommendations (Gomes et al., 2006; Krempien & Barr, 2011; Perret & Stoffel-Kurt, 2011) and could cause the use of NS to meet these needs. For example, despite the importance of the micronutrients involved in bone health such as calcium, vitamin D and magnesium, wheelchair basketball athletes reported inadequate intakes (Grams et al., 2016). The authors recommended a calcium supplement could be used to reach the recommended intakes if they could not be achieved through dietary intake alone (Grams et al., 2016). Importantly, there are no specific guidelines for individuals with physical impairments and hence the macro- and micronutrient recommendations are currently based on AB data, which may not be appropriate.
2.2.2. Safety of nutritional supplements

Some athletes with a physical impairment may use NS to help them consume a healthy, well-balanced diet that meets the demands of their training schedule. Furthermore, the practical implications that occur due to visual impairment or cerebral palsy for example, can make it difficult to prepare fresh nutritious meals which may result in some individuals using convenient NS to meet their requirements. Consequently, athletes who regularly use or are prescribed supplements such as iron, calcium or protein/meal replacement shakes for their health may be more inclined to consume performance-enhancing supplements because it is the ‘norm’. Athletes with a physical impairment may, therefore be unwittingly engaging in behaviours that may have unknown health, performance and potential doping consequences. Athletes with a physical impairment experience the same pressure to succeed and improve their exercise performance as AB athletes. Doping in sport is forbidden by the Olympic and Paralympic movement, an environment in which being on the podium is the ultimate achievement. No matter what the motivation, athletes must remember that they are subject to drug testing and therefore must consider the pros and cons prior to using NS given the small yet real risk of an inadvertent positive doping test (Baylis et al., 2001). Inaccurate labelling has also been found to be a problem in that some NS have been shown not to contain the labelled amount or type of active ingredient, or they contain an unlabelled substance (Geyer et al., 2004; Kohler et al., 2010). This issue is prevalent due to a lack of regulatory laws regarding NS in some countries and the widespread purchase of NS over the internet. Consuming NS containing an incorrectly labelled ingredient may have more serious consequences on the health of an individual with a physical impairment as it may have an unknown effect on their impairment or it may interact with medication use.

The International Olympic Committee discouraged the use of dietary supplements by athletes in its 2010 consensus statement, whilst encouraging them to meet their nutrient requirements from food. They do however recognise that NS such as carbohydrate-electrolyte sports drinks, bars and gels, and a few ergogenic aids such as creatine, caffeine and buffering agents may be of benefit to some individuals. Given the minimal amount of information regarding NS habits and perceptions in elite sportmen and women with physical impairments, it is hard to currently deliver the same message to this population. It is thus essential that current NS habits and perceptions of athletes with a physical impairment are considered prior to the delivery of any such message.

The number of NS available on the market continues to increase and yet many of these proposed ergogenic aids are unsupported by scientific evidence (Abel et al., 2005;
Jeukendrup & Randell, 2011). For example, fat burning NS continue to be popular and yet many lack the evidence to support any form of fat metabolism-enhancing properties (Jeukendrup & Randell, 2011). New supplements are also being used prior to a body of evidence regarding their effectiveness and long-term effects. Using creatine as an example, research in AB individuals shows an ergogenic effect during maximal power/strength, single-effort and repetitive sprint performance, whilst also acting as a training tool to help increase strength, FFM and improve performance during high-intensity protocols (Kreider, 2003; Volek et al., 1999). On the other hand, the evidence is currently equivocal (and under-researched) in athletes with a physical impairment (Jacobs et al., 2002; Perret et al., 2006). Both studies provided 20 g creatine monohydrate for 6-7 d with a 21 d washout period however, the performance tests differed; an peak arm ergometry test (Jacobs et al., 2002) and an 800 m wheelchair test on a training roller (Perret et al., 2006). Jacobs et al. (2002) reported improved peak PO and time to fatigue in individuals with tetraplegia whereas Perret et al. (2006) reported no change in performance in individuals with paraplegia and spina bifida. Despite a lack of evidence, creatine was reportedly used by more Paralympic than Olympic athletes (9.1% vs. 5.1%) during the Athens 2004 games (Tsitsimpikou et al., 2009). There is no evidence regarding the dosage recommendations for supplements such as creatine for individuals with a reduced active muscle mass such as individuals with a SCI, who may be inadvertently consuming more than they require when following AB guidelines. Even in AB athletes, supplements may cause detrimental effects when taken in large doses for prolonged periods (Maughan, 2005).

There is currently insufficient scientific evidence regarding the effects of NS in a population of athletes with a physical impairment and the potential for unknown side-effects or more acute sensitivity to side-effects may exist (Van de Vliet et al., 2011). Some athletes remain uneducated regarding their individual needs and the use of NS to complement their daily diet and could, especially in a population of athletes with a physical impairment, therefore be threatening their health (Dascombe et al., 2010; Rastmanesh et al., 2007).

2.2.3. Athletes’ sources of information

Research from AB populations shows there is a need for athlete education regarding nutrition and NS (Dunn et al., 2007; Economos et al., 1993; Jacobson et al., 2001). Many individuals who consume NS on a regular basis are unaware of the proposed physiological mechanisms or the possible side-effects (Dascombe et al., 2010). Athlete populations also show a lack of understanding regarding NS and their associated effects (Petróczi et al., 2008).
Hence athletes may be using NS without initially assessing the need for them or the associated risks.

From an AB perspective, Froiland et al. (2004) reported that the three most common sources of information used by varsity athletes were family, other athletes and their athletic trainer. These were closely followed by their coach, strength coach, friends and a registered dietitian (Froiland et al., 2004). The use of these sources, except the registered dietitian, is a concern given the lack of professional knowledge likely in these individuals. Others have reported coaches and athletic trainers to be influential when deciding whether to use a NS (Jacobson et al., 2001; Juhn et al., 1999). However, working in the field of sport does not guarantee sufficient knowledge and understanding of NS. Considering the individual nutritional needs of athletes with a physical impairment there may be a heightened requirement for education in this population and it is imperative that athletes understand which sources of information are most knowledgeable and reliable e.g. registered nutritionists/dietitians.

It has been shown that education can change attitudes and behaviours (Rastmanesh et al., 2007). For example, Rastmanesh et al. (2007) provided nutritional education (a booklet and four 3 h courses) to a group of athletes with a SCI or amputation. Following the education, 50% of the athletes reported that they would prefer to receive their nutritional information from a dietitian, compared to only 14% prior to the education. An understanding of current sources of NS information for athletes with a physical impairment will help ensure educational practice is conducted at the correct level and therefore aid its effectiveness upon implementation.

2.2.4. Nutritional supplement use by athletes with a physical impairment

The majority of research suggests that the consumption of NS is common among AB athletes (51-88%) (Braun et al., 2009; Dascombe et al., 2010; Erdman et al., 2006; Sundgot-Borgen et al., 2003) and there is a large body of evidence regarding their efficacy. On the other hand, there is a dearth of evidence regarding the use of NS by athletes with an impairment and further investigation is warranted.

To the author’s knowledge the only study to determine food supplement use in Paralympic athletes was performed at the Athens 2004 Paralympic Games (Tsitsimpikou et al., 2009). The study revealed that food supplements made up 42.1% of the reported preparations. Interestingly, compared to their Olympic counterparts, fewer Paralympic athletes reported the use of food supplements and medications but they did display a similar
consumption pattern. Tsitsimpikou et al. (2009) revealed that vitamins (43.5%), minerals/electrolytes (16.1%) and proteins/amino acids (10.5%) were the most commonly consumed NS. Tsitsimpikou and colleagues (2009) provided important evidence that NS use is common among Paralympic athletes (27%) however; the data was purely descriptive and did not explore athlete’s habits or perceptions of NS and/or attitudes towards (anti-)doping.

As stated earlier, many practitioners will utilise AB findings to make recommendations on NS use. Given the reliance on UBE within many disability and Paralympic sports it is important to assess this information with caution. Research on the impact of NS on (non-strength) UBE performance in individuals with a physical impairment is scarce and the evidence is currently equivocal. Studies include the exploration of caffeine (Flueck et al., 2015; 2014; see Table 2.4), carbohydrate (Spendiff & Campbell, 2002), creatine (Jacobs et al., 2002; Perret et al., 2006) and sodium citrate (Flueck et al., 2014) as ergogenic aids during short-term, high-intensity or endurance UBE protocols (Table 2.1). The former two caffeine studies resulted in no significant change in performance but individual responses were apparent (Table 2.4). Hence, further investigation is required.
Table 2.1. Studies investigating the use of nutritional supplementation (excluding caffeine) related to short-term high-intensity and endurance upper-body exercise performance in individuals with a physical impairment.

<table>
<thead>
<tr>
<th>Publication</th>
<th>Participants</th>
<th>Supplementation</th>
<th>Exercise performance protocol</th>
<th>Enhanced performance</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carbohydrate supplementation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spendiff &amp; Campbell, (2005)</td>
<td>Participants with paraplegia (T5-T12) &amp; spina bifida (8 males)</td>
<td>4% (‘low’) or 11% (‘high’) carbohydrate drink 20 min prior to exercise</td>
<td>1 h at 65% VO₂peak &amp; 20 min performance test on a wheelchair ergometer</td>
<td>Perhaps – tendency (p = 0.08) for greater performance distance &amp; PO following ‘high’ compared to ‘low’</td>
<td>Tendency for greater [GLU], RER &amp; PO, &amp; lower FFA concentrations following ‘high’</td>
</tr>
<tr>
<td><strong>Creatine monohydrate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jacobs et al. (2002) (abstract only)</td>
<td>Participants with cervical level SCI (C5-C7) (16 males)</td>
<td>20 g·d⁻¹ creatine monohydrate / PLA for 7 d (21 d washout)</td>
<td>Incremental peak arm ergometry test</td>
<td>Yes - Improved peak PO &amp; time to fatigue</td>
<td></td>
</tr>
<tr>
<td>Perret et al. (2006)</td>
<td>Competitive wheelchair athletes with paraplegia, spina bifida or hemiparesis (4 male &amp; 2 female)</td>
<td>4 x 5 g creatine monohydrate / PLA for 6 d (21 d washout)</td>
<td>All-out 800 m wheelchair test on a training roller</td>
<td>No</td>
<td>No difference in BM, RPE, peak/mean HR, maximum velocity or [Bla]</td>
</tr>
<tr>
<td><strong>Sodium citrate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flueck et al. (2014)</td>
<td>Elite wheelchair racing athletes with paraplegia &amp; spina bifida (category T53/54) (9 males)</td>
<td>0.5 g·kg⁻¹ sodium citrate / PLA in 700 ml water 120 min prior to exercise</td>
<td>1500 m wheelchair racing TT</td>
<td>No</td>
<td>5/9 participants suffered GI distress Tendency for higher [Bla]</td>
</tr>
</tbody>
</table>

Note: [Bla]=blood lactate concentration, BM=body mass, C=cervical, FFA=free fatty acids, GI=gastrointestinal, GLU=glucose, PLA=placebo, PO=power output, RER=respiratory exchange ratio, RPE=ratings of perceived exertion, SCI=spinal cord injury, T=thoracic and TT=time trial.
2.3. Caffeine

2.3.1. What is caffeine?

Caffeine is a member of a group of stimulants called methylxanthines, or xanthines, and occurs naturally in some plants. Caffeine’s chemical name is 1,3,7-trimethylxanthine and its chemical structure can be seen in Figure 2.1. Caffeine is classed as a pharmaceutical compound or drug, rather than a nutrient, and is used in many commonly consumed foods and drinks. Caffeine is a naturally occurring plant alkaloid that is found in tea leaves, coffee beans, cocoa beans, guarana and kola nuts, and is often artificially added to over the counter products (e.g. weight loss products and cold preparations) and beverages (e.g. energy or sports products). The caffeine content of different types and brands of these foods and drinks (Table 2.2) vary greatly and can also depend on how they are prepared e.g. percolated contains more than instant coffee. Food and drink manufacturers are not legally required to list caffeine as an ingredient on their product label if it occurs naturally due to a plant source. However, it must be listed if it is an added ingredient in products such as sports drinks, gels, capsules and powders. This enables athletes to calculate caffeine dose more easily.

![Chemical structure of caffeine](image)

**Figure 2.1.** Chemical structure of caffeine
Table 2.2. Caffeine content of common foods, drinks and nutritional supplements. (Table adapted from Burke, 2008).

<table>
<thead>
<tr>
<th>Food or drink</th>
<th>Serving</th>
<th>Caffeine (mg)*</th>
<th>Range (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instant coffee</td>
<td>250 ml (8 oz)</td>
<td>60</td>
<td>(12-169)</td>
</tr>
<tr>
<td>Brewed coffee</td>
<td>250 ml (8 oz)</td>
<td>80</td>
<td>(40-110)</td>
</tr>
<tr>
<td>Short black or espresso coffee</td>
<td>1 standard serving</td>
<td>107</td>
<td>(25-214)</td>
</tr>
<tr>
<td>Tea</td>
<td>250 ml (8 oz)</td>
<td>27</td>
<td>(9-51)</td>
</tr>
<tr>
<td>Hot chocolate</td>
<td>250 ml (8 oz)</td>
<td>5-10</td>
<td></td>
</tr>
<tr>
<td>Milk chocolate</td>
<td>60 g</td>
<td>5-15</td>
<td></td>
</tr>
<tr>
<td>Coca-cola</td>
<td>375 ml (12 oz)</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>Red Bull energy drink</td>
<td>250 ml (8 oz)</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>Powerbar caffeinated sports gel</td>
<td>40 g sachet</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Spike Shotgun energy drink</td>
<td>500 ml (16 oz)</td>
<td>350</td>
<td></td>
</tr>
<tr>
<td>Stay Alert Caffeine supplement chewing gum</td>
<td>1 piece</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>ProPlus tablets</td>
<td>1 tablet</td>
<td>50</td>
<td></td>
</tr>
</tbody>
</table>

*These values were gathered from a variety of sources, including manufacturers’ information and nutrition databases (Centre for Science in the Public Interest (available at [http://www.cspinet.org/new/cafchart.htm](http://www.cspinet.org/new/cafchart.htm)), and USDA National Nutrient Database (available at [http://www.nal.usda.gov/fnic/foodcomp/search/](http://www.nal.usda.gov/fnic/foodcomp/search/)). Note that commercial brands may vary slightly from country to country.
Caffeine is one of the most widely used drugs in the world and it has received recent attention as an ergogenic aid in sport since its removal from the WADA prohibited list in 2004 (Del Coso et al., 2011). Caffeine has appeared on the WADA prohibited list intermittently for approximately 40 years; a common sign that it has been shown to have a positive effect on sporting performance. When banned, the urinary cut-off of 12-15 μg·mL\(^{-1}\) did not allow distinction between social and performance-related consumption. Concerns regarding the abuse of caffeine as a performance aid mean that the substance remains on the WADA monitoring programme. These concerns may be unfounded given that the prevalence of caffeine consumption was similar during both the period it was banned and during the four years after it was removed from the prohibited list (2004-2008) (Del Coso et al., 2011).

Caffeine is absorbed quickly in the GI tract and stomach (absorption reaches 99% in the GI tract) in both humans and animals, and it moves easily across cellular membranes including the blood-brain barrier due to its hydro- and lipophilic properties (Fredholm et al., 1999). It can therefore potentially interact with every tissue in the body either via receptors or direct entry into cells, including all organs. The presence of food in the stomach slows the absorption of methyxanthines such as caffeine (McKim, 1996). Caffeine concentrations can be measured in urine, serum and saliva, and good correlations (r=0.93-0.98) have been reported between these methods in AB individuals (Birkett & Miners, 1991; Zylber-Katz et al., 1984). Salivary caffeine concentrations are ~80% of those measured in plasma (Zylber-Katz et al., 1984).

Caffeine is slowly metabolised by the liver and has a half-life of ~5-6 h (Smith, 2002). Caffeine is distributed via the bloodstream with 10-30% being transported by proteins (McKim, 1996). Typical blood concentrations are elevated within 15-45 min and peak 45-60 min post-ingestion in AB individuals (Goldstein et al., 2010b; Smith, 2002). Blanchard and Sawers (1983) reported rapid absorption of 5 mg·kg\(^{-1}\) caffeine in an oral solution in healthy adult males whereby the time to reach a peak plasma concentration (C\(_{\text{max}}\)) was 30(8) min and a C\(_{\text{max}}\) of 51(6) μM. There is no long-term accumulation of caffeine or its metabolites in the body.

Caffeine is metabolised primarily by the cytochrome P450 enzyme system and is converted via demethylation reactions to three main dimethylxanthines (paraxanthine (~80%), theobromine (~11%) and theophylline (~5%)), which accounts for ~95% of metabolism. A small amount is excreted without being metabolized (Arnaud, 2011). The cytochrome 1A2 (CYP1A2) gene carries the instructions for building the cytochrome P450 enzyme and humans can express two variants. Individuals who are homozygous for the A variant are
rapid caffeine metabolisers, and individuals that possess the C allele (heterozygous) are slow metabolisers (McKim, 1996). Hence, individuals that metabolise caffeine slower may be more susceptible to adverse effects such as nervousness, jitters, restlessness, sleeplessness and irritability which may also negatively impact on sports performance. The increased potential for adverse effects may help explain why 16 out of 19 participants with the C allele were voluntarily low caffeine users (Womack et al., 2012). Greater improvements in 40 km TT performance have been reported in individuals who possess the homozygous A allele compared to the C allele (4.9 vs. 1.8%, respectively) (Womack et al., 2012). The authors suggest this difference may be related to the earlier presence of caffeine’s metabolites, theophylline and paraxanthine that have higher binding affinities to adenosine receptors than caffeine and may therefore be more potent (Fredholm et al., 1999; Womack et al., 2012). This specific polymorphism may help to explain some of the large inter-individual variability in responses to caffeine ingestion that have been reported. Of these studies, Astorino et al. (2008) reported improvements in one repetition maximum bench press in 12 resistance trained participants following the ingestion of 6 mg·kg\(^{-1}\) caffeine; while five improved following placebo and five performed the same following both treatments (n=22). Flueck et al. (2014) also reported faster 1500 m wheelchair race times in four out of nine participants following 6 mg·kg\(^{-1}\) caffeine, while two were fastest following placebo and two were faster following an alternative NS.

A number of other factors may influence the pharmacokinetics of caffeine including the presence of food and fluid in the stomach (Brachtel & Richter, 1988), genetics (McKim, 1996), the use of oral contraceptives (Abernethy & Todd, 1985), diet and lifestyle, dosage and sleep deprivation (Kamimori et al., 1995). Obesity has been shown to prolong the elimination half-life of some drugs and therefore an individual’s body composition may also be another influencing factor (Kamimori et al., 1987). An increase in apparent volume of distribution (caffeine clearance divided by elimination rate constant) resulted in a trend towards a prolonged elimination half-life of caffeine in obese individuals (Abernethy et al., 1985). Skinner et al. (2014) also suggested that individual rates of caffeine metabolism may be linked to body composition and training status. The pharmacokinetics of caffeine differs between species of animal and so the extrapolation of animal data to humans must be done with care (Arnaud et al., 2011).
2.3.2. Mechanisms of action

Caffeine appears to have a variety of effects on the human body including as a smooth muscle relaxant, and as a stimulant for cardiac muscle and the central nervous system (CNS). Numerous mechanisms have been proposed to explain the beneficial effects of caffeine on exercise performance. The traditional theory was that caffeine increased the circulating levels of adrenaline, which subsequently stimulated an increase in lipolysis and fat metabolism, and therefore spared muscle glycogen stores (Graham, 2001). It was proposed that the increased availability of FFA (Graham et al., 2000; Van Soeren et al., 1996) led to a change in substrate utilisation following caffeine ingestion and was therefore thought to contribute to improved exercise capacity (Graham, 2001). However, Laurent et al. (2000) opposed this notion by reporting that 6 mg·kg$^{-1}$ caffeine ingested 90 min prior to 2 h cycling at 65% $\text{VO}_2\text{peak}$ did not result in a muscle glycogen sparing effect in athletes with high muscle glycogen content despite increases in both adrenaline and FFA concentrations. Hence, the proposed traditional theory regarding changes in substrate utilisation during endurance exercise is unlikely to be the sole reason for caffeine’s ergogenic nature. Other studies have also revealed that caffeine can be advantageous during exercise protocols in which muscle glycogen stores are not compromised (Beck et al., 2006 (one repetition maximum bench press); Bruce et al., 2000 (2000 m rowing performance); Collomp et al., 1992 (100 m swimming performance)).

Further, despite individuals having an impaired catecholamine response (due to tetraplegia, see section 2.4.1), an increase in plasma FFA concentration and improvements in electrical cycling time to exhaustion have been observed following caffeine ingestion (Mohr et al., 1998). Mohr and colleagues (1998) therefore provided support for the theory that caffeine may have a direct effect on adipocytes and various other tissues independent of the brain and circulating catecholamine concentrations (Mohr et al., 1998; Van Soeren et al., 1996).

Caffeine’s influence on the CNS via adenosine receptor antagonism has been shown to influence mental and physical performance, improving attributes such as alertness, reaction time (Rogers et al., 2013) and exercise capacity (Van Soeren & Graham, 1998). Adenosine is a by-product of adenosine triphosphate (ATP) metabolism and hence concentrations rise when there is activity resulting in ATP metabolism e.g. exercise. Adenosine acts to reduce arousal, wakefulness and motor activity (Fredholm et al., 1999). It is also a potent vasodilator, and inhibits catecholamine release and lipolysis (Keisler & Armsey, 2006). The caffeine molecule (Figure 2.1) has a similar structure to adenosine and therefore acts as a
potent non-selective adenosine receptor antagonist, thereby reducing the inhibitory effect of adenosine on the body (Fredholm et al., 1999; Watson, 2008).

There are four subtypes of adenosine receptor: A₁, A₂A, A₂B and A₃, and these can be found on cell surfaces throughout the human body. Importantly, caffeine, at plasma concentrations reached through dietary intake, acts mainly on adenosine A₁ and A₂A receptors which are found largely in the brain (McKim, 1996). Adenosine inhibits excitatory neurotransmitter release and hence antagonism may affect circulating levels of neurotransmitters such as dopamine (Davis et al., 2003). Therefore, the blockade of adenosine receptors, especially those in the brain can help delay fatigue (Goldstein et al., 2010b).

Caffeine has also been shown to lower the perception of effort experienced by an individual during exercise (Doherty & Smith, 2005). The reduction in pain perception may also be due to the analgesic effects of increased plasma endorphin concentrations. It has been suggested that caffeine may lower the threshold for exercise-induced β-endorphin release, which can consequently reduce pain perception (Laurent et al., 2000). Caffeine consumption has been shown to reduce leg muscle pain during cycling exercise but more so at a submaximal, fixed intensity than during maximal exercise (Black et al., 2015; Motl et al., 2006; O’Connor et al., 2004).

It is likely that a combination of mechanisms is responsible for any improvements in performance and is likely to vary depending on the exercise protocol, caffeine dosage and the participants’ characteristics. Adenosine receptor antagonism appears to be the main mechanism via which caffeine improves performance at physiological concentrations. However, evidence does suggest that under certain conditions other biochemical mechanisms may be active but many have only been explored in vitro (Magkos & Kavouras, 2005). Other proposed mechanisms of action include the inhibition of phosphodiesterase enzymes, increased calcium mobilisation and stimulation of the sodium/potassium pump (Magkos & Kavouras, 2005). Caffeine’s ability to increase the release of calcium from the sarcoplasmic reticulum and therefore influence excitation-contraction coupling only occurs at supraphysiological caffeine concentrations (minimum of 1-2 mM) (Luttgau & Oetliker, 1968). Hence, this is not a mechanism considered to improve exercise performance in humans however it cannot be discounted that some potentiation may occur via other pathways that increase the sensitivity of the calcium release system to caffeine (Mohr et al., 1998; Magkos & Kavouras, 2005). The inhibition of phosphodiesterase enzyme activity following caffeine administration leads to accumulation of cyclic adenosine monophosphate (cAMP), which is
involved in hormone regulation and importantly, increase adipose tissue lipolysis (Magkos & Kavouras, 2005). Once more, [CAF] needs to be greater than those reported with dietary intake or supplementation to induce this mechanism (0.1-6.0 mM) (Magkos & Kavouras, 2005). Caffeine has also been shown to stimulate the sodium/potassium pump and ATPase activity by preventing the rise in potassium in the extracellular fluid and thereby maintaining an electrochemical gradient for optimal muscle contraction (Bittar et al., 1974). Once again this mechanism has only been reported at supra-physiological concentrations (>100 µM) (Bittar et al., 1974).

2.3.3. Caffeine: side-effects, tolerance and withdrawal.

Caffeine is generally well-tolerated in humans in doses up to 400 mg·d⁻¹ with no adverse effects (Riddell et al., 2012). In those that are susceptible however, caffeine can cause adverse effects such as sleeplessness/disturbed sleep, trembling and increased anxiety. Caffeine also inconsistently causes other physiological effects such as an increased HR and breathing rate, and should therefore be avoided by pregnant or nursing women, babies and children, or those that are sensitive to the drug.

Individuals can develop a tolerance and dependency for caffeine, which appears to be related to the up-regulation of adenosine activity and a decrease in adrenergic activity (Latini & Pedata, 2001) making withdrawal from the drug difficult. The removal of caffeine from the diet can cause withdrawal symptoms such as headache, irritability, lethargy and depressed mood (Riddell et al., 2012). Withdrawal has also been associated with sleepiness, lower mental alertness and can cause slower reaction times (Rogers et al., 2013). Upon a re-dose of caffeine, withdrawal symptoms are quickly reversed. Despite the occurrence of these symptoms, Van Soeren and Graham, (1998) published results that showed no effect of short-term withdrawal from caffeine on endurance during high-intensity exercise, compared to no withdrawal. Despite this, it is common to ask research study participants to withdraw from the consumption of caffeine in the 24-48 h prior to trials to ensure all participants have a similar baseline and for their safety, to ensure no participant consumes dangerously high doses.

Caffeine can also act as a mild diuretic when consumed in high doses because it stimulates renal glomerular filtration and inhibits the reabsorption of sodium, which results in increased sodium and water excretion (Arnaud 1999). However, normal daily intakes of <240 mg of caffeine, equivalent to approximately three cups of brewed coffee (Table 2.2), are unlikely to cause a significantly greater diuresis than a control fluid containing no caffeine.
such as water (Armstrong et al., 2007). Any influence of mild diuresis would be minimal and there does not appear to be any basis for the common concern that caffeine will cause hypohydration (Graham, 2001).

2.3.4. Caffeine and exercise performance

2.3.4.1 Caffeine use during whole/lower-body exercise

A substantial amount of evidence has accumulated on the effects of moderate doses (3-6 mg∙kg⁻¹) of caffeine on both physiological and psychological performance in AB individuals during lower-body exercise modes such as running and cycling (see reviews Ganio et al., 2009; Graham, 2001; Keisler & Armsey, 2006; McLellan et al., 2016; Tarnopolsky, 1994). McLellan et al. (2016) suggested that 78%, 66% and 69% of the studies reviewed reported ergogenic effects of caffeine during endurance, high-intensity and muscular strength/endurance exercise protocols, respectively. Ganio et al. (2009) concluded that caffeine ingestion improved endurance TT (>5 min) performance by 3.2(4.3)% but this improvement was highly variable (-0.3-17.3%). Variability is likely dependent on a number of factors such as differences in timing and dosage of caffeine, route of delivery and participant characteristics.

Small-moderate doses of caffeine (≤6 mg∙kg⁻¹) have been shown to improve mental attributes such as reaction time, alertness and attention (Rogers et al., 2013; Smith et al., 1999). Caffeine has been shown to be ergogenic during endurance exercise lasting ~60 min (Kovacs et al., 1998 (3-4 mg∙kg⁻¹); McNaughton et al., 2008 (6 mg∙kg⁻¹); Skinner et al., 2013 (6 mg∙kg⁻¹)). Both McNaughton et al. (2008) and Kovacs et al. (1998) reported improvements in performance during a 1 h cycling performance trial following caffeine ingestion. Skinner et al. (2013) was also able to report a 2% improvement in a more ecologically valid 40 km TT lasting ~1 h. Exercise protocols lasting longer than 60 min have also shown improvements in performance following caffeine (Cureton et al., 2007 (5.3 mg∙kg⁻¹); Cox et al., (2002) (6 mg∙kg⁻¹)). Both Cureton et al. (2007) and Cox et al. (2002) reported improved TT performance following a 120 min preload at 60-75% ·VO₂ peak in addition to the improvements seen following carbohydrate ingestion.

Caffeine may also be effective in exercise scenarios lasting less than 30 min where muscle glycogen depletion is unlikely to be the cause of fatigue (Jenkins et al., 2008; Bruce et al., 2000). Bruce et al., (2000) reported reduced times to complete a 2000 m rowing TT following moderate to large doses of caffeine (6 and 9 mg∙kg⁻¹) whereas Jenkins et al., (2008)
described improvements in 15 min cycling TT performance following much lower and more practical doses (2-3 mg·kg\(^{-1}\)). Caffeine may therefore be useful during a variety of sports/events including endurance events, intermittent team sports and events involving high-intensity activity lasting less than 60 min. However, the evidence for an ergogenic effect of caffeine during single events that require strength and power remains inconclusive (Keisler & Armsey, 2006). Caffeine supplementation has been shown to improve sport performance but the magnitude of the effect is dependent on various factors such as an athlete’s training status, and the intensity, duration and mode of exercise (McLellan et al., 2016). Caffeine appears to be effective in an AB population at doses between 3 and 6 mg·kg\(^{-1}\) without any adverse effects. Caffeine does not appear to respond in a dose dependent manner, with higher doses not producing any further performance enhancement (Goldstein et al., 2010b) but may increase the likelihood of adverse effects (Burke, 2008; Graham & Spriet, 1991).

2.3.4.2 Caffeine use during upper-body exercise and by individuals with a physical impairment

There is a lack of evidence regarding the effects of caffeine on UBE performance, which is highlighted by the number of publications compared to whole/LBE in Table 2.3. There are even fewer studies investigating the effects of caffeine in individuals with a physical impairment/disability (Table 2.3). However, based on the mechanisms discussed in section 2.3.2 caffeine could theoretically be advantageous for those competing in disability sports requiring endurance or short-term, high-intensity exercise performance such as athletics, football, wheelchair sports, triathlon and cycling. The ergogenic benefit of a supplement such as caffeine can be influenced by a number of factors including individual variation and training status, which are two key differences between AB athletes and athletes with a physical impairment. For example, no individual with a SCI will display the exact same physical and neurological issues and hence each athlete needs to be considered as an individual. Furthermore, any athlete who uses a wheelchair for daily ambulation will display vastly different training loads and EEs compared to an AB individual. Individuals with neurological impairments such as CP or SCI must also consider the effects of caffeine on the occurrence of palpitations and tremor (Astrup et al., 1990; Shirlow & Mathers, 1985), and the possible effects it may have on spasticity (anecdotal evidence from athletes). This highlights the importance of considering the dose when using caffeine in an athletic population with physical impairments.
Table 2.3. Number of publications on caffeine and lower/whole-body exercise compared to upper-body exercise.

<table>
<thead>
<tr>
<th>Pubmed search terms</th>
<th>Number of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lower/whole-body exercise studies</strong></td>
<td></td>
</tr>
<tr>
<td>Caffeine and exercise performance</td>
<td>494</td>
</tr>
<tr>
<td>Caffeine and running</td>
<td>159</td>
</tr>
<tr>
<td>Caffeine and running performance</td>
<td>99</td>
</tr>
<tr>
<td>Caffeine and cycling</td>
<td>254</td>
</tr>
<tr>
<td>Caffeine and cycling performance</td>
<td>115</td>
</tr>
<tr>
<td><strong>Upper-body exercise studies</strong></td>
<td></td>
</tr>
<tr>
<td>Caffeine and UBE</td>
<td>19</td>
</tr>
<tr>
<td>Caffeine and wheelchair/wheelchair</td>
<td>2</td>
</tr>
<tr>
<td>Caffeine and arm crank</td>
<td>2</td>
</tr>
<tr>
<td>Caffeine and handcycling/handbiking</td>
<td>0</td>
</tr>
<tr>
<td>Caffeine and disability sport</td>
<td>3</td>
</tr>
</tbody>
</table>

*Note: Searches performed on 05.08.16 and excluded any publications from this thesis.*
Table 2.4. Studies of caffeine supplementation related to upper-body strength, short-term high-intensity and endurance exercise performance.

<table>
<thead>
<tr>
<th>Publication</th>
<th>Participants</th>
<th>Caffeine protocol</th>
<th>Exercise performance protocol</th>
<th>Enhanced performance</th>
<th>Blood lactate concentration (mmol·L⁻¹)</th>
<th>Ratings of Perceived Exertion (RPE)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strength exercise performance</strong></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Duncan &amp; Oxford, (2011)</td>
<td>Moderately trained (13 males)</td>
<td>5 mg·kg⁻¹</td>
<td>Repetitions to failure at 60% 1RM</td>
<td>Yes † repetitions to failure &amp; ↑ weight lifted</td>
<td>↑</td>
<td>Unaffected († scores for vigour)</td>
</tr>
<tr>
<td>Duncan et al. (2013)</td>
<td>Resistance trained (9 males &amp; 2 females)</td>
<td>5 mg·kg⁻¹</td>
<td>Repetitions to failure at 60% 1RM</td>
<td>Yes † repetitions to failure</td>
<td>Unaffected</td>
<td>↓ (↓ pain)</td>
</tr>
<tr>
<td>Beck et al. (2006)</td>
<td>Resistance trained (37 males)</td>
<td>201 mg (mate, guarana, black tea extract) 60 min prior to exercise</td>
<td>1RM bench press Muscular endurance test (total volume of weight lifted with 80% 1RM)</td>
<td>Yes 2.1%↑ 1RM BP</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Goldstein et al. (2010a)</td>
<td>Resistance trained (15 females)</td>
<td>6 mg·kg⁻¹</td>
<td>1RM bench bench &amp; repetitions to failure at 60% 1RM</td>
<td>Yes † 1RM</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Timmins &amp; Saunders, (2014)</td>
<td>Resistance trained (16 males)</td>
<td>6 mg·kg⁻¹</td>
<td>MVC of elbow &amp; wrist flexors</td>
<td>No change in 60% 1RM</td>
<td>Perhaps † mean MVC</td>
<td>n/a</td>
</tr>
<tr>
<td>Jacobs et al. (2003)</td>
<td>Healthy, active (13 males)</td>
<td>4 mg·kg⁻¹</td>
<td>3 supersets of 80% 1RM bench press</td>
<td>No</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Green et al. (2007)</td>
<td>Physically active participants (≥8 wk strength training) (13 males &amp; 4 females)</td>
<td>6 mg·kg⁻¹</td>
<td>3 sets of 10 RM bench press to failure</td>
<td>No</td>
<td>n/a</td>
<td>Unaffected</td>
</tr>
<tr>
<td>Bellar et al. (2011)</td>
<td>Recreationally trained participants (5 male &amp; 5 female)</td>
<td>100 mg caffeine gum (delivered 85% effective dose) immediately prior to exercise</td>
<td>Grip TTE at 30%max</td>
<td>No</td>
<td>n/a</td>
<td>Unaffected (↓ pain)</td>
</tr>
<tr>
<td>Study</td>
<td>Participants Description</td>
<td>Dose</td>
<td>Time Prior to Exercise</td>
<td>Protocol/Briefing</td>
<td>Findings</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
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<td>-------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Black et al. (2014)</td>
<td>Recreational active participants (6 male &amp; 6 female)</td>
<td>5 mg·kg⁻¹ 60 min prior to exercise</td>
<td>MVC &amp; motor unit recruitment of elbow flexors tested pre-capsule, pre- &amp; post-40 min arm cycling</td>
<td>No</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Flueck et al. (2015)</td>
<td>Healthy, trained participants (17 AB, 10 PARA &amp; 7 TETRA males)</td>
<td>6 mg·kg⁻¹ 60 min prior to exercise</td>
<td>3 min all-out arm crank test</td>
<td>Yes ↑ average PO in PARA only Yes ↑ peak PO in AB/PARA only No TETRA (Large inter-individuality)</td>
<td>Unaffected in AB/PARA ↑ in TETRA post-ex</td>
<td>n/a</td>
</tr>
<tr>
<td>Flueck et al. (2014)</td>
<td>Elite wheelchair racing athletes (6 male &amp; 3 female)</td>
<td>6 mg·kg⁻¹ 60 min prior to exercise</td>
<td>1500 m wheelchair racing TT</td>
<td>No but 4 out of 9 athletes improved</td>
<td>↑ post-TT</td>
<td>n/a</td>
</tr>
<tr>
<td>Aedma et al. (2013)</td>
<td>Trained wrestlers (14 males)</td>
<td>5 mg·kg⁻¹ 30 min prior to exercise (1st test)</td>
<td>4 x 6 min UBE intermittent sprint performance tests with 30 min recovery between tests</td>
<td>No ↓peak PO in test 4</td>
<td>↑ in tests 3 &amp; 4</td>
<td>Unaffected</td>
</tr>
<tr>
<td>Stadheim et al. (2013)</td>
<td>Highly trained CC skiers (10 males)</td>
<td>6 mg·kg⁻¹ ~75 min prior to exercise</td>
<td>Incremental warm-up 8 km CC DP performance test</td>
<td>Yes 4%↓ performance time</td>
<td>↑</td>
<td>↓ during sub-maximal intensities</td>
</tr>
<tr>
<td>Stadheim et al. (2014)</td>
<td>Highly trained CC skiers (8 males)</td>
<td>3 &amp; 4.5 mg·kg⁻¹ ~75 min prior to exercise</td>
<td>15 min submaximal exercise &amp; a 10 min all-out CC DP ergometer test</td>
<td>Yes 4%↑ distance on day 1 &amp; ~5%↑ on day 2 Unaffected at rest/during warm-up ↑ post test</td>
<td>↓ during sub-maximal intensities Unaffected during test</td>
<td></td>
</tr>
<tr>
<td>Black et al. (2014)</td>
<td>Recreational active participants (9 male &amp; 5 female)</td>
<td>5 mg·kg⁻¹ 60 min prior to exercise</td>
<td>30 min arm cycling at 60% VO₂peak &amp; 10 min performance trial</td>
<td>No but improved by 2.1% (n.s)</td>
<td>↑ Unaffected post-performance trial</td>
<td>↓ (↓ pain during sub-maximal but not maximal exercise)</td>
</tr>
</tbody>
</table>

**Note:** AB=able-bodied, CC=cross-country, DP=double-poling, MVC=maximal voluntary contraction, PARA=individuals with paraplegia, PO=power output, RM=repetition maximum, TETRA=individuals with tetraplegia, TT=time trial and TTE=time to exhaustion
A summary of studies that have investigated caffeine supplementation during UBE can be seen in Table 2.4. As with the evidence in an AB population, it appears that caffeine is unlikely to consistently enhance UB strength. The evidence is equivocal for short-term, high-intensity UBE but both studies by Flueck et al. (2014; 2015) show positive signs that caffeine may improve performance in some individuals with a physical impairment. The 2014 study investigated the effects of caffeine and sodium citrate on 1500 m wheelchair racing performance (~2:50 min) using elite athletes with a SCI or spina bifida (category T53/54) (Flueck et al., 2014). The authors concluded that caffeine supplementation, or its combination with sodium citrate, did not improve 1500 m race performance compared to placebo. However, individual variability was evident, with four athletes (n=9) producing their fastest time during the caffeine only trial. The differing muscle fibre type composition in the arms compared to the legs and the elite athlete participant pool were among the proposed reasons for the lack of an ergogenic effect. Flueck et al. (2015) suggested that the effects of 6 mg·kg\(^{-1}\) caffeine on 3-min all-out arm crank performance differed depending on an individual’s SCI lesion level in UBE trained participants. Improvements were seen in AB individuals (n=17) and individuals with paraplegia (n=10) but high inter-individuality remained evident in all groups (n=7, individuals with tetraplegia) (Flueck et al., 2015). The authors proposed that the lesser training status of the participants in the 2015 study was one of the reasons for the differing results. During short-term maximal exercise Flueck et al. (2015) suggested that elite athletes may benefit less from caffeine because they are already performing close to their maximum. This opposes Collomp et al. (1992) who suggested that the intra and/or extracellular adaptations resulting from specific swimming training were necessary to reap the benefits of caffeine during 2 x 100 m sprint performance. Both studies published by Flueck et al. (2014; 2015) are notable for their absence of subjective measures of perceived exertion, pain, mood and/or arousal, which are reported to be positively altered following caffeine (Doherty & Smith, 2005; Smit & Rogers, 2000).

The third study to investigate short-term UBE performance employed an UB intermittent sprint performance test on an arm crank ergometer (Aedma et al., 2013). The test was developed specifically to assess anaerobic performance in wrestlers and involved four six min bouts of intermittent sprint arm cranking (repeated 15 s sprints and 40 s unloaded cranking) with 30 min recovery in-between. Aedma et al. (2013) are the only known study to report a negative effect of caffeine supplementation on UBE performance, whereby a significant reduction in peak PO was observed in the fourth intermittent sprint test compared to a smaller decline following placebo. The authors concluded this was due to the increased HR and blood
lactate concentrations [Bla] observed during the caffeine trial, which may have impaired the wrestlers’ recovery between consecutive bouts (Aedma et al., 2013). Increased [Bla] in the absence of performance improvements has been reported previously (Black et al., 2014; Flueck et al., 2014) but the reasons for this are currently unknown.

Three further studies have investigated the effects of caffeine supplementation on UBE endurance performance in AB participants. Stadheim et al. (2013) reported caffeine (6 mg·kg\(^{-1}\)) to enhance endurance performance during an 8 km double-poling performance test lasting ~33-34 min. Stadheim et al. (2014) also reported improvements during a 10 min all-out double-poling TT following a 15 min preload and a lower caffeine dose (3 and 4.5 mg·kg\(^{-1}\)). These results must be assessed with caution given that the double-poling technique used in cross-country skiing also involves the muscles of the trunk and upper-leg, but the arms provide the speed generating force (van Hall et al., 2003). To the author’s knowledge, Black et al. (2015) is the only study that has investigated the influence of caffeine on UB-only endurance performance. The authors compared participant’s performance in a 10 min performance trial during leg and arm cycling following a 30 min submaximal preload at 60% VO\(_2\)\(_{\text{peak}}\). Caffeine (5 mg·kg\(^{-1}\)) ingestion 60 min prior to exercise improved leg but not arm cycling performance, which Black et al. (2015) suggested may have been due to a potential threshold intensity of pain/RPE above which caffeine cannot exert its ergogenic effects. Participants reported near maximal RPE scores of ~19 following both placebo and caffeine, following the 10 min performance trial. There are currently a limited number of studies employing different exercise and caffeine protocols, participant populations and measures of performance making it hard to form any clear conclusions on caffeine’s effects on individuals with physical impairments.

2.4. Spinal cord injury

2.4.1. Spinal cord anatomy and terminology

The spine consists of 33 vertebrae: 24 pre-sacral vertebrae (7 cervical (C), 12 thoracic (T), and 5 lumbar (L)) followed by the sacrum (5 fused sacral (S) vertebrae) and the coccyx (4 fused coccygeal vertebrae) (see Figure 2.2). The spinal cord originates at the caudal end of the medulla oblongata and sits within the spinal vertebra before terminating above the foramen magnum to the level of L1/2. The spinal cord acts as a major conduit for motor, sensory and autonomic neural information. Injury to the spinal cord therefore results in a complex, lesion level dependent challenge to the cardiovascular, respiratory, digestive and
Figure 2.2. Schematic diagram of autonomic cardiovascular (CV) control in individuals with a spinal cord injury (SCI). Adapted from Krassioukov and West, (2014).
skeletal muscle systems. Evidently the higher the lesion level, the greater the loss of functional muscle mass and autonomic control (Haisma et al., 2006; Leicht et al., 2013a). Injury at a thoracic, lumbar or sacral level is commonly referred to as paraplegia and causes lesion level dependent damage to the neural elements within the spinal canal resulting in loss of motor and/or sensory function of the trunk, pelvic area and lower limbs (Maynard et al., 1997). The upper limbs remain functional in individuals with paraplegia. Injury at a cervical level is commonly referred to as tetraplegia and results in the additional loss of motor and/or sensory function in the upper limbs. A SCI can be further classified as complete (no sensory or motor function below the lesion level), or incomplete (partial preservation of sensory and/or motor function below the lesion level and preserved function in the lowest sacral segments (S4 and S5) known as ‘sacral sparing’).

2.4.2. Consequences of a SCI

A SCI results in a range of dysfunctions that extend beyond muscle paralysis. Importantly, the autonomic dysfunction that occurs consequently leads to cardiovascular, respiratory, bladder and bowel, thermoregulatory and/or sexual dysfunction (Krassioukov & West, 2014). Discussion of the consequences of SCI in their entirety is beyond the scope of this thesis however, the reader is directed towards a number of detailed reviews on such topics (Hou & Rabchevsky, 2014; Krassioukov & West, 2014; Price, 2006; West et al., 2012). The current thesis will focus on the consequences most directly linked to the potential ergogenic effect of caffeine in individuals with a SCI; autonomic, cardiovascular and gastrointestinal dysfunction, and changes to skeletal muscle and body composition.

2.4.3. Autonomic and cardiovascular function

The autonomic nervous system (ANS) has two components: sympathetic and parasympathetic, both of which innervate the majority of visceral organs including the heart and bronchial pulmonary tree (Krassioukov & Weaver, 1996). Under normal conditions in AB individuals the sympathetic and parasympathetic systems interact to produce a balanced regulation of the innervated organs (Krassioukov, 2009). The sympathetic component is commonly referred to as the ‘fight or flight’ and the parasympathetic component produces the ‘rest and digest’ response. A complete SCI disrupts the pathways from the brain to the peripheral sympathetic nervous system and therefore disrupts cardiovascular, respiratory, metabolic, urinary, gastrointestinal, sexual and thermoregulatory function.

The loss of sympathetic tone and subsequent blood pooling in the peripheral and splanchnic vasculature in individuals with cervical and high-thoracic SCI results in
bradycardia and low resting arterial blood pressure (Hou & Rabchevsky, 2014; Krassioukov, 2009) (see Figure 2.2). These individuals will face the daily challenge of managing an unstable blood pressure which can result in two serious conditions: orthostatic hypotension (OH) and autonomic dysreflexia (AD). An episode of OH is observed as a sustained (3 min) decrease in systolic/diastolic blood pressure of greater than 20/10 mmHg, respectively upon the assumption of an upright posture from a supine position (Freeman Somers, 2010). Whereas an episode of AD is characterised as an increase in systolic blood pressure of at least 20 mmHg (Krassioukov, 2009) and occurs following noxious or non-noxious stimuli below the SCI lesion level. The sudden uncontrolled increase in blood pressure can be caused by a variety of stimuli including bladder and bowel distention, spasms, pressure sores, urinary bladder catheterisation or something as trivial as a stone in the shoe or laces tied too tight (Krassioukov & Weaver, 1996). Self-induced AD, known as ‘boosting’, is unethical and deemed illegal by the International Paralympic Committee however; it has been reported that some wheelchair athletes induce AD voluntarily to enhance exercise performance (Bhambhani et al., 2010).

The heart has dual innervation: parasympathetic from the vagal nerve and sympathetic from T1-5 (Krassioukov, 2009). Bradycardia therefore occurs in individuals with a SCI above T6 where there is a loss of direct sympathetic outflow to the heart (see Figure 2.2) (Wecht et al., 2015). The influence of lesion level is observed with peak HRs of 181(10) and 127(10) beats·min⁻¹ in trained wheelchair athletes with motor complete paraplegia and tetraplegia, respectively (Paulson et al., 2013b). Innervation of the adrenal medulla (primary source of catecholamine release) derives from T5-9 and hence individuals with cervical and high-thoracic SCIs show reduced adrenaline and noradrenaline responses at rest and during exercise compared to AB controls and individuals with lower SCI lesion levels (Paulson et al., 2013b; Schmid et al., 1998; Van Soeren et al., 1996; see Table 2.5). Catecholamine concentrations have a wide-ranging impact on physiological responses such as HR, blood pressure and glycolytic flux. Reductions in blood volume, muscle pump action below the lesion level, and sympathetically mediated vasoconstriction limit both cardiac preload and ventricular filling (Krassioukov & West, 2014). The consequent volume unloading may be responsible for the cardiac decline observed in individuals with cervical or high-thoracic SCI (Wecht et al., 2015).

Physical capacity can be described as ‘the capacity of the cardiovascular system, muscle groups and the respiratory system to provide a level of physical activity’ (Haisma et al., 2006). The physical capacity of individuals with a SCI is limited due to the loss of
functional muscle mass and diminished sympathetic control below the lesion level (Hoffman, 1986). Unsurprisingly, peak oxygen consumption and other physiological parameters such as peak [Bla], HR and ventilation rates are inversely related to lesion level (Bhambhani, 2002). A review by Haisma et al. (2006) reported mean $\dot{V}O_2$ peak values of 1.51 and 0.87 L·min$^{-1}$ in individuals with paraplegia and tetraplegia, respectively during maximal arm crank ergometry. Anaerobic capacity and strength measures also show decreases which are lesion level dependent whereby trained individuals with low-level paraplegia can produce comparable upper-body muscle strength measures to those of AB individuals (Janssen et al., 2002; Phillips et al., 2000).
Table 2.5. Studies related to the effects of caffeine supplementation on catecholamines, glucose, lactate, free fatty acids (FFA) and respiratory exchange ratio (RER).

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Van Soeren et al. (1996)</td>
<td>6 TETRA 2 PARA</td>
<td>3 h rest</td>
<td>6 mg·kg⁻¹</td>
<td>Unaffected</td>
<td>↑ in PARA only</td>
<td>Unaffected</td>
<td>↑</td>
<td>Unaffected</td>
</tr>
<tr>
<td>Mohr et al. (1998)</td>
<td>7 TETRA 2 PARA</td>
<td>Rest &amp; FES TTE</td>
<td>6 mg·kg⁻¹</td>
<td>Unaffected</td>
<td>Slight increase after 15 min FES</td>
<td>Unaffected</td>
<td>↑ after 60 min rest &amp; 15 min FES</td>
<td>Unaffected</td>
</tr>
<tr>
<td>Batttram et al. (2007)</td>
<td>14 TETRA</td>
<td>60 min rest</td>
<td>4 mg·kg⁻¹</td>
<td>Unaffected</td>
<td>n/a</td>
<td>Unaffected</td>
<td>↑ n.s</td>
<td>n/a</td>
</tr>
<tr>
<td>Flueck et al. (2015)</td>
<td>17 AB 10 PARA 7 TETRA</td>
<td>3 min all-out arm crank test</td>
<td>6 mg·kg⁻¹</td>
<td>↑ in AB only</td>
<td>↑ in AB only</td>
<td>[Bla] unaffected in AB/ PARA ↑ [Bla] in TETRA post-ex</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Graham &amp; Spriet, (1991)</td>
<td>7 AB trained runners</td>
<td>2 x cycling TTE 2 x running TTE</td>
<td>9 mg·kg⁻¹ 60 min prior to exercise</td>
<td>↑ at rest &amp; during exercise</td>
<td>Unaffected at rest or during exercise</td>
<td>↑ [Bla] [GLU] unaffected</td>
<td>Unaffected</td>
<td>Unaffected</td>
</tr>
<tr>
<td>Van Soeren et al. (1993)</td>
<td>7 AB users 7 AB non-users</td>
<td>1 h cycling at 50% VO₂max</td>
<td>5 mg·kg⁻¹ 60 min prior to exercise</td>
<td>Unaffected at rest 2-fold ↑ in users vs. non-users during exercise</td>
<td>Unaffected</td>
<td>↑ [Bla] during exercise in users [GLU] unaffected</td>
<td>↑ at rest only</td>
<td>Unaffected</td>
</tr>
<tr>
<td>Jackman et al. (1996)</td>
<td>14 AB rec. active</td>
<td>2 x 2 min cycle VO₂max with 6 min rest &amp; a TTE at VO₂max</td>
<td>6 mg·kg⁻¹ 60 min prior to exercise</td>
<td>Unaffected</td>
<td>↑ at rest &amp; during exercise</td>
<td>↑ [Bla] (n.s) ↑ muscle lactate concentration</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Note. AB=able-bodied, FES=functional electrical stimulation, PARA=individuals with paraplegia, TETRA, individuals with tetraplegia and TTE=time to exhaustion.
2.4.4. Gastrointestinal function

Cervical SCI above the level of sympathetic outflow to the GI tract disturbs normal interdigestive antral-duodenal motor coordination and delays postprandial GE of liquid meals (Fealey 1984; Segal 1995) (Figure 2.3). The impact of different SCI lesion levels on autonomic voluntary control of bladder and bowel function requires the sacral spinal cord (S2-4) to remain intact to allow communication with the brain. Hence, the majority of individuals with a SCI do not have spontaneous bladder and bowel movements. The alterations in physiological and metabolic functions in individuals with a SCI mean that the fundamental pharmacokinetics derived from AB individuals cannot be directly translated (Mestre et al., 2011). Consequently the standard dose and schedule for some drugs therefore do not achieve the required therapeutic effects or alternatively, they may produce drug concentrations that are toxic (Mestre et al., 2011). Treatment protocols for this heterogenic population must therefore be altered to help optimise absorption, distribution, metabolism and excretion. Delayed GE and intestinal motility may influence the absorption of drugs and/or NS in individuals with a SCI (Mestre et al., 2011).

Oral ingestion is a common drug administration method in a SCI population and yet it may not be the most effective due to impaired GI motility. Slower gastric, intestinal and colonic peristalsis may slow the rate at which the drug is transported to the site of absorption. The absorption of some drugs such as theophylline has been investigated (Segal 1986). Theophylline is a methylxanthine drug, which is structurally and pharmacologically similar to caffeine and is commonly used by individuals suffering from respiratory diseases to help relax the bronchial smooth muscle. When consumed orally by individuals with tetraplegia decreased bioavailability (fraction of dose of unchanged drug to reach the circulation) was apparent compared to individuals with paraplegia and a control group (Segal 1986). This reduced bioavailability could lead to incorrect dosage recommendations in individuals with tetraplegia and therefore patterns of absorption of specific drugs may need to be explored in this population.
Figure 2.3. The influence of spinal cord injury (SCI) lesion level on sympathetic and parasympathetic innervation related to the gastrointestinal and urinary system. Adapted from Tortora and Grabowski, (2003). Note: C=cervical, GE=gastric emptying, GI=gastrointestinal, S=sacral, T=thoracic
2.4.5. Skeletal muscle and body composition

A SCI causes inactivation and consequently results in unloading of skeletal muscle which causes a number of changes. There is a rapid decline in the cross-sectional area (CSA) of muscle in the paralysed lower limbs of individuals with a SCI (Castro et al., 1999; Olive et al., 2003). Intramuscular fat also increases after SCI (Gorgey et al., 2015), which has been linked to impaired glucose tolerance (Elder et al., 2004). Spungen et al. (2003) reported total body percent lean tissue losses of 2.4 and 3.0% per decade for males with paraplegia and tetraplegia, respectively compared to age, height, and ethnicity-matched AB controls in which a 1% loss was reported.

Following the decline in leg muscle CSA, there is a change in the distribution of muscle fibre types (McCully et al., 2011). Within the first 6 months post-injury, it has been noted there are minimal changes to the relative CSA and myosin heavy chain (MHC) content of type I fibres but there is a transformation of type II fibres whereby type IIa decreased and type IIx increased (Castro et al., 1999; Talmadge et al., 2002). The muscle fibre type changes in the leg lead to a reduction in oxidative metabolism, evidenced by ~50% reduction in mitochondrial function in individuals with paraplegia compared to AB individuals (McCully et al., 2011). Reductions in capillary-to-fibre ratio have also been reported to be lower compared to AB controls (Martin et al., 1992). However, larger reductions in type I fibres are seen in individuals 1-9 y post-injury (Greve et al., 1993; Rochester et al., 1995; Round et al., 1993). The utilisation of electrical stimulation of the lower limbs can help prevent the decline in type I muscle fibres and oxidative enzyme activity (Martin et al., 1992).

In the arm however, the opposite appears to occur; increases in type I and reductions in type IIb muscle fibres have been reported (Schantz et al., 1997). Percentage of type I muscle fibres in the deltoid of individuals with paraplegia were 59 and 55% for untrained and trained participants, respectively (Schantz et al., 1997). The untrained and trained participants with tetraplegia had a substantially greater percentage of type I muscle fibres with 66 and 82%, respectively (Schantz et al., 1997). Despite the acute impact of a SCI, adaptations to muscle fibre type distribution, capillarisation, and oxidative and glycolytic enzyme levels following training are similar to those reported in AB individuals (Biering-Søerensen et al., 2009; Schantz et al. 1997).

The consequence of a loss of lean body mass (LBM) is directly reflected in the resting metabolic rate of individuals with a SCI (Monroe et al., 2011). Hence, the higher the lesion level and the longer time since injury (TSI) (and presumably a reduction in lean mass /
increase in fat mass (FM)), the greater the reduction in basal EE (Mollinger et al., 1985). Reductions in metabolic rate, changes in diet and limited mobility in individuals with a SCI lead to changes in body composition. Lower total fat-free mass (FFM), greater upper-limb FFM and higher total FM are observed in individuals with a SCI (Beck et al., 2014; Maggioni et al., 2003) compared to AB participants. The greater FFM seen in the upper-limbs is likely due to the use of the arm musculature during daily wheelchair propulsion. These alterations in body composition below the lesion may be associated with carbohydrate intolerance, insulin resistance and lipid abnormalities (Bauman & Spungen, 2001; Elder et al., 2004).

Paralysis and immobility, leading to the aforementioned adaptations in body composition leave individuals with a SCI at increased risk of the adverse consequences associated with reduced physical activity levels and obesity such as metabolic syndrome (Nelson et al., 2007).

The assessment of body composition in individuals with a SCI is more difficult than in AB populations. A number of measurements use assumptions based on a cross section of the population that may not be valid for individuals with a SCI. For example, the equations used by Durnin and Womersley (1974), and Jackson and Pollock (1978) do not incorporate a lower limb measurement and therefore do not account for the increased regional adiposity in this area following a SCI. The use of dual-energy x-ray absorptiometry (DXA) offers greater accuracy when measuring body composition in individuals with a SCI compared to other field-based assessments such as bioelectrical impedance analysis, skinfolds and waist circumference (Goosey-Tolfrey et al., 2016; Willems et al., 2016). A DXA scan measures the soft tissue by the attenuation of FM to FFM, and the use of a meat calibration technique enables it to bypass traditional assumptions for fat content assessment (Spungen et al., 1995). A DXA scan does not provide three-dimensional imaging, as magnetic resonance and computed tomography techniques do, but it is more accessible, simpler, cheaper and produces lower radiation levels (Sutton et al., 2009). For this reason DXA has become the gold standard for body composition assessment in individuals with a SCI (Sutton et al., 2009). Additional methodologies independent of traditional assumptions, validation of existing methods and the development of specific population equations for individuals with a SCI have been a topic of interest recently (Goosey-Tolfrey et al., 2016; Willems et al., 2016) yet still require further exploration with larger sample sizes.
2.5. Modes of exercise

2.5.1. Physiological responses to lower- and upper-body exercise

Studies comparing LBE and UBE have reported different physiological responses during submaximal and maximal exercise (Bobbert, 1960; Sawka, 1986). Peak oxygen uptake responses during UBE (e.g. handcycling or arm cranking) are ~70% of those obtained during LBE (e.g. cycling) (Bottoms et al., 2015; Sawka & Pandolf, 1991). For example, Black et al. (2015) reported $\dot{V}O_2$ peak values of 3.1 and 2.3 l·min$^{-1}$ in recreationally active AB participants during leg and arm cycling, respectively. These lower values for UBE are due to the lower oxygen extraction in the arms compared to the legs, which is attributed to the smaller diffusional surface area, less capillarisation and shorter oxygen transit time (Calbet et al., 2005; Pendergast 1989; Volianitis et al., 2004). The arms also possess a smaller muscle CSA compared to the legs which results in a smaller oxidative capacity and a reduced muscle force potential (Pendergast 1989; Pimental et al., 1984). Improvements in $\dot{V}O_2$ peak associated with UBE training are attributed to an increase in arm blood flow, a larger extraction of oxygen via a higher capillary surface area, and improved oxidative metabolism (Hooker et al., 1989; Pendergast et al., 1979; Volianitis et al., 2004).

Cardiac output is similar during LBE and UBE but how this is achieved differs greatly; UBE results in a greater HR and lower stroke volume at any given absolute submaximal intensity (Bottoms et al., 2015; Davies & Sargeant, 1974; Pimental et al., 1984). This likely reflects a greater sympathetic outflow (increased HR) and a reduced lower-body skeletal muscle pump (reduced stroke volume) (Bevegard et al., 1966). The gross mechanical efficiency (GME: derived from the ratio between external PO and internal energy liberation) is lower during UBE compared to LBE (Sawka, 1986). The anaerobic threshold therefore occurs at a lower mode-specific oxygen uptake: 46.5% and 58.6% $\dot{V}O_2$ peak for arm cranking and leg cycling, respectively (Davis et al., 1976). Exercise at the same relative load results in higher carbohydrate and lower fat oxidation in the arms compared to the legs (Helge, 2008). Consequently, UBE is associated with larger lactate release than LBE at comparable exercise intensities (Jensen-Urstad & Ahlborg, 1992; Killierich et al., 2008; Mizuno et al., 1990). There also appear to be fewer type I muscle fibres in the arms (triceps brachii/deltoid = 32-54%) compared to the legs (vastus lateralis/gastrocnemius = 52-69%) (Killierich et al., 2008; Mizuno et al., 1990; Mygind, 1995), and type II muscle fibre area is reported to be larger in the triceps brachii compared to the gastrocnemius (Mizuno et al., 1990). The distribution of
muscle fibre type in the arms may be dependent on training status and level of SCI (Gollnick et al., 1972; Schantz et al., 1997), which will in turn influence a person’s ability to perform UBE and the type of substrate utilised (Astorino & Harness, 2009; Knechtle et al., 2004). These aforementioned factors highlight that whole- or LBE research on the effects of NS cannot necessarily be directly translated to UBE.

2.5.2. Wheelchair propulsion, arm crank ergometry and handcycling

Individuals with lower limb impairments (e.g. SCI, cerebral palsy or lower limb amputations) are often dependent on manual wheelchair propulsion, which means a transfer from leg to arm work for daily ambulation (Woude et al., 2005). Participation in sports such as wheelchair basketball, rugby and tennis also require the use of a manually propelled wheelchair. Due to the discontinuous and complex movement patterns required during wheelchair propulsion, the GME is low and rarely exceeds 11% (Dallmeijer et al., 2004; Hintzy et al., 2002; Lenton et al., 2008). For reference, the GME of leg cycling is ~20% in trained and recreational cyclists (Hopker et al., 2007). Since wheelchair propulsion is inefficient and is of a repetitive nature it often leads to pain, discomfort and repetitive strain injury (Woude et al., 2001). An individual’s GME during wheelchair propulsion can however be improved with training (de Groot et al., 2002).

Other less straining and more efficient modes of exercise used for fitness or for sports training include arm cranking (GME ~14-15%; Hopman et al., 1995) and recreational handcycling (GME ~13%; Hettinga et al., 2013). The latter is easily accessible using an attachment for the daily use handrim wheelchair to form a three-wheeled handcycle (see Figure 2.4). The use of asynchronous arm cranking has therefore been recommended as an alternative mode of ambulation to help reduce the risk of overuse injuries (Martel et al., 1991; Woude et al., 2001). The sport of handcycling also allows individuals to achieve higher speeds and therefore cover longer distances compared to wheelchair propulsion (Hettinga et al., 2010). The majority of modern handcycles now employ synchronous propulsion which produces constant application of force throughout the propulsion cycle. Consequently, due to athletes’ adopting this technique while in an aerodynamic supine position in the handcycle (Figure 2.5), GME in trained individuals has been reported as ~21% (Goosey-Tolfrey et al., 2008). Handcycling is therefore an effective mode of exercise to improve an individual’s physical capacity; four months of handcycle training resulted in significant increases in $P_{O_{peak}}$ (123 to 141 W; $p<0.001$) and $\dot{V}O_2\text{ peak}$ (1.98 to 2.11 l·min⁻¹; $p=0.002$) in individuals
with a physical impairment (Hoekstra et al., 2016). Furthermore, \( \dot{V}O_2 \text{peak} \) values of \( \approx 2.3(0.5) \) l·min\(^{-1}\) have been reported in trained handcyclists (7.7(2.6) h·wk\(^{-1}\) handcycle training) with paraplegia (T2-8) (Fischer et al., 2015).

The employment of untrained, AB participants has been used as a model of novice wheelchair users and handcyclists previously (Hettinga et al., 2016; Paulson et al., 2013a). Experienced manual wheelchair users display higher GME (8-11%) than novice users (4-8%), which highlights the need to familiarise and habituate participants to allow improvements in co-ordination and force production prior to experimental trials (Brown et al., 1990; Dallmeijer et al., 2004; Lenton et al., 2008). Findings cannot be directly applied to the wheelchair user population, particularly for individuals with a high level SCI. Yet the application of novice, AB participants reduces confounding factors of UBE training, wheelchair propulsion experience and upper-limb pain within research design. Experimental findings from the study of AB individuals can, where appropriate be extended to novice and experienced wheelchair users and handcyclists for verification.

Figure 2.4. Arm crank ergometer set-up in a laboratory (a) and an attachment for the daily use handrim wheelchair to form a three-wheeled handcycle (b).
2.5.3. Assessment of upper-body exercise performance

Assessment of UBE performance is important to enable the measurement of physical capacity of individuals taking part in UBE sports. Reliable and valid test protocols also allow the assessment of NS such as caffeine on exercise performance. Determination of UBE maximal aerobic responses during arm crank ergometry (ACE) and handcycling utilise similar protocols to LBE tests with adaptations to the initial and incremental PO values (Price & Campbell, 1997; Smith & Price, 2007). Maximal ACE tests have been reported to reliably determine $\dot{VO}_2$ peak (Price & Campbell, 1997). A crank rate of 60 or 70 rev·min$^{-1}$ can reliably determine UBE $\dot{VO}_2$ peak in AB participants and a verification phase is not deemed necessary (Price & Campbell, 1997). Wheelchair propulsion testing (usually in a sport-specific wheelchair) can also be performed in the laboratory on an ergometer or a wide belt treadmill and will follow similar protocols whereby participants will complete constant load exercise bouts at ascending velocities or gradients (Goosey-Tolfrey et al., 2014b; Paulson et al., 2013a; West et al., 2015).

Given the smaller muscle mass involved during UBE, and due to some individuals not having UBE-specific training there is a tendency for peripheral fatigue and consequent early cessation of exercise during maximal UBE (Smith & Price, 2007). Traditional criteria for $\dot{VO}_2$ max attainment such as i) RER >1.00-1.15 or ii) 90-100% HRpeak are not necessarily appropriate during UBE (Leicht et al., 2013b). The maximal HR achieved during UBE is ~10-20 beats·min$^{-1}$ lower than during LBE because of the smaller active muscle mass (Hill & Price, 2016; Janssen & Hopman, 2005). The use of HR as a secondary criterion is also less useful in individuals with a high-level SCI (>T6) due to the interruption of sympathetic
pathways to the heart which limit cardioacceleration (Janssen & Hopman, 2005). Hence, in the absence of a plateau, \( \dot{V}O_2 \) secondary criteria must be adjusted based on the participant pool.

Other anaerobic and sport-specific UBE tests that have been used to assess the impact of NS on performance include ACE Wingate tests (Aedma et al., 2013) and maximal performance tests (Flueck et al., 2015 (3 min maximal test); Spendiff & Campbell, 2005 (20 min performance trial)). There are also a number of validated field-based tests such as the 6 or 4 min push tests (Cowan et al., 2012; West et al., 2014), multi-stage fitness tests (Vanderthommen et al., 2002), TTs (Flueck et al., 2014), and sprint, skill and agility tests (West et al., 2014; Yilla & Shirrel, 1998). For a review of field-based exercise testing see Goosey-Tolfrey & Leicht, (2013).

**2.6. Summary**

The use of NS is common in the AB athlete population and a large body of evidence exists exploring their potential ergogenic properties. One such NS is caffeine, which has been extensively researched during various short and long-term exercise protocols involving whole- or LBE in AB individuals. A recent review of nutritional strategies to increase exercise performance highlighted caffeine as a NS with considerable evidence behind its effectiveness (Close et al., 2016). The review however, did not include any insight into the effectiveness of caffeine during UBE.

The physiological responses to whole- and LBE differ to those of UBE (Pendergast, 1989), and it is therefore debatable whether the findings of caffeine studies during the different modes of exercise are transferable. The current research exploring the use of caffeine as an ergogenic aid during UBE is limited (Table 2.4) and has focused mainly on strength exercise. Hence, no conclusions can currently be drawn regarding caffeine’s effectiveness during short-term, high-intensity or endurance UBE protocols. Further UBE-specific investigations employing non-strength-related exercise protocols are therefore required.

To the authors knowledge only two studies have previously explored the impact of caffeine on performance in individuals with a physical impairment (SCI and spina bifida) (Flueck et al., 2015; 2014). The findings indicate individual responses to the NS, which may be related to SCI lesion level (Flueck et al., 2015). The further complications of a SCI (e.g. reduced active muscle mass, slower GI transit times, changes in muscle fibre type distribution
and an impaired catecholamine response) highlight the need for impairment-specific investigations into the impact of caffeine on UBE performance.

The proceeding experimental chapters therefore aim to answer the following questions:

- What type of NS are used, how and why are they used, and who do athletes with a physical impairment consult for advice regarding NS use? (Chapter three)
- Do the effects of caffeine differ between LBE and UBE performance in the same participants? (Chapter four)
- Does caffeine improve short-term, high-intensity (Chapter five) and endurance (Chapter four and seven) UBE performance?
- Does the rate of caffeine absorption in individuals with paraplegia and tetraplegia differ to AB individuals at rest? Do AB guidelines need to be adjusted for individuals with a SCI? (Chapter six)
3

Study 1: Nutritional supplement habits of athletes with an impairment and their sources of information.

This chapter has been published in a slightly modified form in *International Journal of Sport Nutrition and Exercise Metabolism*:

3.1. Abstract

The consumption of NS is common among AB athletes yet little is known about NS use by athletes with an impairment. This study aimed to examine the: (i) prevalence of NS use by athletes with an impairment; (ii) reasons for use/ non-use; (iii) sources of information regarding NS; and (iv) whether age, gender, impairment, performance level and sport category influence NS use. The questionnaire was completed by 399 elite (n=255) and non-elite (n=144) athletes (296 males, 103 females) online or at a sporting event/training camp. Data were evaluated using chi-square analyses. Fifty-eight percent (n=232) of athletes used NS in the previous 6-month period and 41% (n=102) of these followed the instructions on the label to determine dose. Adherence to these AB recommendations may partly explain why 9% (n=37) experienced negative effects from NS use. As expected, the most popular NS were: protein, carbohydrate-electrolyte sports drinks, multivitamins and carbohydrate supplements, which were obtained from health food/sport shops, the internet and supermarkets (top 3) where evidence-based, impairment-specific advice is limited. The nutritionist/dietitian was the most used and trusted source of information, which is a promising finding. The most prevalent reasons for use were to support exercise recovery, support the immune system and provide energy. Elite athletes were more likely to use NS, which may reflect greater training hours and/or access to nutritionists. Fifty-two percent of athletes (n=209) requested more information and education regarding NS. NS use is prevalent in this population and therefore education on dosage and appropriate sources of information is required.
3.2. Introduction

It is widely accepted that nutrition can influence exercise performance (Rodriguez et al., 2009) and that it should be integrated into an athlete’s programme to fully capitalise on their athletic potential (Broad, 2014). Likewise, the use of some NS, defined by the Dietary Supplement Health and Education Act of 1994 as ‘any product intended to supplement the diet’, may have the ability to improve sporting performance (Maughan et al., 2004). It is therefore unsurprising that the consumption of NS is common among AB athletes (Braun et al., 2009; Erdman et al., 2006; Sundgot-Borgen et al., 2003). With the increased popularity of disability and Paralympic sport in recent years there is a need to also understand the nutritional practices of athletes with an impairment. That said few studies have focused on the nutritional requirements and behaviours of athletes with a physical impairment (Bertoli et al., 2006; Goosey-Tolfrey & Crosland, 2010; Krempien & Barr, 2012; Rastmanesh et al., 2007). The only study to investigate the NS habits of Paralympic athletes (Athens 2004 Paralympic Games), revealed that vitamins (43.5%), minerals/electrolytes (16.1%) and proteins/amino acids (10.5%) were most commonly consumed (Tsitsimpikou et al., 2009). This study however failed to report the athletes’ reasons for NS use or the sources of information they consulted.

The nutritional requirements for AB athletes are almost certainly not directly transferable to athletes with a physical impairment (Broad, 2014). For example, athletes who use a wheelchair utilise a smaller working muscle mass during movement, which will lead to lower energy requirements than those of AB athletes (Glaser, 1985). Furthermore, within this population there are likely to be a wide range of requirements based on individual impairment characteristics, including level and completeness of SCI (Goosey-Tolfrey et al., 2014a). In cases where a wheelchair is used for mobility, there may be considerable muscle atrophy in the lower limbs, leading to a lower resting metabolic rate, and in turn, a further reduction in daily energy expenditure (Goosey-Tolfrey & Sutton, 2012; Goosey-Tolfrey et al., 2014a). To prevent unwanted weight gain, energy intake must be correspondingly reduced. This lower total food intake could encourage a reliance on vitamin and mineral supplementation to meet micronutrient needs. In addition, there are practical issues to consider associated with food preparation. For example, individuals with an upper-limb amputation or visual impairment may have difficulties accessing, purchasing or preparing food (Meyer & Edwards, 2014), and some individuals with cerebral palsy may use NS to overcome feeding difficulties (Crosland & Boyd, 2014). Athletes’ reasons for NS use may therefore reflect a nutritional requirement
and hence some NS may be viewed as ‘essential’ rather than ‘optional’ in some circumstances.

The number of NS available on the market continues to increase despite insufficient supporting scientific evidence (Abel et al., 2005; Jeukendrup & Randall, 2011) and many are ineffective despite their widespread use (Maughan et al., 2004). There is currently very little evidence regarding the effects of ergogenic aids and macronutrient-providing NS in athletes with a physical impairment (Tables 2.1 and 2.4). This raises concern given the potential for, or more acute sensitivity to, side-effects in some sportspeople with a physical impairment (Van de Vliet et al., 2011). The potential risks associated with NS use in AB athletes such as inadvertent doping and unknown concentrations of active ingredients have been well-researched (Molinero & Márquez, 2009) and are acknowledged by the authors; however, this will not be the central theme of this study.

The use of NS is often a personal choice made by the athlete and/or in conjunction with their dietitian/nutritionist, ideally following a full cost-benefit analysis. Previous AB research shows that athletes are often more likely to report the use of family members, themselves, coaches and fellow athletes than more informed sources such as registered dietitians/nutritionists (Dolan et al., 2011; Froiland et al., 2004; Krumbach et al., 1999). The sources of information used by athletes with an impairment are currently unknown despite the importance of impairment-specific advice. Therefore, the objectives of this study were to determine the: (i) prevalence of NS use by athletes with an impairment; (ii) reasons for use/non-use; (iii) sources of information regarding NS; and (iv) whether age, gender, impairment, performance level and sport category influence NS use.

3.3. Methods

3.3.1. Participants

A total of 399 athletes (74% male, 26% female) across five impairment categories (42% SCI, 19% amputation, 18% Les Autres, 11% CP and 10% VI), 28 sports and 21 Nationalities (44% British, 17% American and Canadian, 13% Swiss, 11% other, 8% German, 6% Brazilian) completed the questionnaire. Athletes were aged 18-24 (24%), 25-30 (24%), 31-35 (18%), 36-40 (12%), 41-45 (9%) and 46+ (13%) years, and reported weekly average training hours of 0-5 (17%), 6-10 (30%), 11-15 (23%), 16-20 (20%) and 21+ (10%) h. Sixty four percent (n=255) and 36% (n=144) of athletes reported playing at an elite (currently represent their country Nationally or Internationally) and non-elite (train and compete for a club, regional or development team) performance level, respectively. Seventy-
nine percent of athletes completed the questionnaire online (n=317) and the remainder completed a paper version (n=82).

3.3.2. Survey instrument and survey procedure

A self-designed questionnaire which was developed by six professionals (a dietitian, a qualitative scientist and sport nutritionists/ scientists) and tested for reliability using McNemar and Cronbach’s Alpha tests in a representative sample (n=10; p(range)=0.582-1.000, with the exception of one question where p=0.125). It included; i) 12 closed and 9 open-ended; ii) 10 multiple-choice; iii) 7 Likert-type rating scale; and iv) 2 ranking questions. The questionnaire captured data pertaining to individual characteristics (e.g. age, gender, sport participation, impairment etc.), NS habits, reasons for NS use/ non-use and sources of information. The questionnaire took approximately 20 minutes to complete electronically or on paper. A copy of the questionnaire can be viewed in Appendix A and was made available in English, French, German, Portuguese and Spanish. The study was approved by the University Research Ethics Committee and informed consent was provided prior to completion of the questionnaire.

Participants were recruited during the 2012-13 athletic season at training camps/competitions across a variety of sports (e.g. Wheelchair Rugby/Tennis/Basketball, Sitting Volleyball and Athletics) in Great Britain, Canada, America, Switzerland and Germany following event organisers’ approval. Despite unsuccessful attempts to gather information from Powerlifting, Swimming and Boccia events, the investigators distributed links to the online questionnaire through their own network of coaches, sport scientists and at the International Paralympic Congress to widen the participant pool.

Athletes with a VI were aided by one of the authors to complete the questionnaire where necessary. Since the questionnaire was developed without consideration of athletes with an intellectual impairment, only athletes with a physical or visual impairment, over 18 years of age, who regularly took part in disability or Paralympic sport were included. Sighted guides were excluded.

In order to maintain the accuracy of participant responses, a 6-month recall period was set. For the purpose of this questionnaire the term ‘nutritional supplement’ was defined as ‘any product intended to supplement the diet, provide nutrients and/or improve performance.’ Examples of health-related and performance-enhancing NS were provided, and reported NS were categorised prior to analysis (Table 3.1). Categories were based on the macro- and micro-nutrient components i.e., ‘carbohydrate supplements’ contained
predominantly carbohydrate for the purpose of providing energy, ‘protein’ contained predominantly protein for the purpose of power, strength, muscle building etc.; whereas ‘recovery’ contained both carbohydrate and protein for the purpose of recovery.

3.3.3. Statistical analysis

The Statistical Package for the Social Sciences version 20 software (SPSS Inc., Chicago, IL) was used to analyse the data. All descriptive data are presented as frequencies (%, n). Data were evaluated by age, gender, impairment, performance level and sport category (intermittent, speed and power, endurance, skill-based) (Table 3.2)) using chi-square ($\chi^2$) analyses. Where appropriate, data were subsequently interpreted using odds ratios. Significance was determined at $p<0.05$.

3.4. Results

3.4.1. Nutritional supplement habits

In total, 58% of athletes (n=232) used NS in the previous six months. The use of multiple NS was commonplace with 33%, 30%, 15%, 8%, 6% and 8% reporting the use of 1, 2, 3, 4, 5 or 6 different types of NS, respectively. Forty percent (n=259) of NS consumed were used daily (at least 4-5 times per week), 36% (n=231) were used before/during/after training, 6% (n=38) were competition-specific, with only 2% (n=13) used rarely. Other options were ‘unknown’ (10%), ‘reason-specific’ (3%) and ‘weekly’ (2%).

The most popular health-related NS were multivitamins, other health-related NS (e.g. aloe vera, coenzyme Q10, mushroom extract, evening primrose oil and chromium) and essential fatty acids; and the most popular performance-enhancing NS were protein, carbohydrate–electrolyte sports drinks and carbohydrate supplements (Figure 3.1). Caffeine was the most used NS (5%) beyond any macronutrient providing NS such as sports drinks and protein. The three most common outlets where athletes obtained NS were the supermarket (23%, n=71), internet (22%, n=67) and health food/sports shop (21%, n=65); others included pharmacy, sports nutritionist/dietitian and team sponsor. The most prevalent reasons reported for use/ non-use of NS are reported in Table 3.3.

When NS users were asked ‘How do you decide how much of a supplement to take?’, 102 (41%) followed the (AB) recommendations on the label/manufacturers website, 60 (24%) were told by a sports nutritionist/dietitian, 35 (14%) calculated it based on their body mass, 22 (9%) were unsure and 32 (13%) indicated ‘other’ (e.g. ‘doctor’s advice’, ‘how I feel’, ‘a third of the recommended as I have roughly a third of body function’, ‘half the
instructions,’ and ‘trial and error’). Nine percent of all athletes (n=37) reported having experienced a negative effect from using NS such as GI/digestive problems (protein, carbohydrate–electrolyte sports drinks/gels, creatine, cherry juice, beetroot juice), itchiness (beta-alanine) and palpitations (caffeine).

### 3.4.2. Comparisons by age, gender, impairment, performance level and sport category

Whether an athlete used NS did not differ by age ($p>0.05$). However, when the two oldest categories were combined, those over 41 y were most likely to use multivitamins compared to the younger age categories ($p<0.05$). Whether an athlete used NS or which type they used did not differ between gender ($p=0.661$) or impairment ($p=0.489$). Of note however, 9% of athletes (14 of 152) with a SCI reported using cranberry.

Elite athletes trained significantly more hours per week ($p<0.05$) and odds ratio analysis revealed they were 1.6 times more likely to use NS than non-elite athletes. Elite athletes were significantly more likely to use multivitamins, amino acids and carbohydrate–electrolyte sports drinks compared to non-elite ($p<0.05$). There was a significant association ($p<0.05$) between sport category and whether an athlete used NS. Individuals who took part in predominantly endurance sports were most likely to use carbohydrate–electrolyte sports drinks, carbohydrate supplements, protein, multivitamins and NS in general, compared to those in skill-based, intermittent or speed/power sports ($p<0.05$). Figure 3.2 indicates the use of NS within the sport categories. Caffeine was used mostly by wheelchair court sports, cycling, athletics and goalball athletes.

### 2.4.3. Sources of information

Athletes ranked sports nutritionist/dietitian (18%, n=155), coach (14%, n=122) and training partner/athlete (13%, n=114) as their top three sources of information. When asked who provided the most trusted source (top 3), athletes chose the sports nutritionist/dietitian (24%, n=248), doctor/medical professional (21%, n=214) and coach (12%, n=128). Other sources included friends/family, physiotherapist, supplement/health food store, evidence-based/scientific journals and books/magazines. Elite athletes had greater access to nutritionists/dietitians (60%, n=153) compared to non-elite (22%, n=31). Fifty-two percent of athletes (n=209) would like more information and education regarding NS. The type of information sought by athletes is shown in Figure 3.3.
Table 3.1. Nutritional supplement categories and frequency of use.

<table>
<thead>
<tr>
<th>Category</th>
<th>Types of nutritional supplement included</th>
<th>Frequency ((%) (n))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate–electrolyte sports drinks</td>
<td>Isotonic and hypotonic drinks/powders</td>
<td>20% (81)</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>Energy drinks (&gt;10% carbohydrate), carbohydrate gels and energy bars</td>
<td>13% (53)</td>
</tr>
<tr>
<td>Protein</td>
<td>Protein bars, powders and ready-to-drink shakes (&lt;20 g carbohydrate per serve)</td>
<td>26% (102)</td>
</tr>
<tr>
<td>Recovery</td>
<td>Products containing carbohydrate (&gt;20 g carbohydrate per serve) and protein to aid recovery</td>
<td>6% (25)</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Any product containing caffeine/guarana as an active ingredient</td>
<td>5% (20)</td>
</tr>
<tr>
<td>Buffering agents</td>
<td>Beta-alanine, sodium bicarbonate, sodium citrate</td>
<td>2% (7)</td>
</tr>
<tr>
<td>Amino acids</td>
<td>Any amino acids/BCAAs e.g. leucine, glutamine, l-carnitine</td>
<td>8% (31)</td>
</tr>
<tr>
<td>Creatine</td>
<td>Any pure creatine products</td>
<td>4% (16)</td>
</tr>
<tr>
<td>Combination</td>
<td>Products containing carbohydrate and/or protein, and other ingredients e.g. vitamins</td>
<td>3% (13)</td>
</tr>
<tr>
<td>Essential fatty acids</td>
<td>Omega 3 and 6 fish oils/cod liver oil</td>
<td>8% (30)</td>
</tr>
<tr>
<td>Joint care</td>
<td>Glucosamine and chondroitin</td>
<td>4% (14)</td>
</tr>
<tr>
<td>Multivitamin</td>
<td>Multivitamins</td>
<td>14% (55)</td>
</tr>
<tr>
<td>Probiotics</td>
<td>Probiotics</td>
<td>2% (9)</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Vitamin C only</td>
<td>4% (17)</td>
</tr>
<tr>
<td>Vitamin</td>
<td>Vitamin D and/or calcium only</td>
<td>5% (20)</td>
</tr>
<tr>
<td>D/calcium</td>
<td>Iron</td>
<td>2% (7)</td>
</tr>
<tr>
<td>Cranberry</td>
<td>Cranberry tablets/extract/capsules</td>
<td>4% (15)</td>
</tr>
<tr>
<td>Herbal</td>
<td>Any product containing herbal ingredients e.g. Echinacea, turmeric, arnica</td>
<td>3% (18)</td>
</tr>
<tr>
<td>Unknown (health or performance)</td>
<td>If a product’s content could not be identified it was recorded as unknown</td>
<td>1% (2) health</td>
</tr>
<tr>
<td>Other (health or performance)</td>
<td>Products which do not fit into the other categories were recorded as other</td>
<td>10% (38) health</td>
</tr>
</tbody>
</table>

Note: Total number of supplements reported = 594.
Figure 3.1. Frequency distribution for the type of nutritional supplement used.
Table 3.2. Sport grouping according to the nature of the sport (n=399).

<table>
<thead>
<tr>
<th>Group</th>
<th>Sports</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermittent</td>
<td>Badminton (3), Football (16), Sitting Volleyball (26), Sledge Hockey (15), Wheelchair Basketball (48), Wheelchair Tennis (39), Wheelchair Rugby (80), Wheelchair Flag Football (1)</td>
</tr>
<tr>
<td>Speed/power</td>
<td>Athletics (Field/Sprint) (6), Goalball (20), Kickboxing (1), Paracanoeing (2), Paraclimbing (1), Rowing (4), Swimming (17), Powerlifting (2), Alpine Skiing (8)</td>
</tr>
<tr>
<td>Endurance</td>
<td>Biathlon (1), Cycling (24), Paratriathlon (23), Athletics (mid-long distance running) (26)</td>
</tr>
<tr>
<td>Skill-based</td>
<td>Archery (1), Boccia (4), Equestrian (3), Shooting (6), Table Tennis (7), Wheelchair Curling (7), Wheelchair Dance (1), Wheelchair Fencing (7)</td>
</tr>
</tbody>
</table>

Values reported as frequency (n).
Table 3.3. Reasons for use and non-use of nutritional supplements.

<table>
<thead>
<tr>
<th>Reasons for use of performance-enhancing NS (%, n))</th>
<th>Reasons for use of health-related NS (%, n))</th>
<th>Reasons for non-use of NS (%, n))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Support exercise recovery (32%, 224)</td>
<td>Support immune system (32%, 114)</td>
<td>I don’t know enough about them (30%, 77)</td>
</tr>
<tr>
<td>Provide energy (28%, 200)</td>
<td>Medical need/deficiency (22%, 80)</td>
<td>I don’t need them (25%, 65)</td>
</tr>
<tr>
<td>Increase strength/power (20%, 142)</td>
<td>Inadequate diet (11%, 40)</td>
<td>I am concerned about a positive drugs test (18%, 47)</td>
</tr>
</tbody>
</table>

Note: Athletes could select as many responses as were applicable. Reasons in the health-related ‘other’ category included anti-inflammatory, joint care, I thought I’d give it a go, heart health, to help promote lean body mass, and to support female reproduction. Total number of supplements reported = 594.
Figure 3.2. Frequency distribution of nutritional supplement use within sport categories.
Figure 3.3. Frequency distribution for the type of information sought by athletes who indicated they would like more information/education regarding nutritional supplements and anti-doping. *Note: Athletes were able to select multiple responses where applicable.*
3.5. Discussion

3.5.1. Nutritional supplement habits

This study demonstrates that a wide-variety of NS are currently being used across a range of disability and Paralympic sports, and that 58% of athletes surveyed used NS in the previous six months. To our knowledge the only other study to investigate the use of NS by athletes with an impairment reported that 64% of athletes tested for doping control at the Athens 2004 Paralympic Games declared the use of medications and food supplements (58% and 42%, respectively) (Tsitsimpikou et al., 2009). Interpretation of these data would suggest that 27% of all athletes tested used at least one food supplement, which is less than half that reported in the current study. The higher reported NS use in the current study may reflect an increase in i) NS use over the previous decade, ii) the popularity and availability of NS, and/or iii) the training load/demand placed on the modern day athlete.

The prevalence of NS use in the current study was at the lower end of that reported by elite and collegiate AB athletes where 51-88% reported the use of NS (Dascombe et al., 2010; Erdman et al., 2006; Sundgot-Borgen et al., 2003). Thus, this supports the observations of Tsitsimpikou et al. (2009), who found Paralympians to use a more rational intake pattern compared to their Olympic counterparts. However, the lower reported use in the current study may also reflect a non-homogenous sample that included elite and non-elite athletes, which when separated suggests that more elite athletes used NS than non-elite. The lower reported use may also reflect a lack of knowledge regarding their effectiveness, side-effects and the dosage recommendations for this specific population given that 52% indicated they would like more information on these topics.

The most common NS were similar to those reported by the Athens 2004 Paralympic athletes (vitamins, minerals/electrolytes and proteins/amino acids) (Tsitsimpikou et al., 2009) but also included carbohydrate–electrolyte sports drinks. Previous research has shown that some athletes do not consider calorie/fluid replacement products as NS (Froiland et al., 2004) and may therefore fail to report them as such. The addition of carbohydrate–electrolyte sports drinks in the current study may reflect its inclusion on the list of NS examples. The prevalence of some macro- and micronutrient-providing supplements such as carbohydrate–electrolyte sports drinks, protein and multivitamins appears to be lower in this population of athletes with an impairment compared to AB athletes; used by 20%, 26% and 14% in the current study. Kristiansen et al. (2005) reported the use of sports drinks, protein and vitamins/minerals by 87%, 51% and 52% of male varsity athletes. Similarly, Froiland et al.
(2004) reported the use of energy drinks, protein and multivitamins by 73%, 48% and 47% of varsity athletes. Potential reasons for these differences may include; i) some athletes with an impairment may be more aware of eating a well-balanced diet for health reasons and therefore may not deem multivitamins and protein supplements necessary, ii) some individuals may be aware of their lower daily EE and therefore avoid sports drinks and protein supplements which provide additional energy to help prevent weight gain, iii) athletes may lack an understanding of the role that sports foods can play in improving performance/training capability, and iv) some athletes with an impairment may not understand their training needs and how NS may support their training goals compared to weight management goals which are common in a rehabilitation setting. Caffeine was the most used NS beyond any that provided a macronutrient. The 5% of athletes with an impairment that reported using caffeine is very low compared to AB sports such as cycling (60%) and track and field athletics (33%) since its removal from the WADA prohibited list in 2004 (Chester & Wojek, 2008). This low frequency of use may be related to a lack of knowledge of the benefits of caffeine for sports performance compared to daily use as a ‘stimulant’.

Athletes used various methods to calculate NS dosage but 41% indicated that they follow the (AB) instructions on the label/manufacturers website. The NS dose for some individuals with a SCI, amputation or CP may need to be adjusted from the AB recommendations due to a reduced active muscle mass, or the potential side-effects that may occur. The use of AB guidelines may therefore have been a contributing factor to the 9% that experienced side-effects having consumed a NS. It is encouraging that a number of athletes did however indicate that they use a proportion of the recommended dose, or adapt the dose based on personal experience. Given the nature of a questionnaire we cannot be sure whether these adaptations are the athlete’s decision or those of a nutritionist/dietitian. Although there are no specific recommendations for NS dosage, some individuals may be aware of emerging evidence regarding the segmental body composition (obtained via DXA) of athletes with a SCI (Goosey-Tolfrey & Sutton, 2012) and also the energy requirements of some disability sports (Abel et al., 2008). This type of evidence provides some basic information on which to base NS dosage recommendations, however, further research is required.

It may be concerning that the internet (22%) was a popular place to obtain NS. Previous research suggests that there are issues with NS being improperly tested, containing substances not declared on the label and/or not containing significant amounts of the active ingredients listed on the label (Geyer et al., 2004; Kohler et al., 2010; Maughan, 2005). A lack of regulatory controls on the internet may increase the likelihood of inadvertent doping
when purchasing products in this manner. Unfortunately in some countries, these problems also occur with products bought over-the-counter or in stores. The nature of the questionnaire means we cannot be sure if athletes checked whether the products they purchased were regularly tested for prohibited substances (e.g. via Informed-Sport) but it does suggest that ‘where to obtain NS’ should be a topic of education for these athletes. This topic is usually included in National Anti-Doping education sessions for elite funded athletes.

3.5.2. Reasons for nutritional supplement habits

Athletes reported similar reasons for the use of performance-enhancing NS (support recovery, support the immune system, to improve strength/power and to provide energy) and non-use (I don’t know enough about them and I don’t need them) to those of AB athletes (Froiland et al., 2004; Neiper, 2005). The most popular health-related answer in the current study was ‘to support the immune system’ (32%). This is understandable given the depressed immune function experienced by individuals with a SCI (Leicht et al., 2013a), who formed a large proportion of the athletes (42%). The top reason for non-use was ‘I don’t know enough about them’ (30%), which suggests that NS information may be either unavailable, inaccessible or the athletes are not interested. One athlete’s reason for non-use was ‘I take enough medication as it is’. The use of medication by Paralympic athletes’, highlighted by Tsitsimpikou and colleagues (2009), may help to explain the lower reported use of NS by athletes with an impairment because they do not want to take anything beyond what they need to maintain health.

3.5.3. Comparisons by age, gender, impairment, performance level and sport category

There was no influence of age on whether an athlete used NS. However, individuals 46+ y were more likely to use ‘other health supplements’ and when the upper two age categories were combined, individuals >41 y were more likely to use multivitamins. The increased use by older athletes has not been seen in previous AB literature because it is rare to find a group of athletes in this age category. Older athletes may feel the need to consume NS such as multivitamins to maintain health and this may be heightened in athletes with an impairment if their diet is restricted in some way.

A number of AB studies show that female athletes tend to use more NS than males (Froiland et al., 2004; Krumbach et al., 1999; Neiper, 2005; Ziegler et al., 2003). This can partly be explained by the fact that females may be more aware of their nutritional needs and that their actual need for certain micronutrients may be heightened due to their gender (Neiper, 2005). In contrast there was no influence of gender on NS use in the current study.
Zeigler et al. (2003) reported that female AB elite figure skaters were more likely to use multivitamin-minerals than their male counterparts. In aesthetic sports such as figure skating low energy intakes are common, especially in females, and multivitamins may be used to help maintain overall diet quality. This difference may not have been apparent in the current study because both male and female athletes may reduce their EI due to their impairment and therefore feel the need to consume a multivitamin to meet their micronutrient needs.

There was no significant influence of impairment on NS use however, 9% of athletes with a SCI reported the use of cranberry supplements which is likely due to the perceived prevention of urinary tract infections which are common in this population (Dermen et al., 2014). The limited evidence available however, shows that cranberry supplements are ineffective at preventing and/or treating urinary tract infections (Opperman, 2010).

It is well-documented that AB athletes report the use of more NS than the general population (Erdman et al., 2006, Sobal & Marquart, 1994). The current study supports ‘level of performance’ as a key indicator of NS use because elite athletes were 1.6 times more likely to use them. The significant positive association between training hours and performance level may help to explain the greater use by elite athletes. The energy requirements of greater training hours may influence an athlete’s (perceived) need for NS. Elite athletes also had greater access to nutritionists/dietitians and may thus have more knowledge regarding NS for performance or enhanced training capacity, and therefore the confidence to use them.

The energy requirements of an endurance athlete may also influence their use of NS. Heikkinen et al. (2011) found that endurance and speed/power athletes reported the use of NS significantly more often than team sport athletes. This partly agrees with the finding that athletes who took part in endurance sports in the current study were most likely to use carbohydrate–electrolyte sports drinks, carbohydrate supplements, protein, multivitamins and NS in general.

3.5.4. Sources of information

Knowledge of where athletes seek advice regarding NS is essential to devise and implement educational strategies (Erdman et al., 2006). Athletes in the current study reported the use of similar sources of information as AB athletes (Erdman et al., 2006; Froiland et al., 2004; Krumbach et al., 1999) and the top three were sports nutritionist/dietitian, coach and training partner/athlete. Registered nutritionists/dietitians should be knowledgeable and trustworthy sources; however, athletes and even coaches may lack the desired level of NS
knowledge. The coach-athlete relationship however, puts the coach in a unique position to influence his/her athlete’s diet, which emphasises the need to educate coaches regarding issues pertaining to the use of NS. It also highlights that there may be a need to educate athletes themselves on who is a knowledgeable source. It is clear that impairment-specific information and education regarding NS for this population is required, with 52% of all athletes indicating they would like more.

When the question was rephrased to ask ‘who the most trusted sources of information are’ the athletes’ replaced training partner/athlete with doctor/medical professional (top 3). This change may be due to regular consultations/visits regarding their impairment, medication or secondary complications, and the on-going relationship that may develop as a result. Despite being trustworthy, doctors/medical professionals do not necessarily possess the area-specific expertise to advise athletes on their use of NS for sport and should therefore be educated on how to deal with these questions should they arise.

Direct athlete education should be provided through sources of information that they trust and already use e.g. sports nutritionists/dietitians and coaches. Education regarding impairment-specific advice should therefore be directed at these professions. This type of information could be included within the coach education curriculum to make future disability sport coaches more aware of potential questions that may arise and who to contact for advice. Any impairment specific advice and information on NS for athletes should also be made available to a wider audience online through organisations such as WADA, National governing bodies and sport science/nutrition/medicine providers.

3.5.5. Limitations
As with all questionnaire-based data, the results of the current study rely on the honesty, recall, and self-report accuracies of athletes. An alternative to using an open-ended approach would be to prompt athletes with a list of common NS to choose from (Erdman et al., 2006), which may help reduce recall error. We appreciate the limitations of a 6-month recall period and that a longer survey period (i.e. 12 months) or biannual reporting may provide a more accurate representation of seasonal NS usage. However, the accuracy of recall and/or participant adherence may be reduced.

3.6. Conclusion
This study provides previously unknown information regarding NS habits and sources of information used by athletes with an impairment. Fifty-eight percent of those surveyed used NS. Athletes with an impairment appear to require and more importantly want more
information and advice regarding NS. Ultimately, further impairment-specific NS investigations are required in order to provide evidence-based recommendations.

The current chapter confirms the use of caffeine as an ergogenic aid in athletes with an impairment. Caffeine was the most used NS beyond any macronutrient providing NS such as sports drinks and protein, and hence it warrants further investigation in the following experimental chapters.

3.7. Practical applications

For the sports practitioner working with athletes with a physical or visual impairment it is important to understand that NS use is common in this population and that they may face questions on this topic. It is therefore vital to ensure athletes and practitioners are well educated on their use of NS to ensure practices are safe and effective. The current study indicated that education should be delivered directly to athletes and/or through those they trust e.g. sports nutritionists/dietitians and coaches. Education topics should include impairment-specific information (where available) regarding effective and safe NS and doses, where to buy NS and who to use as a source of information.
Study 2: Improvements in cycling but not handcycling preloaded 10 km time trial performance in habitual caffeine users

This chapter has been published in a slightly modified form in *Nutrients*:

4.1 Abstract

Caffeine supplementation during whole-/lower-body exercise is well-researched, yet evidence of its effect during UBE is equivocal. The current study explored the effects of caffeine on cycling/handcycling 10 km TT performance in habitual caffeine users. Eleven recreationally trained males (mean(SD) age 24(4) y, body mass 85.1(14.6) kg, cycling/handcycling $\dot{V}O_2$ peak 42.9(7.27)/27.6(5.1) ml·kg·min$^{-1}$, 160(168) mg·d$^{-1}$ caffeine consumption) completed two maximal incremental tests and two familiarisation sessions. During four subsequent visits, participants cycled/handcycled for 30 min at 65% mode-specific $\dot{V}O_2$ peak (preload) followed by a 10 km TT following the ingestion of 4 mg·kg$^{-1}$ caffeine (CAF) or placebo (PLA). Caffeine significantly improved cycling (2.0(2.0)%; 16:35 vs 16:56 min; $p=0.033$) but not handcycling (1.8(3.0)%; 24:10 vs 24:36 min; $p=0.153$) TT performance compared to PLA. The improvement during cycling can be attributed to the increased power output during the first and last 2 km during CAF. Higher [Bla] was reported during CAF compared to PLA ($p<0.007$) and was evident 5 min post-TT during cycling (11.2(2.6) and 8.8(3.2) mmol·L$^{-1}$; $p=0.001$) and handcycling (10.6(2.5) and 9.2(2.9) mmol·L$^{-1}$; $p=0.006$). Lower overall RPE were seen following CAF during the preload ($p<0.05$) but not post-TT. Lower peripheral RPE were reported at 20 min during cycling and at 30 min during handcycling, and lower central RPE was seen at 30 min during cycling ($p<0.05$). Caffeine improved cycling but not handcycling TT performance. The lack of improvement during handcycling may be due to the smaller active muscle mass, elevated [Bla] and/or participants’ training status.
4.2. Introduction

Low-moderate doses of caffeine (3-6 mg·kg$^{-1}$) have been shown to positively influence cycling TT performance (Astorino et al., 2012; Santo et al., 2014). During cycling the leg musculature provides the speed-generating force. However, there are numerous sports and activities such as kayaking, handcycling, double-poling and wheelchair sports during which the arms produce this force. It is apparent that NS such as caffeine are commonly used in both AB (Braun et al., 2009; Erdman et al., 2006) and disability sports (Chapter three), including many that involve UBE. The physiological responses to whole- and lower-body exercise (LBE) differ to those of UBE (Pendergast, 1989), and it is therefore debatable whether the findings from the aforementioned cycling studies are transferable to an UBE sport such as handcycling.

Caffeine is proposed to influence central nervous system (CNS) function by acting as an adenosine receptor (most likely A$_1$ and A$_{2A}$) antagonist (Davis et al., 2002; Fredholm et al., 1999). Antagonism reduces the influence of adenosine and produces motor-activating and arousing effects. Caffeine can therefore have a positive influence on subjective feelings such as RPE, mood and cognitive performance (Doherty & Smith, 2005; Smit & Rogers, 2000). Lower RPE during submaximal exercise have been reported following caffeine ingestion, and/or similar RPE when a higher workload has been achieved (Cureton et al., 2007; Stadheim et al., 2013). Caffeine has also been shown to produce hypoalgesic effects during submaximal cycling in male and female participants (Motl et al., 2006; O’Connor et al., 2004). It has been suggested that the inhibition of adenosine receptors following caffeine ingestion could also influence neuromuscular function (Kalmar, 2005; 1999). It is likely that a combination of factors contribute to improved endurance performance but with caffeine’s influence on the CNS in mind, a similar ergogenic benefit could be expected during UBE as has been reported during LBE. However, the evidence for a positive influence of caffeine during UBE remains equivocal.

An 8 km double-poling TT performance lasting ~34 min was enhanced following the consumption of 6 mg·kg$^{-1}$ caffeine in regular caffeine users (Stadheim et al., 2013). Double-poling is considered primarily to be an UBE however; the trunk and legs also play a role in the performance of this technique. On the other hand, when LBE and asynchronous UBE were directly compared in very low caffeine users (<40 mg/d) during a preloaded 10 min all-out performance trial (40 min total exercise time), caffeine (5 mg·kg$^{-1}$) improved LBE but failed to statistically impact UBE in a mixed AB group (Black et al., 2015). The opposing
results may be linked to differences in the exercise testing protocols, caffeine dose, training status of the participants’, or the participants’ level of habitual caffeine consumption. The contrasting responses may also be due to a number of factors related to the physiology of the leg and arm muscles. Firstly, the arms possess a smaller muscle CSA and hence a reduced absolute muscle force. Arm muscles may possess a higher percentage of fast-twitch muscle fibres (Mizuno et al., 1990; Mygind, 1995) and have a lower oxygen extraction capacity compared to the legs (Calbet et al., 2005; Pendergast, 1989). The onset of anaerobic metabolism during UBE therefore occurs at a lower level of oxygen uptake, and lactate concentrations are reported to be higher than during a comparable bout of LBE (Cerretelli et al., 1979; Pendergast, 1989). These factors can be altered with training however (Gollnick et al., 1972) and may help explain differences between performance outcomes in recreationally active participants (Black et al., 2015) and those that are specifically UBE trained (Stadheim et al., 2013).

It has been previously reported that caffeine increases muscular strength (maximal voluntary contraction) and motor unit recruitment in the knee extensors but not in the elbow flexors (Black et al., 2015; Warren et al., 2010). These observations may help to explain the lack of performance improvement during short-term UBE in AB participants (Aedma et al., 2013). The influence of caffeine on longer UBE endurance performance however, requires further investigation given the protocols of Stadheim et al. (2013) and Black et al. (2015) both allowed involvement of the trunk to some extent to produce force yet report opposing effects. Black et al. (2015) also used a mixed male and female participant pool of very low caffeine users (<40 mg·d⁻¹), which makes their findings less applicable to the many competitive athletes who consume caffeine regularly. Therefore, the purpose of the current study was to explore the effects of caffeine on both LBE and UBE endurance performance. The study will employ an ecologically valid LBE and UBE endurance protocol whereby male habitual caffeine users will complete preloaded (30 min at 65% \( \text{VO}_2 \text{peak} \)) 10 km TTs following the ingestion of caffeine and placebo. Importantly they will adopt a synchronous handcycling modality for the UBE aspect, which is akin to the sports of handcycling and the cycling discipline of Paralympic triathlon.
4.3 Methods

4.3.1. Participants

Eleven recreationally active, healthy males (age 24(4) y, body mass 85.1(14.6) kg, lower and upper body relative $\dot{V}O_2$ peak 42.9(7.3 and 27.6(5.1) ml·kg·min⁻¹) participated in the current study. Caffeine users, with average daily caffeine intake 160(168) mg·d⁻¹ were recruited to represent the usual dietary habits of athletes. All procedures were approved by the University’s Ethical Advisory Committee and performed in accordance with the Declaration of Helsinki. All participants provided written informed consent and none revealed contraindications for participating in the study.

4.3.2. Experimental design

The study employed a double-blind, placebo-controlled, repeated measures design. Participants attended the laboratory on eight separate occasions which consisted of a $\dot{V}O_2$ peak test, a familiarisation and two (caffeine and placebo) experimental trials (Figure 4.1) for both cycling and handcycling. Famililiarisation sessions aimed to limit a potential learning effect. Familiarisation procedures were the same as the experimental procedures described in Figure 4.1 with the exception of capsule consumption and blood sampling. Experimental trials were separated by ≥48 h and were conducted at the same time of day within participants (07:30-09:30) to avoid any influence of circadian rhythm (Drust et al., 2005).

4.3.3. Equipment

The cycling trials were performed on a Viking Jetstream 14 road bike and the handcycling trials were performed on a Draft handbike (operating in synchronous crank mode). Both pieces of equipment were mounted on a Cyclus II ergometer (Avantronic Richter, Leipzig, Germany). Bike settings were individually adjusted and standardised for each participant across trials (Figure 2.5). The differentiated Borg 6-20 RPE scale (Borg, 1998) was explained to participants prior to the commencement of preliminary trial testing.

4.3.4. Preliminary testing

On separate occasions, participants performed incremental cycling and handcycling tests until exhaustion to determine mode-specific $\dot{V}O_2$ peak. The ergometer was set in power control mode, which ensured a pre-set power output (PO) was automatically regulated independent of cadence or gear selection by continuous adjustment of the degree of electromagnetic braking. The participants’ performed a 5-min warm-up at a self-selected
pace. The continuous step tests consisted of 3-min submaximal stages with an initial load of 70 W for the cycling and 20 W for the hand-cycling test. Increments of 30 W for the cycling and 10 W for the hand-cycling test were then applied. Participants reported differentiated RPE scores at the end of each stage and upon completion. [Bla] were determined using a Biosen C-Line (EKF Diagnostic GmbH, Barleben, Germany) at the end of each stage from earlobe capillary blood samples. When the participant’s [Bla] increased beyond 4 mmol·L⁻¹ the resistance was increased by 5 W every 15 s until volitional exhaustion (failure to maintain a cadence of ≥50 rpm following 2 warnings and an overall RPE=19-20). Secondary criteria included RER >1.15 and/or a HR_{peak} > (220-age)-20. Online respiratory gas analysis was carried out via a breath by breath system (MetaLyzer 3B, Cortex Biophysik GmbH, Leipzig, Germany). Prior to each test, gases were calibrated according to the manufacturer’s recommendations. The highest 30 s rolling average \dot{V}O₂ value was used as the participant’s \dot{V}O₂_{peak} and HR was monitored continuously (Polar RS400, Polar, Kempele, Finland).

4.3.5. Experimental trials

Participants refrained from exercise, caffeine and alcohol consumption in the 24 h preceding each trial, as previously utilised [23]. They completed 24 h dietary diaries prior to the first experimental trial and were asked to replicate their diet for all subsequent trials. Participants were asked to consume a self-selected standardised meal 1.5 h prior to arriving at the laboratory, which was noted upon arrival (62(10)% carbohydrate, 18(9)% protein, 20(9)% fat) and replicated prior to all subsequent trials.

The experimental trials involved the consumption of either 4 mg·kg⁻¹ caffeine anhydrous (CAF) (My Protein, Northwich, UK) or dextrose placebo (PLA) capsules (Bulk Powders, Colchester, UK) 45 min prior to the warm-up. A 4 mg·kg⁻¹ caffeine dose has previously increased [CAF] to 14.6 µM, 50 min post-ingestion (Skinner et al., 2010) and was therefore deemed suitable for the current study. The protocol can be seen in Figure 4.1 and is based on that used previously to assess the effects of glucose ingestion on UBE performance (Spendiff & Campbell, 2002). The preload and TT provide information on the effect of caffeine on physiological parameters and performance, respectively. Previous data show preloaded and unloaded TTs to be highly reproducible with CVs of 3.5 and 3.4%, respectively (Jeukendrup et al., 1996). Participants were instructed to complete the 10 km TT in the shortest time possible, during which they could change gear at any time. Cycling 10 km
TTs have been shown to be reproducible in active and endurance-trained participants with a coefficient of variation of 1.5% for performance time (Astorino et al., 2012). No motivation was provided during the TT and to avoid test-retest influence the only feedback provided was cumulative distance covered. Experimental trial conditions were temperature 19.7(1.1)°C, pressure 1004(11) hPa and humidity 52(12)%.

The 6-20 RPE scale (Borg, 1998) was used as a measure of perceived exertion during exercise at 10, 20 and 30 min during the preload, and post-TT. Participants were asked for three RPE scores: peripheral (muscle and joint exertion) (RPE_p), central (ventilatory and circulatory exertion) (RPE_c) and overall (integrated) (RPE_o).

4.3.6. Statistical analysis

Statistical Package for the Social Sciences version 20 software (SPSS Inc., Chicago, IL) was used to analyse the data. Normal distribution was confirmed using the Shapiro-Wilk test and consequently [Bla], performance times, HR, PO, respiratory exchange ratio (RER) and $\dot{V}O_2$ data are reported as mean(standard deviation) (SD). Repeated measures analysis of variance (ANOVA) was used to examine differences in [Bla], and preload HR, RER and PO. Post-hoc paired samples t-tests using the Bonferroni correction were applied following significant findings. Ten km TT performance was also analysed using a repeated measures two-way ANCOVA, with time and treatment as within participant factors and trial order as a covariate. Cohen’s d ESs are included to supplement important findings. An ES of 0.2 was considered small, 0.5 moderate and 0.8 large (Cohen, 1992). One-way ANOVAs with habitual caffeine intake (low, moderate, high users) as a factor were also employed. Nonparametric ordinal RPE data are reported as median (quartiles) and were analysed using Friedman and Wilcoxon tests. Statistical significance was accepted at $p<0.05$. 
Figure 4.1. Schematic outline of the preloaded time trial (TT) experimental protocol. R=rest, WU=warm-up, HR=heart rate and RPE=ratings of perceived exertion.
4.4 Results

4.4.1. Performance tests

Caffeine significantly improved 10 km TT performance during cycling by 2.0(2.0)% compared to PLA (ES=0.4, \( p=0.033 \)) (995(46) s and 1016(58) s, respectively). Ten (of 11) participants cycled faster during CAF (Figure 4.2). Participants (7 of 11) also handcycled 1.8(3.0)% faster during CAF compared to PLA (1450(86) and 1476(67) s, respectively) (Figure 4.2) however, this failed to reach statistical significance (ES=0.34, \( p=0.153 \)). The CVs were 4.6 and 5.7% for cycling, and 5.9 and 4.3% for handcycling following caffeine and placebo, respectively. There was no significant influence of trial order during cycling (\( p=0.164 \)) or handcycling (\( p=0.298 \)). The PO was significantly greater during CAF compared to PLA during cycling only (\( p=0.003 \)), and this was apparent during the first and last 2 km of the TT (\( p<0.006 \)). Participants’ followed similar pacing strategies during both modes of exercise; the second km was completed at the greatest PO, and the final 2 km end-spurt was evident (Figure 4.3). There was no influence of habitual caffeine intake on TT performance (\( p>0.470 \)). Participant’s with a handcycling \( \dot{V}O_2 \text{peak} \) greater than the mean relative value (27.6 ml·kg·min\(^{-1}\)) (\( n=7, 30.9 \) ml·kg·min\(^{-1}\)) improved their handcycling TT performance by 3.2% whereas those with a \( \dot{V}O_2 \text{peak} \) less than the mean (\( n=4, 21.9 \) ml·kg·min\(^{-1}\)) had a 0.3% reduction in handcycling performance (Figure 4.2).

A significantly lower relative \( \dot{V}O_2 \text{peak} \) was recorded during handcycling compared to cycling (27.6(5.1) and 42.9(7.3) ml·kg·min\(^{-1}\), \( p=0.001 \)). The target relative exercise intensity of the 65% \( \dot{V}O_2 \text{peak} \) during the preload was matched experimentally with average \( \dot{V}O_2 \) values of 64.5(2.5)% during cycling, and 59.7(4.8)% during handcycling but importantly, did not differ between mode-specific CAF and PLA trials (\( p>0.217 \)). Average preload HR and RER did not differ between CAF and PLA (\( p>0.180 \)).

4.4.2. Blood lactate concentration

There was a significant increase in [Bla] over time during all trials (\( p=0.001 \)). This was evident between 10 and 20 min during cycling following CAF only (\( p=0.006 \)), and at both 20 and 30 min compared to 10 min during handcycling following both CAF and PLA (\( p<0.005 \)). The TT resulted in a significant increase in [Bla] post-TT and five min post-TT during all trials (\( p<0.017 \)). The ingestion of CAF resulted in significantly higher [Bla] compared to PLA during cycling (\( p=0.001 \)) and handcycling (\( p=0.007 \)), but differences were
only evident post-TT ($p<0.012$) (Figure 4.4). The handcycling preload (despite a slightly lower relative workload) produced significantly greater [Bla] than during cycling regardless of trial ($p=0.004$ and 0.016 during PLA and CAF, respectively). However, there was no difference in [Bla] pre-exercise or post-TT between modalities ($p>0.134$).
Figure 4.2. Individual change in 10 km (a) cycling and (b) handcycling time trial (TT) performance. Negative bars indicate a reduction in time to complete the TT during caffeine (CAF) compared to placebo (PLA). Open/filled bars indicate participants with a \(\dot{\text{VO}_2}\) peak above (30.9 ml·kg·min\(^{-1}\))/below (21.9 ml·kg·min\(^{-1}\)) the mode-specific mean (27.6 ml·kg·min\(^{-1}\)). Participant data are ordered the same in a and b.
Figure 4.3. Mean power output (W) throughout the 10 km time trial during (a) cycling and (b) handcycling following the consumption of 4 mg·kg\(^{-1}\) caffeine (CAF) or placebo (PLA).

*Significantly different from placebo (PLA) (p<0.05).
Figure 4.4. Group mean(SD) blood lactate concentrations (mmol·L⁻¹) throughout the 30 min preloaded (65% $\dot{V}O_2_{peak}$) 10 km time trial protocol during (a) cycling and (b) handcycling following the consumption of 4 mg·kg⁻¹ caffeine (CAF) or placebo (PLA). *Significantly different from placebo (PLA) ($p<0.05$).
Table 4.1. Overall, central and peripheral ratings of perceived exertion (RPE) at 10, 20 and 30 min during the preload and immediately post-time trial (TT).

<table>
<thead>
<tr>
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<th>Preload 10 min</th>
<th>Preload 20 min</th>
<th>Preload 30 min</th>
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<td>Overall RPE</td>
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<tr>
<td>C PLA</td>
<td>13 (12, 13)</td>
<td>13 (13, 14) †</td>
<td>14 (13, 14) †‡</td>
<td>19 (17, 20) †‡#</td>
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<td>C CAF</td>
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<td>HC CAF</td>
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<td>Central RPE</td>
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<td>C CAF</td>
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<tr>
<td>Peripheral RPE</td>
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<td>C CAF</td>
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<td>HC CAF</td>
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*Note. Data are median (quartiles). *Significantly different from placebo (PLA), † significantly different from Preload 10 min, ‡ significantly different from Preload 20 min and # significantly different from Preload 30 min (p<0.05).*
4.4.3. Subjective measures

Participant’s RPE responses can be seen in Table 4.1. Only one participant, a low caffeine user, experienced side-effects during CAF (cycling), which were reported as feelings of sickness post-preload. Only two participants correctly identified the treatment in all four trials.

4.5 Discussion

This is the first study to assess the effect of caffeine on 10 km TT performance during both cycling and handcycling in habitual caffeine users. The main finding was that the ingestion of caffeine (4 mg·kg⁻¹) significantly improved cycling 10 km TT performance, whereas the same dose did not statistically improve handcycling performance. This study compliments the work of Black et al. (2015) by investigating the influence of caffeine on longer-term endurance performance during LBE (~47 vs. 40 min) and UBE (~54 vs. 40 min). It also supports a large body of evidence on the positive impact of caffeine on endurance cycling performance (Astorino et al., 2012; Black et al., 2015; Cureton et al., 2007; McNaughton et al., 2008).

4.5.1. Preload

The ingestion of CAF resulted in changes in RPE but not average RER, HR or \( \dot{V}O_2 \) during the submaximal preload, which agrees with earlier studies (Bell & McLellan, 2003; Greer et al., 2000). While there was a trend for greater [Bla] during the preload following CAF, in contrast to previous steady state exercise data (Black et al., 2015) this did not reach significance.

Recent reviews on caffeine and its ergogenic effects propose the antagonism of adenosine receptors as the primary mode of action leading to enhanced performance (Ganio et al., 2009; Graham, 2001). This mechanism of action has been shown to influence the CNS (Davis et al., 2002) through which perceived pain, effort and fatigue are reduced. The current results show caffeine to reduce RPE during constant rate LBE and UBE. During cycling, RPEO was lower at all preload time-points and RPEP and RPEC was lower at 20 and 30 min following CAF, respectively. During handcycling, RPEO was lower at 10 and 20 min and RPEP was lower at 30 min only following CAF. The reduction in perceived effort during the preload may have influenced the participant’s effort during the subsequent cycling TT yet appears not to have impacted the handcycling TT.
The higher [Bla] evident during the handcycling (5.55 and 5.14 mmol·l⁻¹) compared to the cycling (3.39 and 2.98 mmol·l⁻¹) preload following caffeine and placebo, respectively (Figure 4.4) is likely a consequence of lower oxidative capacity and greater carbohydrate utilisation (RER=1.04 vs. 0.98 for handcycling and cycling, respectively). The higher preload [Bla] could have influenced subsequent self-paced TT performance and hence a TT with no preload may have elicited a different ergogenic response to caffeine but this is unknown. Future studies could employ a preload at a percentage of lactate threshold rather than VO₂_peak to help limit its impact.

4.5.2. Time trial performance

The 10 km TT provided data from which the influence of caffeine on endurance performance could be assessed in a sport-specific manner. The ingestion of CAF resulted in a significant improvement in cycling performance (2.0(2.0)%) compared to PLA, which was due to the increased PO during the first and last two km. On the other hand, it failed to significantly improve handcycling performance (1.8(3.0)%) and there was large intra-individual variability. The small ESs (-0.4 and -0.34 for cycling and handcycling, respectively) reflect the large standard deviations for both sets of results. Individual responses to caffeine supplementation have often been attributed to differing rates of caffeine metabolism, which may in turn be linked to training status (Skinner et al., 2014). Unfortunately the rate of caffeine absorption and metabolism were not measured in the current study. Participant three, who produced the greatest handcycling VO₂_peak of the group, improved handcycling TT performance by 8.3% following CAF, yet only improved cycling TT performance by 0.2%. Aside from the participant displaying a learning effect or having an unexplained good/bad performance, a further explanation for some of the inter-individual variability may therefore be an individual’s training status. Despite a non-significant finding, some sports practitioners would argue that if a 1.8% improvement held true for individual elite handcyclists, caffeine could positively impact performance and ultimately influence finishing positions in a sport where winning margins are small (~0.5%) (Perret, 2015).

The ingestion of CAF resulted in higher post-TT [Bla] during both modes of exercise. This increase in [Bla] following the ingestion of caffeine is common in the literature during both LBE (Bell & McLellan, 2003) and UBE (Stadheim et al., 2013). The increase is understandable when seen in conjunction with improved performance such as during the current cycling trials, yet remains to be explained when a performance improvement is absent.
as seen during the handcycling trials. The metabolic responses to exercise differ in arm and leg muscles. Arm exercise is physiologically more stressful than leg exercise at a given PO and can increase adrenaline concentration, which in turn is a potent stimulant for muscle glycogenolysis (Hooker et al., 1990). The arms also have a lower oxygen extraction capacity which results in an earlier onset of anaerobic metabolism (~50% and 75% $\text{VO}_2\text{max}$ during arm and leg exercise, respectively) (Pendergast, 1989). Accumulation of [Bla] during the handcycling TT, which was further increased during CAF may have limited the participants’ ability to improve performance.

Evidence from biopsy studies suggest that the triceps muscle (an important force producing muscle during synchronous handcycling) exhibits a greater proportion of type II muscle fibres than the legs (vastus lateralis) (Mizuno et al., 1990; Mygind, 1995). This may partly explain a lack of performance improvement during the endurance handcycling TT (~24 min) during which type I fibres would dominate. Furthermore, type II fibres have been shown (in vitro) to be less sensitive to caffeine compared to type I fibres (Mitumoto et al., 1990). Hence performance gains may be less likely following the ingestion of caffeine during exercise which relies on the arms (with a lower proportion of type I fibres). Endurance training can improve the oxidative capacity of muscle fibres (Gollnick et al., 1972) and hence may help to explain the observed handcycling TT improvements following caffeine in those that had an above average mode-specific $\text{VO}_2\text{peak}$ (Figure 4.2).

Previous research suggests caffeine increases muscular strength (maximal voluntary contraction) and motor unit recruitment in the knee extensors but not in the elbow flexors (Black et al., 2015; Warren et al., 2010). More and larger muscles are recruited during LBE compared to UBE and hence caffeine’s influence on muscle contractility may enhance LBE performance to a greater extent. This potential mechanism is supported by the improvement in cycling but not handcycling TT performance in the current study.

Although RPE was not reduced following the cycling TT, PO was higher during CAF suggesting that participants were able to cycle at a higher PO with no change in RPE. This is in line with previous literature that has shown caffeine to increase PO for a given RPE during a TT (Astorino et al., 2012; Santos et al., 2014). It has previously been suggested that the limitation to maximal UBE is likely due to localised fatigue rather than central circulatory factors (Price & Campbell, 1997). At the end of the handcycling preload (30 min) RPE$_P$ was reduced by CAF but this reduction in perceived arm and shoulder effort did not translate to improvements in TT performance. It has been suggested that caffeine is unable to have a
hypoalgesic effect during heavy-severe fixed intensity exercise (Black et al., 2015), and the same study reported no change in RPE during a 10 min asynchronous UBE performance trial. The current study adds further evidence that the reduced RPE and hypoalgesic effects seen during submaximal synchronous UBE do not translate to improved performance during a maximal performance trial. It is likely that the nociceptive stimuli contributing to the peripheral muscle pain during handcycling may be too great for the antagonism of adenosine receptors to reduce RPE and pain, and hence are unlikely to translate to improved performance.

The \( \dot{V}O_2 \) peak achieved during handcycling was 64% of that achieved during cycling (range: 52-83%), which is similar to previous reports (~70%) (Sawka & Pandolf, 1991). The lower handcycling \( \dot{V}O_2 \) peak is due to the training status of the current participants who were not specifically UBE trained. The use of recreationally trained participants helped to limit the potential difference in performance between the cycling modalities and yet meant that participants were unfamiliar with the pacing strategies required, especially during handcycling. This was evident in that participant’s adopted a similar pacing strategy for both modes of cycling (Figure 4.3). Given the smaller muscle mass involved during handcycling and the lower UBE training status of the participants, a negative pacing strategy whereby speed gradually increases throughout the TT may have been advantageous to prevent early RPE\(_p\). It is worth noting that those with a relative handcycling \( \dot{V}O_2 \) peak above the mean improved their handcycling TT performance by 3.2%, which is much closer to the handcycling group CVs of 5.9 and 4.3% for caffeine and placebo, respectively. Hence the performance improvement seen in these individuals is less likely due to chance. Unfortunately further specific repeatability testing would be required to indicate smallest worthwhile change for future interventions. Whereas participants with a handcycling \( \dot{V}O_2 \) peak below the mean had a 0.3% reduction in performance (Figure 4.2). An individual’s training status may increase the amount of recruitable muscle mass during maximal exercise and it appears to affect how they respond to caffeine during UBE. This theory is supported by improvements in swimming velocity (during which a large proportion of the force is generated by the upper-body) following the ingestion of caffeine by trained but not untrained participants (Collomp et al., 1992). The authors suggested that the intra and/or extracellular adaptations resulting from specific training such as improved buffering capacity are

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necessary to benefit from caffeine during sprint performance (Collomp et al., 1992). The current results suggest that this holds true for endurance UBE performance also.

It has been suggested that one familiarisation session is sufficient for reproducible results in recreationally active individuals (cycling $\dot{V}O_2$peak = 3.9 compared to 3.6 L·min⁻¹ in the current study) completing a preloaded cycling TT (Sewell & McGregor, 2008) but it is unknown whether this is also the case for handcycling. That said, there was no statistical evidence of a trial order effect on cycling or handcycling performance, which suggests that the results cannot be solely attributed to a learning effect.

4.6 Conclusion

Pre-exercise ingestion of caffeine (4 mg·kg⁻¹) significantly improved preloaded cycling 10 km TT performance but there was no statistical improvement in handcycling in habitual caffeine users. The positive effects of caffeine on cycling performance may be related to reductions in RPE during the preload. The lack of a statistical improvement during handcycling is possibly due to elevated [Bla] owing to both the mode of exercise and the ingestion of CAF. Furthermore, participants’ training status appears to influence the ability of caffeine to improve UBE performance.

4.7 Practical applications

The results of the current study confirm caffeine’s ergogenic benefits during cycling endurance performance in recreationally active AB participants, and moderate doses of the supplement can therefore continue to be recommended during this type of event. The use of caffeine prior to endurance handcycling on the other hand should be considered further. The results suggest that it may be advantageous in more UBE trained individuals (e.g. kayak, canoe or wheelchair athletes) but the evidence is still insufficient. Hence, the authors would recommend an ‘n=1’ approach whereby a practitioner would investigate the effects of caffeine on an individual athlete’s performance quantitatively and qualitatively, as seen in Chapter seven.
Study 3: Improvement of sprint performance in wheelchair sportsmen with caffeine

This chapter has been published in a slightly modified form in *International Journal of Sport Physiology and Performance*:

5.1. Abstract

Caffeine can be beneficial during endurance and repeated sprint exercise in AB individuals performing leg or whole-body exercise. However, little evidence exists regarding its effects during UBE. This study therefore aimed to investigate the effects of caffeine on sprint and 4 min maximal push (PUSH) performance in wheelchair sportsmen. Using a double-blind, placebo-controlled, crossover design, 12 male wheelchair rugby players (age 30.0(7.7) y, body mass 69.6(15.3) kg, training hours 11.1(3.5) h·wk⁻¹) completed two exercise trials, separated by 7-14 d, 70 min after ingestion of 4 mg·kg⁻¹ caffeine (CAF) or dextrose placebo (PLA). Each trial consisted of four 4-min PUSH and three sets of 3x20 m sprints (SPR), each separated by 4 min rest. Participants reported Felt arousal (a measure of perceived arousal), Feeling (a measure of the affective dimension of pleasure-displeasure) and RPE using subjective scales. Salivary caffeine secretion rates were measured. Average SPR times were faster during CAF relative to PLA during SPR1 and SPR2 ($p=0.037$ and $0.016$). There was no influence of supplementation on PUSH2-4 ($p>0.099$) however, participants pushed significantly further during PUSH1 following CAF relative to PLA (mean(SD), 677(107) and 653(118) m, $p=0.047$). There was no influence of CAF on arousal or RPE scores ($p>0.132$). Feeling scores improved over the course of the CAF trial only ($p=0.017$) but did not significantly differ between trials ($p>0.167$). Pre-warm-up (45 min post-ingestion) salivary caffeine secretion rates were 1.05(0.94) and 0.08(0.05) µg·min⁻¹ for CAF and PLA, respectively. Acute caffeine supplementation can improve both 20 m sprint performance and a one-off bout of short-term high intensity performance in wheelchair sportsmen.
5.2. Introduction

Since its removal from the WADA list of prohibited substances in 2004, there has been substantial research into the effects of caffeine on exercise performance. Low-moderate doses of caffeine (3-6 mg·kg\(^{-1}\); 210-420 mg for a 70 kg individual) typically ingested 60 min before exercise have been shown to have a beneficial effect on both short-term, high intensity (Astorino et al., 2010) and endurance (Burke, 2008; Ganio et al., 2009) performance. The available evidence on repeated sprint (running) performance also appears to support the use of caffeine (Carr & Dawson, 2008; Glaister et al., 2008).

Caffeine’s effects are wide ranging but a possible mechanism for its ergogenic effect relates to its influence on the CNS. Caffeine is a lipid soluble molecule which can pass through cell membranes and importantly cross the blood-brain barrier. Caffeine is structurally similar to adenosine and can therefore act as an adenosine (most likely A\(_1\) and A\(_2A\)) receptor antagonist (Fredholm et al., 1999) thereby reducing the influence of adenosine and producing motor-activating and arousing effects. Adenosine receptor antagonism may also act by increasing the turnover of some neurotransmitters (e.g. adrenaline and noradrenaline) resulting in the central stimulatory effects seen following the ingestion of caffeine (Fredholm et al., 1999). The exact mechanisms explaining caffeine’s beneficial effects in humans remain unknown however, non-selective adenosine antagonism has received much support in recent years. It has been suggested that certain participant/athlete characteristics such as genetics (Cornelis et al., 2007), training status (Collomp et al., 1992), impairment (Flueck et al., 2014) and an individual’s habitual intake (Bell & McLellan, 2002) may affect how they respond to caffeine. An individual’s response will also depend on the duration, intensity and time of caffeine ingestion, and the mode of exercise.

The majority of the aforementioned studies have employed running or cycling exercise modalities in which the leg musculature provides the speed-generating force. The physiological responses to these modes of exercise differ to those of UBE (Pendergast, 1989) which is largely due to the smaller skeletal muscle mass used. The response to UBE in individuals with an impairment such as a SCI also differs to AB individuals due to the amount of active muscle mass available, (Maggioni et al., 2003) the distribution of muscle fibre types (Schantz et al., 1997) and the potential issue of prolonged GI transit times (Williams et al., 2012). Consequently, it may not be possible to directly transfer the findings from AB running/cycling exercise modalities to individuals with a physical impairment performing UBE. However, given that the potential mechanism of action for performance
enhancement following caffeine ingestion is the same in individuals with an impairment, a similar ergogenic benefit could be expected during UBE. Use of NS is common among athletes with an impairment (Chapter three) and yet data investigating their efficacy in this population is scarce (Table 2.3 and 2.4). Aside from an uncertainty whether caffeine is beneficial in this population, a lack of evidence raises concern given the potential for, or more acute sensitivity to side-effects in some sportspeople with a physical impairment (Van de Vliet et al., 2011).

The influence of caffeine on subjective feelings and mood has also been investigated in AB participants whereby low to moderate doses of caffeine appear to improve mood and increase arousal (Smit & Rogers, 2000). A meta-analysis also revealed that caffeine can reduce RPE during exercise (Doherty & Smith, 2005). These factors, in part, contribute to the performance-enhancing effects seen during various exercise modalities but have not been investigated during UBE in a physically impaired population. For this reason, the current study employed both the Feeling (Hardy & Rejeski, 1989) and Felt arousal (Svebak & Murgatroyd, 1985) scales to assess the influence of caffeine on feelings of pleasure/displeasure and perceived arousal pre-, during and post-exercise. Both scales were validated using student populations and have since been regularly used in the caffeine and exercise literature (Ali et al., 2016; Richardson & Clarke, 2016).

Given the dearth of evidence in the area of caffeine and UBE, this study aimed to determine the effects of caffeine supplementation on aspects of wheelchair sports performance. Wheelchair sports such as rugby, basketball and tennis are intermittent in nature and require short bursts of high intensity movements superimposed on a background of aerobic activity. The current study employed previously used wheelchair sport field tests (West et al., 2014; Yilla & Sherril, 1998) to assess both sprint and short-term, high intensity exercise performance.

5.3 Methods

5.3.1. Participants

Twelve male wheelchair rugby players (mean(SD)): age 30.0(7.7) y, body mass 69.6(15.3) kg, wheelchair rugby experience 6.7(6.0) y, and training hours 11.1(3.5) h·wk⁻¹, volunteered to participate in this study. Participants impairments were cervical level SCI (n=7), cerebral palsy (n=2), osteogenesis imperfecta (n=1), distal weakness of limbs (n=1) and vanishing white matter disease (n=1). The participant’s wheelchair rugby classifications ranged from 0.5-3. A health screening questionnaire was completed by all participants to
ensure they were free from any injury or illness which may have prevented them from safely completing the protocol. Average daily caffeine intake was assessed using a standardised caffeine consumption questionnaire (Landrum, 1992). All procedures were approved by the local Ethical Advisory Committee and performed following the Declaration of Helsinki. Informed consent was obtained from all participants included in the study.

5.3.2. Experimental design

A double-blind, placebo-controlled, randomised, cross-over design was employed. Participants performed two experimental trials separated by 7-14 d. All data collection occurred at the wheelchair sportsmen’s training venues, which was standardised within participants.

5.3.3. Preliminary testing

During the familiarisation session participants’ body mass was measured to the nearest 0.1 kg, using wheelchair beam scales (Marsden MPWS-300, Henley-on-Thames, UK). Participants were familiarised to the experimental testing procedures by completing: three 20 m sprint tests (SPR), at least two 4-min maximal pushes (PUSH) and a 3-min saliva sample collection. Participants were also familiarised with the Feeling (Hardy & Rejeski, 1989), Felt arousal (Svebak & Murgatroyd, 1985) and Borg 6-20 RPE scales (Borg, 1998).

5.3.4. Experimental trials

Participants were asked to refrain from caffeine consumption in the 48 h, and from exercise and alcohol consumption in the 24 h preceding each trial. Participants were asked to complete a 24 h food diary prior to the first experimental trial and to replicate this prior to the second. Participants were asked to consume only water in the hour preceding each trial to help reduce the influence of eating on the saliva sampling procedure. Upon arrival at the testing venue participants responded to the Feeling and Felt arousal scales. Participants provided a pre-capsule 3-min saliva sample via the passive dribble method (Leicht et al., 2012) prior to ingesting placebo (PLA) (4 mg·kg⁻¹ dextrose) or caffeine (CAF) (4 mg·kg⁻¹) (My Protein, Northwich, UK). Both CAF and PLA were consumed in powder form in cellulose capsules (G & G Food Supplies Ltd, West Sussex, UK).

Participants then rested and prepared for exercise (wheelchair set-up, gloves, standardisation of wheel tyre pressure, clothing, bladder voiding etc) for 45 min prior to repeating the two perceptual scales and 3-min saliva collection pre-warm-up. A standardised 20-min warm-up was started at 50 min and completed prior to the performance tests: three
SPR sets and four PUSH (alternate anti-clockwise and clockwise), each with a 4-min rest in-between (Figure 5.1). The two perceptual scales and saliva collection were repeated immediately post-exercise. Participants were also asked whether they had experienced any side-effects during the protocol and to indicate which trial they believed they were on. Participants were permitted to consume only water ad libitum throughout each trial. Environmental conditions across the two training venues were: temperature 20.9(2.4°C), humidity 45(8)% and pressure 999(110) hPa.

The SPR performance test was adapted from West et al. (2014). From a stationary position participants were asked to sprint through 20 m. Times to complete the SPR were recorded using wireless timing gates (Brower, Utah, USA) at 0 and 20 m. Participants were given ~30 s to recover in-between each SPR. One SPR set was composed of three single SPR.

For the PUSH test, markers were placed every 2 m (1.5 m at the corners) to produce a rectangle with rounded corners and to enable the total distance covered to be recorded (One lap=72 m). Participants self-selected their speed with the goal of covering the greatest distance possible in 4 min. Communication between participants was encouraged to ensure overtaking was completed efficiently. Verbal encouragement was provided throughout all experimental trials by the same investigators, all of whom were blind to which trial the participants were completing. Participants were blinded to their results.

Subjective feelings were assessed using the Feeling scale (Hardy & Rejeski, 1989) and the Felt Arousal scale (Svebak & Murgatroyd, 1985). The Feeling scale assessed the participant’s mood on a scale of +5 (Very good) to -5 (Very bad). The Felt arousal scale was used to assess how aroused a participant was on a scale of 1 (Low arousal) to 6 (High arousal). The Borg 6-20 (Borg, 1998) category scale was used to attain participants’ overall RPE scores following each PUSH and SPR set.
Figure 5.1. Schematic of the experimental trial protocol.
5.3.5. Saliva collection and analyses

For analysis, samples were weighed to the nearest 10 mg. Saliva volume was estimated assuming saliva density to be 1.00 g·ml⁻¹, and saliva flow rate was calculated from saliva volume and collection time. Saliva samples were transferred into Eppendorfs and centrifuged at 12,000 rpm for 3 min in a high speed microcentrifuge. Salivary caffeine concentration was determined using a commercially available kit (Emit Caffeine Assay, Dade-Behring, Milton Keynes, UK) and a microplate reader (Opsys MR, Dynex Technologies, Chantilly, USA) (see Appendix B). The intra-assay coefficient of variation for salivary caffeine concentration was 3.5%. Salivary caffeine secretion rates were subsequently calculated by multiplying caffeine concentration by saliva flow rate due to the high variability in saliva flow in this population (Leicht et al., 2012).

5.3.6. Statistical analyses

The Statistical Package for the Social Sciences version 20 software (SPSS Inc., Chicago, IL) was used to analyse the data. Distance per PUSH and total PUSH distance (sum of all four PUSH) were calculated. Total SPR time (all 9 sprints) and average SPR time for each set was calculated. Normal distribution of the outcome variables was confirmed by the Shapiro-Wilk test for PUSH and therefore data are reported as mean(SD). Subsequently, a repeated measures 2 x 4 (trial x time) ANOVA was used to analyse all PUSH data. To assess the effect of caffeine on each individual PUSH and total PUSH, paired samples t-tests were employed. Non-normally distributed SPR data and ordinal Felt arousal, Feeling and RPE scales are reported as median (quartiles) and were analysed using Friedman and Wilcoxon tests. Statistical significance was accepted at $p<0.05$.

5.4 Results

5.4.1. Performance tests

Average 20 m SPR times were significantly faster during CAF compared to PLA during SPR1 and SPR2 ($p=0.037$ and 0.016, respectively) (Figure 5.2). Total SPR time was significantly faster during CAF compared to PLA (61.2 (58.5, 68.6) and 62.5 (58.5, 69.7) s, respectively) ($p=0.006$). Ten (of 12) participants produced faster total SPR times. Times did not significantly change between SPR sets during CAF or PLA ($p=0.254$ and 0.212).

There was no significant difference in PUSH distance between CAF and PLA ($p=0.111$), nor did it differ over the course of the protocol in either trial (PUSH1, 2, 3 and 4) ($p=0.864$). However, participants did cover more distance during PUSH1 during CAF (677(107) m)
compared to PLA (653(118) m) \( (p=0.047) \) (Figure 5.3). Total PUSH distance was not significantly different between supplementation (2686(416) m) and PLA (2634(392) m) \( (p=0.111) \). Overall, seven participants covered a greater total PUSH distance during CAF compared to PLA.

**5.4.2. Subjective feelings**

Felt arousal \( (p=0.001 \) and 0.006 for CAF and PLA, respectively), SPR RPE scores \( (p=0.002 \) and <0.001 for CAF and PLA, respectively) and PUSH RPE scores \( (p<0.001 \) and 0.015 for CAF and PLA, respectively) increased progressively over the course of each trial but there was no significant effect of CAF \( (p>0.132) \) (Table 5.1 and 5.2). Feeling scores improved significantly over the course of the CAF trial \( (p=0.017) \), but not during PLA \( (p=0.197) \), and this occurred pre-capsule (0 (0, 3)) to post-exercise (3 (2, 3)) \( (p=0.041) \) (Table 5.1). Side-effects during CAF including increased spasticity, struggling with decision making, headaches (also experienced during PLA) and nausea were reported by five participants. Trial order was correctly identified by seven participants. Mean(SD) daily caffeine intake was 211(201) mg/d. No participant reported experiencing a prior adverse reaction to caffeine. Three participants reported the regular use of caffeine supplementation (80-220 mg) in capsule format prior to training or competition (supplementation was not included in daily intake data).

**5.4.3. Salivary caffeine**

Salivary caffeine analysis revealed that participants followed the 48 h caffeine withdrawal procedure prior to both PLA (0.06(0.06) \( \mu g \cdot min^{-1} \)) and CAF (0.13(0.17) \( \mu g \cdot min^{-1} \)) (Figure 5.4) and these did not differ \( (p=0.201) \). The consumption of CAF caused an increase in salivary caffeine secretion rates pre-warm-up (1.05(0.94) \( \mu g \cdot min^{-1} \)) \( (p=0.009) \) and post-exercise (1.34(1.09) \( \mu g \cdot min^{-1} \)) \( (p=0.003) \).
Figure 5.2. The effects of caffeine supplementation (CAF) on 20 m sprint performance (3 sprints per set). All data are median (quartiles). *Significantly different from placebo (PLA) ($p<0.05$).

Figure 5.3. The effects of caffeine supplementation (CAF) on 4-min maximal push (PUSH) distance. Data are mean(SD). *Significantly different from placebo (PLA) ($p<0.05$).
**Table 5.1.** Felt arousal and Feeling scale responses pre-capsule, pre-warm-up and post-exercise (n=12).

<table>
<thead>
<tr>
<th></th>
<th>PLA</th>
<th>CAF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Felt arousal scale</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-capsule</td>
<td>2.5 (2.0, 3.0)</td>
<td>2.0 (1.5, 3.0)</td>
</tr>
<tr>
<td>Pre-warm-up</td>
<td>3.0 (2.5, 4.0) †</td>
<td>3.5 (3.0, 4.0) †</td>
</tr>
<tr>
<td>Post-exercise</td>
<td>4.0 (3.5, 4.0) †</td>
<td>4.0 (3.0, 5) †</td>
</tr>
<tr>
<td><strong>Feeling scale</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-capsule</td>
<td>2.0 (0.0, 3.0)</td>
<td>0.0 (0.0, 2.5)</td>
</tr>
<tr>
<td>Pre-warm-up</td>
<td>2.0 (1.0, 3.0)</td>
<td>3.0 (1.0, 3.0)</td>
</tr>
<tr>
<td>Post-exercise</td>
<td>3.0 (1.0, 4.0)</td>
<td>3.0 (2.5, 3.0) †</td>
</tr>
</tbody>
</table>

*Note. Data are median (quartiles) to the nearest 0.5. †Significantly different from pre-capsule (p≤0.05).*

**Table 5.2.** Ratings of Perceived Exertion (RPE) immediately post each sprint set (SPR) and 4-min maximal push (PUSH) (n=12).

<table>
<thead>
<tr>
<th></th>
<th>PLA</th>
<th>CAF</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPR1</td>
<td>12 (9,14)</td>
<td>12 (11,13)</td>
</tr>
<tr>
<td>SPR2</td>
<td>13 (10,15) †</td>
<td>14 (12,14) †</td>
</tr>
<tr>
<td>SPR3</td>
<td>14 (11,16) †‡</td>
<td>14 (10,15) †</td>
</tr>
<tr>
<td>PUSH1</td>
<td>16 (13,19)</td>
<td>15 (15,17)</td>
</tr>
<tr>
<td>PUSH2</td>
<td>17 (15,18) †</td>
<td>18 (15,19) †</td>
</tr>
<tr>
<td>PUSH3</td>
<td>17 (16,17) †</td>
<td>17 (16,18) †</td>
</tr>
<tr>
<td>PUSH4</td>
<td>18 (16,19) †*</td>
<td>18 (17,19) †‡*</td>
</tr>
</tbody>
</table>

*Note. Data are median (quartiles). †Significantly different from (set) 1, ‡Significantly different from SPR2 and *significantly different from SPR3 (p≤0.05).*
Figure 5.4. Individual participants’ salivary caffeine secretion rates pre-capsule (0 min), pre-warm-up (45 min) and post-exercise (2 h) (n=12) following (a) placebo and (b) 4 mg·kg⁻¹ caffeine. Dotted/full lines indicate participants with/without a spinal cord injury.
5.5 Discussion

The current study demonstrates that the consumption of 4 mg·kg\(^{-1}\) caffeine can improve wheelchair sprint performance. On the other hand, caffeine did not significantly influence PUSH performance in wheelchair sportsmen. The following paragraphs will discuss the potential reasons behind these results.

5.5.1. Sprint performance

Caffeine improved repeated sprint performance in athletes with a physical impairment, which was apparent in the first and second SPR sets but not the third (Figure 5.2). This corroborates previous research in AB individuals that has shown initial improvements in performance following caffeine ingestion with a subsequent null or negative influence on latter bouts (Glaister et al., 2008; Greer et al., 1998; Santos et al., 2014). Faster 30 m sprint times in the first three (of 12) sprints following 5 mg·kg\(^{-1}\) caffeine supplementation has previously been reported (Glaister et al., 2008). The authors hypothesised that the mechanism responsible for this initial improvement was a CNS effect mediated by antagonism of adenosine receptors. A CNS effect may also be responsible for the current study results in which participants produced faster average and total SPR times. These improvements are small yet meaningful for individuals competing in intermittent sports as they may allow a player to lead their opponent in a sprint situation and therefore meet the ball, player or line faster.

The effects of caffeine (5 mg·kg\(^{-1}\)) on performance in simulated-contest taekwondo has been investigated, whereby athletes performed two combats (3 x 2 min rounds with 1 min rest periods) separated by 20 min (Santos et al., 2014). The ingestion of caffeine i) improved reaction times before the first combat, ii) increased the intensity of round one, and iii) maintained the intensity observed in the first combat in the second (Santos et al., 2014). These findings provide support for the initial performance improvements seen during SPR1 and SPR2 in the current study. Participants were able to push faster in the first two SPR sets which potentially led to the development of fatigue, and contributed to a lack of subsequent performance improvement. Caffeine may therefore result in a performance improvement initially yet lead to a lack of improvement or decrement in successive exercise bouts.

5.5.2. PUSH performance

Interestingly, the same initial performance improvement was also observed in the PUSH results (Figure 5.3) despite no overall significant effect of supplementation.
Participants benefited from caffeine for a one-off performance, covering a greater distance during PUSH1, yet failed to show improvements in PUSH2, 3 or 4 compared to PLA. Previous research investigated the use of caffeine prior to two 200 m freestyle TTs (~2 min duration) separated by 30 min rest (Pruscino et al., 2008). The authors revealed that caffeine improved performance in TT1 ($p=0.027$) but participants swam 0.9(1.1)% slower in TT2 following caffeine compared to placebo and the conclusion was that the initial effort during TT1 may have hindered performance in TT2 (Pruscino et al., 2008). This may also be true for the current PUSH results. However, another study reported opposing findings whereby caffeine improved 100 m swim times in trained participants and prevented a drop in performance during a second 100 m swim (20 min passive recovery) (Collomp et al., 1992). The race distance (200 vs. 100 m), caffeine dose (~6.2 vs. ~4.3 mg·kg$^{-1}$) and recovery time (30 vs. 20 min) may help explain the differing results in these aforementioned studies.

5.5.3. Gastrointestinal issues

Gastrointestinal emptying and transit times can be delayed in individuals with a SCI (Williams et al., 2012) and this may be more prominent in those with a high lesion level (Kao et al., 1999) such as those in the current study (7 of 12 participants with tetraplegia). The pre-warm-up (45 min post-ingestion) saliva results suggest that 45 min may be inadequate time to develop sufficient caffeine concentrations in some participants with a physical impairment (Figure 5.4). However, the participants then prepared for exercise and performed a 20 min warm-up prior to the performance tests. The early performance improvements in SPR1 and 2, and PUSH1 indicate that the supplement was absorbed prior to the start of these tests (70 min post-ingestion). The only current study to investigate caffeine use in wheelchair athletes, showed no improvement in 1500 m performance (~3 min duration) following the ingestion of 6 mg·kg$^{-1}$ caffeine, 60 min prior to exercise (Flueck et al., 2014). The authors did not measure caffeine concentration and therefore could not use this measure to help explain their results (Flueck et al., 2014). The promising finding however was that 4 (of 9) participants produced their fastest times in the caffeine trial compared to three other conditions (placebo, sodium citrate and a combination of both). Furthermore, the current results suggest that the 60 min absorption time employed by Flueck et al. (2015) may have been sufficient for their athletes with paraplegia and spina bifida to produce these individual results. In support of this, Van Soeren et al. (1996) suggested that the time to $C_{\text{max}}$ (6 mg·kg$^{-1}$) in individuals with tetraplegia did not differ to those of AB individuals. Given the large inter-individuality highlighted by
the salivary caffeine results, the time course for caffeine absorption in individuals with a SCI, especially those with tetraplegia should be further explored.

5.5.4. Subjective feelings

The side-effects reported by five participants were similar to those reported in AB participants, which include muscle trembling and shakiness/jitters but were described as ‘increased spasticity’ by those with a SCI or cerebral palsy. These side-effects occurred despite a relatively moderate dose of 4 mg·kg\(^{-1}\) caffeine administered in this study compared to often larger doses of 5-10 mg·kg\(^{-1}\) in the AB literature. Interestingly, the reported side-effects occurred in two of the three participants who reported the use of caffeine supplementation prior to training/competition. The dose of 4 mg·kg\(^{-1}\) was greater (1.5-2 times more) than their usual intake, which may explain the incidence of side-effects in these individuals. This highlights the need to consider caffeine dose on an individual basis. It is likely that experiencing such issues during exercise could limit performance however; there was no link between those that experienced side-effects and those that did/did not improve.

Despite the reported side-effects during CAF, Feeling scores improved over the course of the trial following ingestion of the supplement. The psychostimulatory effect of caffeine is common (Smit & Rogers, 2000) and may have contributed to the improved SPR performance. Other common findings include increased arousal and an altered perceptual response following the ingestion of caffeine (Doherty & Smith, 2005), neither of which were apparent in the current study. However, an absence of significant changes in RPE were seen in conjunction with a greater distance covered during PUSH1 and faster SPR times during CAF, which may suggest that the supplement influenced perceptual responses to some extent. The ability to successfully determine CAF or PLA is common in the caffeine literature due to familiar side-effects (e.g. jitteriness and energetic sensations). In the current study only seven participants correctly identified both trials, which increased the authors’ confidence that the NS is responsible for the reported performance improvements.

5.5.5. Limitations

A relatively small sample size was used and participants had a variety of physical impairments, hence the findings can only be generalised to the sport not to a specific impairment. As with all on court testing, a combination of factors associated with the participant, the wheelchair and the interfacing between the two may also have influenced performance, especially during cornering in the PUSH during which a high element of skill was required. Given the nature of field study protocols, the participants also performed in the
presence of external interference (e.g., participant’s, coaches and researchers) which may have influenced performance. An attempt to minimise this influence was employed; participants performed the PUSH protocol with the same fellow participants where possible, participants were motivated by the same investigators, and they were blind to their results.

5.6 Conclusion
This study supports the beneficial effects of caffeine on sprint performance and on a one-off bout of short-term high intensity exercise in wheelchair sportsmen. The findings provide some support for the psychostimulatory effect of caffeine seen as improved Feeling scores and yet the supplement did not improve participant’s RPE or arousal scores. The combination of side-effects and potentially delayed caffeine absorption highlights that its use in persons with a physical impairment is highly individual.

5.7 Practical applications
The study protocol utilised moderately trained (club level) wheelchair rugby players performing in their own sports wheelchairs, and reflected real-life pre-training/competition nutrition and hydration practices. Athletes taking part in, and coaches working with similar intermittent wheelchair sports now have some evidence to show that caffeine supplementation can be beneficial during wheelchair sprinting. The measurement of salivary caffeine concentrations highlighted considerations for the timing of caffeine supplementation in individuals with a physical impairment. Caffeine should therefore be trialled on an individual basis by wheelchair sportsmen (especially individuals with a SCI) and should initially utilise low doses of 1-3 mg·kg⁻¹ at least 60-70 min prior to exercise.
Study 4: Does caffeine absorption differ in individuals with a spinal cord injury?

This chapter has been published in a slightly modified form in *Medicine and Science in Sports and Exercise*:

6.1. Abstract

Delayed GI transit times and therefore the time required to reach a therapeutic dose following the oral ingestion of some drugs has been reported in individuals with a SCI. Large inter-individual variability in the effects of caffeine on performance in individuals with a SCI may be linked to this delayed absorption. Therefore, this study aimed to investigate whether the absorption curve and acute effects of caffeine at rest varies in individuals with different SCI lesion levels. With institutional ethics approval 24 healthy males (8 AB, 8 individuals with paraplegia (PARA) and 8 with tetraplegia (TETRA)) consumed 3 mg·kg⁻¹ caffeine (CAF) in a fasted state. The [CAF], glucose, lactate, free-fatty acid [FFA] and catecholamine concentrations were measured during a 150 min rest period. A greater C_max was apparent in TETRA (21.5 µM) compared to AB (12.2 µM) and PARA (15.1 µM), and mean time to C_max occurred at 70, 80 and 80 min, respectively. Moderate and large ESs were revealed for TETRA compared to PARA (0.55) and AB (1.14) for the total area under the [CAF] versus time curve. Large inter-individual responses were apparent within both SCI groups. The change in plasma catecholamine concentrations following CAF did not reach significance (p>0.05) however both adrenaline and noradrenaline concentrations were lowest in TETRA. Significant increases in [FFA] were seen over time (p<0.0005) but there was no significant influence of SCI level. Participants’ [Bla] reduced over time (p=0.022) whereas [GLU] did not change (p=0.695), and no difference between groups was apparent (p>0.05). The results suggest that SCI level does influence the pattern of the caffeine absorption curve, and there was large inter-individual variation within and between groups. Individual curves should be considered when using caffeine as an ergogenic aid. Low doses should be trialled in training by TETRA, and PARA may consider consuming caffeine greater than 60 min prior to exercise performance. The study also supports caffeine’s direct effect on adipose tissue, which is not secondary to catecholamine release.
6.2. Introduction

Supplementation with caffeine (3-6 mg·kg\(^{-1}\)) can improve long and short-term endurance performance (Ganio et al., 2009; Graham, 2001) in AB participants. However, there is a paucity of research on the effects of caffeine on exercise performance in physically impaired populations (Table 2.3 and 2.4). While current evidence is equivocal, an inconsistent beneficial effect of caffeine (4-6 mg·kg\(^{-1}\) in capsule form) on short-term wheelchair propulsion performance has been reported (Flueck et al., 2014; Chapter five). These studies highlighted that there was great inter-individual variability in wheelchair performance responses during a 1500 m TT, 4 min maximal push and repeated sprints, especially in individuals with a SCI. The authors highlighted the potential for slower caffeine absorption due to delayed GI transit times and prolonged GE, especially in those with a cervical lesion level (Kao et al., 1999). Understanding an individual’s time to C\(_{\text{max}}\) has been shown to have little impact on prolonged AB endurance cycling performance (Skinner et al., 2013) but is likely to be important prior to short-term exercise, and may require further consideration in persons with a SCI.

Both metabolic and physiological functions are altered in individuals with a SCI, and the level and completeness of injury has been shown to influence drug pharmacokinetics (Halstead et al., 1985; Mestre et al., 2011). A review of the literature by Mestre et al. (2011) indicated that the delayed absorption seen in some individuals with a SCI increased the time to achieve the required therapeutic dose. One drug reportedly affected by delayed GE and decreased GI motility is theophylline (Segal et al., 1986), which can be used by individuals with a SCI to help treat bradycardia. Diminished bioavailability could result in underestimating the load and maintenance dose of theophylline in individuals with tetraplegia (Segal et al., 1986). As a methylxanthine drug, theophylline has similar pharmacodynamic actions to caffeine (Raguso et al., 1996) and it has also been linked to improved endurance performance (Greer et al., 2000; Marsh et al., 1993). There is therefore reason to believe that caffeine absorption may also be delayed in persons with a SCI. In disagreement however, Van Soeren et al. (1996) suggested that the time to C\(_{\text{max}}\) (6 mg·kg\(^{-1}\)) in individuals with tetraplegia (~47 µM at 40 min (n=6)) did not differ to those of AB individuals. The authors however could not assess the influence of SCI lesion level on caffeine absorption because there was no direct control group and only two individuals with paraplegia. They also did not report individual participant data, which may help to explain inter-individual performance responses. Flueck et al. (2015) measured median [CAF] at 60 min only following 6 mg·kg\(^{-1}\)
caffeine in AB individuals (45.1 µmol·L⁻¹) and individuals with paraplegia (~54.0 µmol·L⁻¹) and tetraplegia (66.1 µmol·L⁻¹). With only a single measurement of [CAF] it remains difficult to determine whether the time course of caffeine absorption differs based on an individual’s SCI lesion level but it is evident that the absolute [CAF] differs.

Numerous mechanisms of action have been proposed to explain the beneficial effects of an acute dose of caffeine on exercise performance. Current research suggests the main mechanism at physiological caffeine doses is the blockade of central nervous system (CNS) adenosine receptors, which indirectly affects neurotransmitter release (Keisler & Armsey, 2006) to increase arousal, alertness and attention. Individuals with tetraplegia are therefore an interesting study population given the reduced sympathetic activity caudal to the lesion level and associated impaired catecholamine response (Paulson et al., 2013b; Table 2.5). The study of this population has lent support to the hypothesis that caffeine can have a direct effect on tissues following reports of adrenaline-independent FFA mobilisation (see Table 2.5). No study has directly investigated the acute effects of caffeine in a group of individuals with paraplegia and tetraplegia, as well as a non-SCI control group. Hence, the current study aimed to explore the time course of caffeine absorption and its effects at rest in these three groups, with the aim of providing safe and accurate recommendations for its use as an ergogenic aid by individuals with a SCI.

6.3. Methods

6.3.1. Participants

Twenty-four recreationally active males (8 AB controls, 8 individuals with paraplegia (PARA) and 8 with tetraplegia (TETRA)) provided informed consent to participate in the current study. Participants were classified using the American Spinal Injury Association (ASIA) impairment scale (Kirschblauem et al., 2011). A health screening questionnaire was completed by all participants and individuals were excluded if any of their medication had known interactions with caffeine. Average daily caffeine intake was assessed using a modified version of the caffeine consumption questionnaire (Landrum, 1992). All procedures were approved by the University Ethical Advisory Committee and performed following the Declaration of Helsinki. Participants’ characteristics are shown in Table 6.1.
6.3.2. Experimental design

The study followed a cross-sectional, repeated measures design whereby participants were naturally placed into groups based on their SCI lesion level. Participants visited the laboratory only once and were aware of the caffeine dose being consumed.

6.3.3. Experimental trials

In the days prior to visiting the laboratory, participants maintained their normal dietary and activity patterns (light-moderate exercise only) and their individual medication regimes. Participants were provided with a list of caffeine containing foods and drinks, and were asked to abstain from consumption in the 36 h preceding their laboratory visit. Participants were also asked to refrain from alcohol consumption for 24 h prior to their visit. Participants arrived at the laboratory between 08:00-10.00 following an overnight fast (no food intake after 21:00). Water consumption was encouraged to help ensure the participant arrived euhydrated. On arrival participants were asked to void their bladder, if necessary, prior to lying in a semi-supine position on a laboratory bed. Participants were asked to report any side-effects to the investigators immediately at any point during the trial. A cannula (Venflon, Becton Dickinson, Helsingborg, Sweden) was inserted into an antecubital vein for subsequent venous sampling. The cannula was kept patent using 5-10 ml sodium chloride (0.9%) after each blood sample.

After a minimum of 15 min rest, a baseline venous blood sample was taken. Participants then consumed cellulose capsules (Bulk Powders, Colchester, UK) containing 3 mg·kg⁻¹ caffeine (My Protein, Northwich, UK). Participants remained rested for 150 min during which a further 9 blood samples were taken. The blood sampling schedule can be seen in Figure 6.1. After the final blood sample, participants were asked once more whether they experienced any side-effects during the experimental trial.
Table 6.1. Participants’ characteristics

<table>
<thead>
<tr>
<th></th>
<th>AB (n=8)</th>
<th>PARA (n=8)</th>
<th>TETRA (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>25(4)</td>
<td>38(10) †</td>
<td>33(9)</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>83.2(9.8)</td>
<td>74.5(12.9)</td>
<td>73.2(9.8)</td>
</tr>
<tr>
<td>Lesion level</td>
<td>n/a</td>
<td>T4-L1</td>
<td>C5-7</td>
</tr>
<tr>
<td>ASIA A/B</td>
<td>n/a</td>
<td>3/5</td>
<td>2/6</td>
</tr>
<tr>
<td>Time since injury (y)</td>
<td>n/a</td>
<td>4.3(4.3)</td>
<td>12.2(0.3) ‡</td>
</tr>
<tr>
<td>Habitual caffeine intake (mg·d⁻¹)</td>
<td>218(157)</td>
<td>220(145)</td>
<td>224(140)</td>
</tr>
<tr>
<td>Low/moderate/high group</td>
<td>2/2/4</td>
<td>1/4/3</td>
<td>1/4/3</td>
</tr>
<tr>
<td>Use of caffeine as a performance aid</td>
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<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

Notes: Data presented as mean(SD). AB=Able-bodied, ASIA=American spinal injury association impairment scale, C=cervical, L=lumbar, PARA=individuals with paraplegia, TETRA=individuals with tetraplegia, S=sacral and T=thoracic. Low <50 mg·d⁻¹, moderate 50-250 mg·d⁻¹ and high >250 mg·d⁻¹. †Significantly different from AB, ‡significantly different from PARA (p<0.05).
Figure 6.1. Schematic of the experimental protocol
6.3.4. Blood analysis

At every sampling time-point 5 ml blood was added to an EDTA K2 vacutainer for subsequent [CAF] analysis. A 20 µl blood sample was removed and analysed in duplicate for [Bla] and glucose ([GLU]) concentrations using an automatic analyser (Biosen C-Line, EKF Diagnostic GmbH, Barleben, Germany). For catecholamine and FFA analysis (baseline, 60, 90 and 150 min), a further 10 ml of blood was dispensed into two lithium-heparin tubes containing 37.5 µl of EGTA-Glutathione for the subsequent analysis of plasma adrenaline ([A]), noradrenaline ([NA]) and FFA ([FFA]) concentrations. In addition, 25 µl of 3 mg·ml⁻¹ tetrahydrolipstatin (THL) was added to the tube for [FFA] analysis. All tubes were centrifuged at 1000g for 10 min at 4°C. Plasma samples were aliquoted into Eppendorfs and stored at -80°C until analysis.

Analysis of [CAF] was performed using reverse-phase high-performance liquid chromatography (HPLC) as described by Holland et al. (1991) with the following minor modifications; prior to injection onto the HPLC column each sample was individually filtered (Mini-UniPrep syringeless filters, Fisher Scientific, UK) and no guard column was used (see Appendix C). The method produced a coefficient of variation (CV) of 1.06% (range 0.24-1.45%).

Plasma [A] and [NA] were also determined using HPLC as previously described by Forster & Macdonald, (1999). A plasma volume of 500 µl was used for analysis. The method produced CVs of 0.31 and 0.17% for [A] and [NA] respectively. Plasma was analysed enzymatically for [FFA] using an in vitro enzymatic colorimetric method (Wako Instrument kit) and a Pentra 400 analyser (Horiba Medical, California, USA). The method produced an intra-assay CV of 1.68 and 1.28% for high and low FFA quality controls (QC) (4 repeats of the QC samples at intervals during the analysis). Plasma [A], [NA] and [FFA] analysis was performed by qualified personnel at the University of Nottingham Medical School, UK.

6.3.5. Statistical analysis

Data were analysed using the Statistics Software Package for the Social Sciences (SPSS) version 22 (SPSS Inc., Chicago, IL). The trapezium rule was used to calculate the total area under the variable versus time curve for [CAF] (TAUC-CAF), [FFA] (TAUC-FFA), [A] (TAUC-A) and [NA] (TAUC-NA). The incremental area under the plasma concentration versus time curve for [FFA] (iAUC-FFA), [A] (iAUC-A) and [NA] (iAUC-NA) was also calculated using the same method after adjusting for baseline concentrations.
Normal distribution was checked using Shapiro-Wilk tests and the data are presented as mean(SD). Data for [FFA] were not normally distributed and were log transformed prior to analysis. These data are presented as geometric mean (95% confidence intervals (CI)) and analysis is based on the ratios of geometric means and 95% CI for ratios. Homogeneity of variances was confirmed by Mauchly’s test of sphericity, and where the sphericity assumption was violated, the Greenhouse Geisser correction was applied to the degrees of freedom.

Repeated measures ANOVAs for group and time were used to examine differences between [FFA], [A], [NA], [Bla] and [GLU]. Where a significant interaction was evident, post-hoc one-way ANOVAs explored the effects of group and time with a Bonferroni adjustment for repeated comparisons.

An analysis of covariance (ANCOVA) was used to examine differences between [CAF], with daily caffeine consumption (low <50 mg·d\(^{-1}\), moderate 50-250 mg·d\(^{-1}\) and high >250 mg·d\(^{-1}\)) as a covariate. One-way repeated measures ANOVAs were used to analyse TAUC and iAUC data. Planned simple and difference contrasts were applied to explain any significant results.

Statistical significance was accepted at \(p \leq 0.05\) and absolute standardised ESs are included to supplement important findings. An ES of 0.2 was considered small, 0.5 moderate and 0.8 large according to Cohen (1992). Due to incomplete data sets (e.g. insufficient blood flow or a cannula change) the number of participants included in each analysis differs. Data sets were A (7/6/7), NA (7/7/8), FFA (7/7/7), Bla (5/5/6) and GLU (8/6/8) for AB, PARA and TETRA groups, respectively.

Power analysis was performed using the [CAF] observed in 3 groups of participants with no SCI, paraplegia and tetraplegia 60 min post-ingestion of 6 mg·kg\(^{-1}\) caffeine (46.4(6.8), 55.3(19.8) and 64.1(6.9) µM, respectively) (Flueck et al., 2015). The a priori analysis, conducted in G*Power 3.1, revealed that six participants would be required in each group to detect a similar change in [CAF] with ES of 0.59, 0.66 and 2.74, 90% power, and an \(\alpha\) of 5%. Given the novel nature of this investigation and the heterogeneity of the population, an additional two participants per group were recruited to increase statistical power (n=8).

6.4. Results

6.4.1. Plasma caffeine

At baseline, [CAF] was either undetectable or very low, which indicates that all participants adhered to the withdrawal guidelines. Differences over time and across groups
were revealed (main effect time \( p<0.0005 \); main effect group \( p=0.026 \); time by group interaction \( p=0.019 \)) (Figure 6.2). Planned simple contrasts revealed these group differences occurred between AB and TETRA \( (p=0.017) \), whereas no difference was observed between AB and PARA \( (p=0.913) \). The \( C_{\text{max}} \) for AB, PARA and TETRA were 12.2(2.3), 15.1(8.1) 21.5(7.0) µM, respectively. The \( C_{\text{max}} \) in TETRA was significantly greater than AB \( (p=0.008) \) yet non-significantly \( (p=0.058) \), but meaningfully (ES=0.9) greater than PARA. Time to \( C_{\text{max}} \) varied greatly between individuals but group mean (range) was 80 (45-90), 80 (45-150) and 70 (30-90) min for AB, PARA and TETRA, respectively. There was no influence of habitual caffeine use on [CAF] \( (p=0.943) \).

No significant difference in TAUC-CAF was observed between groups \( (p=0.135) \); AB 19.8(5.0) µM, PARA 22.6(16.1) µM, and TETRA 31.3(11.1) µM). However, small (AB vs. PARA, ES=0.38), moderate (PARA vs. TETRA, ES=0.55) and large (AB vs. TETRA, ES=1.14) ES were apparent.

Seven participants (3 AB/2 PARA/2 TETRA) reported adverse effects prior to/during the first 30 min of testing (headache/light-headed (2)) and during testing (struggling with quick decision making (1), tingling arm (1), a twitching eye (1)). Five participants also reported feeling more alert.
Figure 6.2. (a) Mean(SD) plasma caffeine concentrations following the consumption of 3 mg·kg\(^{-1}\) caffeine (CAF), (b) individual data from able-bodied participants (AB), (c) participants with paraplegia (PARA), and (d) participants with tetraplegia (TETRA). Dotted/bold lines in c and d represent participants with an ASIA A/B classification.
6.4.2. Plasma catecholamines

All catecholamine analysis excluded the participant with a T4 lesion level due to a missed sample and hence statistical analysis for PARA was calculated based on injuries at or below T6/7. The change in [A] over the course of the resting protocol did not reach statistical significance but did differ between groups (main effect of time \( p = 0.088 \); main effect of group \( p = 0.027 \); time by SCI level \( p = 0.618 \)) (Figure 6.3). Planned difference contrasts revealed these group differences occurred between PARA and TETRA (\( p = 0.019 \)) only. There was no significant difference in TAUC-A (\( p = 0.075 \)) between groups (AB 0.43(0.17) nmol·L\(^{-1}\), PARA 0.57(0.22) nmol·L\(^{-1}\), and TETRA 0.22(0.10) nmol·L\(^{-1}\)) though ES were large for both AB (ES=2.02) and PARA (ES=1.04) compared to TETRA. There was no difference in iAUC-A (\( p = 0.733 \)) (Figure 6.3).

The [NA] did not change significantly during the 150 min protocol (\( p = 0.423 \)) but did differ between groups (\( p = 0.003 \)), and no interaction was evident (\( p = 0.772 \)). Planned difference contrasts revealed these group differences occurred between AB and TETRA (\( p = 0.001 \)), and PARA and TETRA (\( p = 0.006 \)), but no significant difference was observed between AB and PARA (\( p = 0.505 \)). There was a significant difference in TAUC-NA (\( p = 0.003 \)) between groups (AB 4.04(0.92) nmol·L\(^{-1}\), PARA 3.68(1.01) nmol·L\(^{-1}\), and TETRA 2.01(1.21) nmol·L\(^{-1}\)). Small (AB vs. PARA, ES=0.38) and large (AB vs. TETRA, ES=1.89, and PARA vs. TETRA, ES=1.50) ES were revealed. However, no significant difference in iAUC-NA was observed (\( p = 0.827 \)).

6.4.3. Plasma FFA, lactate and glucose

Differences in [FFA] were observed over time and between groups, however the latter failed to reach significance (main effect time \( p < 0.0005 \); main effect group \( p = 0.054 \); time by group interaction \( p = 0.035 \)). Geometric mean [FFA] was 51% (95% CI 31 to 73%), 64% (95% CI 44 to 88%) and 84% (95% CI 58 to 116%) higher than baseline at 60, 90 and 150 min. Geometric mean [FFA] was 26% lower and 9% higher than AB in PARA (95% CI -46 to 2%) and TETRA (95% CI -21 to 50%), respectively. Mean [FFA] results were 47% higher in TETRA compared to PARA (95% CI 6 to 103%).

No significant difference in TAUC-FFA was observed (\( p = 0.072 \)) yet moderate (AB vs. PARA, ES=0.47, AB vs. TETRA, ES=0.85) and large (PARA vs. TETRA, ES=1.16) ES were revealed. No significant difference in iAUC-FFA was observed (\( p = 0.357 \)). Differences in [Bla] were observed over time but not between groups (main effect time \( p = 0.022 \); main effect group \( p = 0.463 \); time by group interaction \( p = 0.065 \)) (Figure 6.3d).
Planned difference contrasts revealed a significant decrease in [Bla] between baseline and 60 min ($p=0.049$), and between 90 and 150 min ($p<0.0005$). No significant difference in [GLU] was seen over the course of the 150 min protocol ($p=0.695$) or between groups ($p=0.983$) (Figure 6.3e).
Figure 6.3. (a) Plasma adrenaline (b) noradrenaline, (c) free fatty acid, (d) lactate and (e) glucose concentrations following the consumption of 3 mg·kg⁻¹ caffeine in able-bodied (AB) participants and participants with paraplegia (PARA) and tetraplegia (TETRA). *Significant main effect for group. †Significant time-group interaction effect.
6.5. Discussion

The current study is the first to report inter-individual differences in the caffeine absorption curve within and between groups when separated for level of SCI (AB, PARA and TETRA). Consequently, dosage and timing recommendations provided to individuals with a SCI may need to be adapted from the AB literature. In addition, the pattern of caffeine absorption differs in TETRA compared to AB and PARA (Figure 6.2). There were small differences in [A], [NA] and [FFA] between the AB and SCI groups, which were non-significant when baseline values were accounted for using the incremental area under the curve. No differences in [Bla] and [GLU] were seen between groups.

6.5.1. Plasma caffeine

Participant’s [CAF] increased in all three groups following the ingestion of 3 mg·kg⁻¹ caffeine. The [CAF] in AB at 60 min (10.8(3.1) µM) is in line with that reported 60 min post-ingestion of 2, 3 and 4 mg·kg⁻¹ caffeine (5.7, ~15.0 and 14.6 µM, respectively) (Graham & Spriet, 1995; Skinner et al., 2010). This study is the first to investigate the caffeine absorption curve in a group of participants with paraplegia. The AB results did not differ from the PARA responses at 60 min (11.1(7.9) µM), and both groups reached mean C_max at 80 min (12.2(2.3) and 15.1(8.1) µM). Individual time to C_max differed greatly however as AB participant peaks occurred between 45 and 90 min, and PARA peaks occurred between 45 and 150 min. The TETRA responses were significantly greater than AB and the mean C_max (21.5(7.0) µM) was reached 10 min earlier (70 min), with an individual range from 30 to 90 min. Flueck et al. (2015) also reported a greater [CAF] 60 min post-ingestion of ~6 mg·kg⁻¹ caffeine in individuals with tetraplegia compared to those with paraplegia (66.1 and 45.1 µM, respectively). Interestingly, Van Soeren et al. (1996) also reported a high C_max of 46.7(5.0) µM in individuals with tetraplegia (n=6) yet this was reached after only 40 min post-ingestion of 6 mg·kg⁻¹ caffeine. The current study therefore adds further support to reports of higher [CAF] in TETRA compared to individuals with lower lesion levels and no SCI. Furthermore, these findings also highlight the variability that exists within each group. Based on the current study there does not appear to be an influence of habitual caffeine use on the participants’ [CAF] in response to a single dose, as seen previously (Bell & McLellan, 2002). Seven participants reported adverse effects which were likely a result of withdrawal (headache), fasting (light headed) and CAF (tingling arm, twitching eye and struggling to make quick decisions). All symptoms were mild, only lasted for a short duration and occurred
in participants across all three groups. The 3 mg·kg$^{-1}$ caffeine dose is therefore deemed safe in this population.

An interaction effect occurred due to the sharp increase in [CAF] in TETRA while both AB and PARA groups [CAF] increased gradually followed by a plateau. The rapid increase in [CAF] displayed by the majority of TETRA participants indicates that these individuals did not display signs of slowed absorption. The sharp rise may be due to a number of factors. Firstly, individuals with tetraplegia have a smaller blood volume compared to AB individuals due to atrophy of the musculature and vessels of the lower limbs (Houtman et al., 2000). This reduced blood volume may result in a falsely large [CAF] in TETRA following the administration of a standardised dose per kilogram body mass. Secondly, following a cervical or thoracic SCI sympathetic outflow to the liver is also disrupted, which in turn can lead to hepatic pathology (Sauerbeck et al., 2015). The liver is innervated by both sympathetic and parasympathetic nerves, and the sympathetic splanchnic nerves originate from neurons which are located between T7-T12 (Yi et al., 2010). Acute changes to the liver occur due to the complete (cervical level) and partial (thoracic level) disruption to the descending control of sympathetic neurons innervating the organ (Sauerbeck et al., 2015). It has been suggested previously that abnormal liver function may affect the metabolism and bioavailability of drugs (Mestre et al., 2011; Sauerbeck et al., 2015). The half-life of many drugs can be prolonged in individuals with a SCI who display suboptimal liver function and slow renal clearance (Mestre et al., 2011; Sauerbeck et al., 2015). Serum caffeine half-life has also been shown to be severely prolonged in individuals with compromised liver function e.g. those with alcoholic hepatic liver disease (Statland & Demas, 1980). The half-life of caffeine in healthy individuals is ~4-6 h (Bell & McLellan, 2002). This may help explain the sharp rise to $C_{\text{max}}$ in TETRA (slowed metabolism) which remains higher than AB and PARA (slowed renal clearance). This TETRA response indicates that individuals with a cervical SCI may consider using a lower dose of caffeine to produce similar [CAF] as AB and PARA while avoiding any potential side-effects that are reported anecdotally and in Chapter five. Further investigation would be required to determine if a lower dose was as effective as higher doses and/or whether the higher [CAF] potentially results in an ergogenic benefit for longer in these individuals. It also suggests that individuals with a cervical level SCI may need to consider reducing the frequency of caffeine intake to prevent the potential negative effects of high doses of caffeine e.g. nervousness, jitters, restlessness, sleeplessness and irritability.

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It has previously been suggested that the pharmacokinetics of caffeine may be modified by an individual’s FM (Abernethy et al., 1985; Kamimori et al., 1987). Caffeine is highly lipophilic and therefore can be transported into various tissues throughout the body. The increased distribution of caffeine with no change in clearance resulted in a non-significantly longer elimination half-life in obese individuals (Abernethy et al., 1985). Kamimori et al. (1987) also reported than three obese individuals had lower elimination rate constants and longer serum caffeine half-lives compared to three lean individuals. Given the sample size in the 1987 study (n=3) and the non-significant trend in the 1985 study, this is purely speculative but the increased FM in individuals with a SCI cannot be discounted as a potential influencing factor on the pharmacokinetics of caffeine (Spungen et al., 2003).

The TAUC-CAF did not statistically differ between groups yet a large ES of 1.14 was evident between AB and TETRA. Large inter-individual responses were seen in both SCI groups evidenced by large standard deviations of 16.1 and 11.1 µM in PARA and TETRA, respectively (Figure 6.2), likely due to the heterogeneous nature of this population. The equivocal findings regarding the beneficial effects of caffeine during short-term exercise performance (Flueck et al., 2015) may be partly explained by these inter-individual differences, highlighted by the current PARA and TETRA responses. Examination of individual data within PARA reveals some interesting findings. Participant nine (L1 lesion; ASIA B) produced a similar curve to the AB participants, with a \( C_{max} \) (albeit larger at 29.0 µM) at 45 min followed by a steady decline. However, caffeine did not appear in the bloodstream of participant 10 (T7 lesion; ASIA B) until 70 min and continued to rise for the remaining 80 min. Hence, participant 10 did not reach a \( C_{max} \) during the 150 min resting protocol. The implementation of a standard caffeine protocol whereby caffeine is administered 60 min prior to short-term exercise performance would result in participant 10 exhibiting a [CAF] associated with a placebo dose at the commencement of exercise. For short-term exercise performance it is therefore recommended that athletes with a SCI determine their individual absorption curve to produce individualised dose and timing recommendations. If this is impractical it is recommended that caffeine prior to short-term exercise performance is provided earlier to ensure it appears in the bloodstream prior to commencement. Research into the use of caffeine gum or mouth rinse is emerging yet the evidence of a consistent positive effect is currently limited (Paton et al., 2015; Ryan et al., 2012). Consuming caffeine in this format allows direct absorption into the bloodstream through the buccal mucosa and may eliminate any potential issues regarding caffeine absorption in individuals with a SCI.
The groups’ body mass and habitual caffeine intakes were similar between all three
groups. There was however, a significant difference between the mean age (AB vs. PARA)
and TSI (PARA vs. TETRA) which cannot be discounted as influencing factors on [CAF]
responses. Previous research has however suggested that age was not associated with peak,
total or time to peak [CAF] following caffeine ingestion ($p>0.612$) (Skinner et al., 2014). Age
and TSI have also been reported not to affect gastric emptying (Kao et al., 1999).

6.5.2. Plasma catecholamines

Resting plasma catecholamine concentrations did not significantly increase over the
course of the 150 min protocol in any group (Figure 6.3a/b). In contrast, Flueck et al. (2015)
and Van Soeren et al. (1996) reported increases in [A] in both AB individuals and individuals
with paraplegia (Table 2.5), which may in part be due to the larger 6 mg·kg$^{-1}$ dose
administered in these studies. In line with previous findings, baseline catecholamine
concentrations were lower in TETRA compared to AB and PARA due to the impaired
sympathetic activation of the adrenal medulla (Paulson et al., 2013b; Schmid et al., 1998).

6.5.3. Plasma FFA, lactate and glucose

Mean resting [FFA] increased over time from 0.36(0.19) mmol·L$^{-1}$ at baseline to
0.61(0.25) at 150 min (Figure 6.3c), in agreement with previous research in an AB and a SCI
population (Graham et al., 2000; Van Soeren et al., 1996; Table 2.5). In the absence of a
catecholamine response, the current results lend further support for a direct effect of caffeine
on human tissue, specifically adipocytes at rest. The majority of research suggests that FFA
availability does not result in greater FFA oxidation and therefore does not alter substrate use
at rest or during exercise (Desbrow et al., 2009; Graham & Spriet, 1991; Mohr et al., 1998). It
is also unlikely to aid performance during short-term UBE where participants/athletes
predominantly work anaerobically, and therefore utilise carbohydrate as the primary
substrate. Unfortunately no body composition or RER data were collected to enable a greater
understanding of the [FFA] responses and whether substrate use was influenced at rest.
However, previous research would suggest this does not occur (Graham & Spriet, 1991; Van
Soeren et al., 1996).

Baseline [FFA] was higher in TETRA than AB or PARA (Figure 6.3c). The lack of
muscle innervation of paralysed lower limbs in individuals with a SCI leads to rapid muscle
atrophy and a reduction in resting metabolic rate (Monroe et al., 1998). Alongside potentially
poor nutritional choices (Perret & Stoffel-Kurt, 2011) and a disruption in the secretion of
anabolic hormones, these changes can result in an increase in fat mass (Spungen et al., 2003).
An expanding fat mass which releases more FFA and a potential reduction in FFA clearance leads to increased plasma [FFA] (Bjorntorp et al., 1969). The [FFA] were significantly greater in TETRA compared to PARA only. One possible explanation for this could be the difference in the group’s time since injury (PARA 4.3(4.3) y and TETRA 12.2(6.3) y) which has been positively associated with loss of lean tissue and increased fat mass (Spungen et al., 2003).

The current data show [Bla] decreased slightly over the course of the 150 min protocol, which is in line with previous resting data (Van Soeren et al., 1996). The [GLU] also decreased modestly (non-significantly) during the current protocol, as previously reported (Mohr et al., 1998) and is unlikely a result of caffeine ingestion. Neither [Bla] nor [GLU] was influenced by CAF.

6.6. Conclusion

The current study demonstrates that there is large inter-individual variability in the pattern of caffeine absorption in individuals with a SCI and that this should be assessed prior to making specific recommendations for its use. Individuals with tetraplegia may consider using a lower dose and individuals may consider consuming supplementary caffeine earlier than the 60 min recommended prior to short-term exercise performance.

6.7. Practical applications

Where possible, if an athlete is using caffeine prior to short-term, high intensity exercise performance it is recommended that the individual athlete’s absorption curve is determined. Where this is not possible, the current data would suggest that both AB and TETRA should allow 70 min between ingestion and performance. Whereas, PARA should ingest caffeine (in capsule form) 80 min prior to exercise to ensure caffeine is present in the bloodstream during short-term exercise. Caffeine can be consumed closer to the start of endurance events given their longer total duration.

The results also suggest that an athlete with tetraplegia should trial a low dose of caffeine (1-2 mg·kg⁻¹) in the first instance. If they do not experience any side-effects then a larger dose can be trialled, ideally in conjunction with controlled performance tests to assess whether it is ergogenic for the individual athlete. They may also need to be cautious of the frequency of caffeine intake to help prevent the possibility of any adverse effects due to high [CAF].

The influence of caffeine on catecholamine release in AB individuals is not replicated in TETRA due to their impaired sympathetic activity. Any mechanism of action reliant on
circulating catecholamines is unlikely to work in individuals with impaired autonomic function. The increase in [FFA] occurs in individuals with or without a SCI despite no significant change in catecholamine concentrations. However, the increase in [FFA] following caffeine ingestion will not necessarily lead to increased lipolysis. Practitioners should investigate the effects of caffeine on an individual’s performance where possible to determine whether it works for the n=1 of an elite athlete.
Study 5: Caffeine improves 20 km handcycling time trial performance in an elite Paralympic triathlete:
A case study

Photo courtesy of Phil Wilson.
7.1. Abstract

Chapter four suggests that caffeine’s ability to influence UBE endurance performance may be related to an individual’s training status. This case study therefore aimed to investigate the ergogenic effects of caffeine on 20 km TT performance of an elite male Paralympic triathlete with paraplegia (T7, ASIA A) who competes in the PT1 (wheelchair user) category. At the time of testing he was aged 46 y, with a body mass of 76.9 kg and a handcycling $\text{VO}_2\text{peak}$ of 3.45 l·min$^{-1}$. Preliminary testing determined the athlete’s individual caffeine absorption curve at rest which resulted in a peak 45 min post-ingestion, which was adopted in the subsequent TT’s. The study followed a single-blind, randomised, placebo-controlled, repeated measures design. The athlete completed four 20 km TT’s on a Cyclus II ergometer under laboratory controlled conditions following the ingestion of 2, 4 and 6 mg·kg$^{-1}$ caffeine (CAF) or placebo (PLA). [GLU], [Bla], PO, Felt arousal and Borg 6-20 RPE were recorded. Ingestion of 2, 4 and 6 mg·kg$^{-1}$ CAF resulted in 20 km TT performance times of 36:56, 37:06 and 36:39 min:sec which were 2, 1.5 and 2.7% faster than PLA (37:40 min:sec). There was no significant change in [GLU] during any trial. The participant’s [Bla] increased throughout all trials and was greater during CAF compared to PLA. There were no apparent differences in RPE between trials. Baseline Felt arousal responses differed between PLA and 4 mg·kg$^{-1}$ (‘1-low’), and 2 and 6 mg·kg$^{-1}$ (‘3-moderate’). Arousal increased at each time-point following the ingestion of 4 and 6 mg·kg$^{-1}$ CAF. The largest CAF dose resulted in a positive pacing strategy, which when combined with an end spurt resulted in the fastest TT. The increased PO at the start of the TT was likely linked to the higher arousal scores reported. Different baseline arousal responses may help explain the lack of a dose response following CAF. The athlete experienced spasticity during two trials but attributed this to the maximal effort delivered, not the ingestion of CAF. Caffeine (2, 4 and 6 mg·kg$^{-1}$) improved 20 km TT performance of an elite male Paralympic PT1 category triathlete, which appears to be related to greater arousal and an increased PO for a given RPE.
7.2. Introduction

It was shown in chapter three that caffeine is commonly used by athletes with a physical impairment and yet very few studies have been conducted using elite (Flueck et al., 2014) and trained (Flueck et al., 2015) participants. Evidence of caffeine’s ergogenic effects during UBE remains equivocal. Findings in Chapters three, four and five suggest that caffeine may be more advantageous during short-term, explosive UBE compared to endurance UBE. This supports previous research (Black et al., 2015; Flueck et al., 2015; 2014). Black et al. (2015) reported improvements in cycling but not arm cranking 10 min all-out performance following 5 mg·kg⁻¹ and a 30 min preload at 60% $\dot{V}O_2$ peak. In chapter four, 4 mg·kg⁻¹ caffeine improved cycling 10 km TT performance but failed to statistically improve handcycling performance following a 30 min preload at 65% $\dot{V}O_2$ peak. The participants’ used in Chapter four and by Black et al. (2015) were recreationally active males with no previous knowledge or experience of pacing their handcycling/arm cranking performance. However, participants with a handcycling $\dot{V}O_2$ peak above and below the mean in Chapter four improved their handcycling TT performance by 3.2% and -0.3%, respectively (see earlier Figure 4.2). This indicates that there may be some influence of training status on caffeine’s ability to influence performance. This theory is also supported by improvements in swimming velocity (during which a large proportion of force is generated by the upper-body) by trained but not untrained participants following the ingestion of a moderate dose of caffeine (250 mg) (Collomp et al., 1992). Collomp and colleagues (1992) suggested that the intra and/or extracellular adaptations (e.g. enhanced buffering capacity) resulting from specific training are necessary to benefit from the NS. Training status has also been suggested as a possible explanation for the equivocal data regarding caffeine’s ability to alter high-intensity exercise (Astorino & Rowerson, 2009). Well-trained/elite athletes are also likely to have greater motivation to perform maximal exercise (Burke, 2008). It is understandable given the practicalities involved that there are limited studies utilising elite athletes. However, in this instance the author was provided with a unique opportunity to investigate the ergogenic effects of caffeine in an elite male PT1 category (wheelchair user) Paralympic athlete.

At the London 2012 Paralympic Games the medal winning times for handcycling and wheelchair racing were within a 0.3-0.6% time frame (Perret, 2015). In Paralympic sport, winning margins are small and every second/goal/metre advantage counts. Paralympic triathlon is a new sport in the Rio 2016 Games in which male wheelchair athletes can
compete in the PT1 category. The sport involves three separate disciplines and is comprised of a 750 m swim, 20 km bike and 5 km run. Athletes in the PT1 category complete the latter two disciplines in a handcycle followed by a racing wheelchair over a total race duration of approximately one hour. Previous AB cycling research suggests that caffeine supplementation would be advantageous during 1 h TT events where ~6% improvement in performance has been reported (Kovacs et al., 1998 (3-4 mg·kg⁻¹); McNaughton et al., 2008 (6 mg·kg⁻¹)). However, there is currently limited evidence to support its use during UBE and by athletes with a physical impairment.

As part of the nutritional support package for a Paralympic triathlete who competes in the PT1 category, the author was asked to explore the potential for caffeine use by this triathlete. In elite sport, the ‘n=1’ research is important and can mean the difference between a podium finish or not. The handcycle section of a Paralympic triathlon event comprises more than half the competition time (~00:36 in a ~01:02 h:min performance) and hence this section was chosen as part of the laboratory controlled exercise protocol. The aim of the current case study was therefore to investigate the effects of caffeine supplementation (2, 4 and 6 mg·kg⁻¹) on 20 km handcycling TT performance.

7.3. Methods

7.3.1. Participants

One male Paralympic triathlete with paraplegia (T7, ASIA A) (age 46 y, body mass 76.9 kg, body fat 25.4%, handcycling \(\overline{VO_2}_{\text{peak}}\) 3.45 l·min⁻¹ and habitual caffeine intake 160 mg·d⁻¹) provided written informed consent to take part in the current case study. All medication was checked to ensure there were no known interactions with caffeine. All procedures were approved by the University’s Ethical Advisory Committee and performed in accordance with the Declaration of Helsinki.

As part of the athlete’s sport science support the authors were provided with the results from a \(\overline{VO_2}_{\text{peak}}\) test (3 weeks prior to visit 1) and a DXA (Lunar iDXA, GE Healthcare, Buckinghamshire, UK) (during the study) to enable greater understanding of the athlete and their training status. The athlete’s physiology support package also includes the completion of 20 km handcycling TTs in the same laboratory every three months and consequently the athlete was familiar with the testing procedures and the RPE scale (Borg, 1998). The participant was familiarised with the Felt Arousal scale (Svebak & Murgatroyd, 1985) during visit 1.
7.3.2. Experimental design

The athlete visited the laboratory on five separate occasions. Preliminary testing (visit 1) was a resting trial in which the athlete’s rate of caffeine absorption was determined. Visits 2-5 were experimental trials in which the participant performed four 20 km handcycling TTs following the consumption of placebo (PLA), 2, 4 or 6 mg·kg$^{-1}$ caffeine (CAF). The experimental trials followed a single-blind, placebo controlled, randomised, repeated measures design and were separated by at least five days. Trials were conducted at the same time of day (10:15am) to avoid any influence of circadian rhythm (Drust et al., 2005).

7.3.3. Equipment

The athlete performed the TTs in their own handcycle so the configuration and set-up matched that used in daily training and competition. This was standardised across trials. The handcycle was mounted on a Cyclus II ergometer (Avantronic Richter, Leipzig, Germany) for all exercise trials as in Chapter four (Figure 2.5 shows the Cyclus II handcycle set-up).

7.3.4. Preliminary trials

The athlete arrived at the laboratory 1.5 h post-ingestion of a self-selected standardised meal (1891 kJ: 64% carbohydrate, 18% protein, 18% fat) and water consumption was encouraged to help ensure the participant arrived euhydrated. The athlete was asked to void his bladder, if necessary prior to lying in a semi-supine position on a laboratory bed. A cannula (Venflon, Becton Dickinson, Helsinborg, Sweden) was inserted into an antecubital vein for subsequent venous sampling. The cannula was kept patent using 5-10 ml sodium chloride (0.9%) after each blood sample.

After a minimum of 15 min rest, a baseline venous blood sample was taken. The athlete then consumed cellulose capsules (Bulk Powders, Colchester, UK) containing 4 mg·kg$^{-1}$ caffeine (MyProtein, Northwich, UK). The 4 mg·kg$^{-1}$ caffeine dose was selected for the preliminary trial because it was the median experimental dose (2, 4 and 6 mg·kg$^{-1}$ caffeine). Absolute [CAF] may differ between doses (Desbrow et al., 2009) but they will provide the author with an indication of the time-course of caffeine absorption across all three caffeine trials as this is not affected to the same extent (Graham & Spriet, 1995). The athlete remained rested for 120 min during which a further 8 blood samples were taken (15, 30, 45, 60, 70, 80, 90 and 120 min).
7.3.4. Experimental trials

Prior to visiting the laboratory, the athlete maintained normal dietary and activity patterns, and their individual medication regime. These were standardised across trials using a 24 h food (5319 kJ: 55% carbohydrate, 34% protein, 11% fat) and training log which was replicated prior to each trial. The same standardised meal as above (7.3.4.) was consumed 1.5 h prior to arrival at the laboratory. The athlete was provided with a list of caffeine containing foods and drinks, and was asked to abstain from consumption in the 24 h preceding all laboratory visits.

The exercise trials involved the consumption of either 2, 4 or 6 mg·kg\(^{-1}\) CAF, or dextrose PLA in cellulose capsules (Bulk Powders, Colchester, UK) 45 min prior to commencement of the TT. The timing recommendation was based on preliminary trial results. As in Chapter four the athlete was instructed to complete the 20 km TT in the shortest time possible, during which the gear could be changed at any time. In line with the usual competition environment, motivation was provided during the TT but was standardised and provided upon the completion of each kilometre and throughout the final 3 km. To avoid test-retest influence the only in-test feedback provided was cumulative distance covered. [GLU] and [Bla] were determined using a Biosen C-Line (EKF Diagnostic GmbH, Barleben, Germany) via earlobe capillary blood samples pre-warm-up, pre-TT, and upon completion of 5, 10, 15 and 20 km during the TT. Heart rate was monitored continuously (Polar RS400, Polar, Kempele, Finland). Exercise trial environmental conditions were mean(SD) temperature 19.4(0.6)°C and humidity 51(5)%.

The 6-20 RPE scale (Borg, 1998) was used as a measure of perceived exertion during the TT upon completion of 5, 10, 15 and 20 km. As in Chapter four the athlete was asked for three RPE scores: RPE\(_P\), RPE\(_C\) and RPE\(_O\). The athlete was asked to rate their arousal on the Felt Arousal scale pre-capsule, pre-warm-up, pre-exercise and post-exercise as in Chapter five. See Figure 7.1 for the schematic of the exercise protocol.
Figure 7.1. Schematic of the 20 km time trial protocol. PLA=placebo, RPE=rating of perceived exertion, TT=time trial
7.3.5. Blood sampling and analysis

All blood sampling and analysis procedures to assess [CAF] at rest were performed as described in Chapter six (see section 6.3.4) and Appendix C.

7.4. Results

The participant’s [CAF] peaked 45 min post-ingestion (43.2 µM) followed by a gradual decline. Ingestion of 2, 4 and 6 mg·kg⁻¹ CAF resulted in 20 km TT performance times of 36:56, 37:06 and 36:39 min:sec, which were 2, 1.5 and 2.7% faster than PLA (37:40 min). The athlete reported symptoms of spasticity during the 2 and 4 mg·kg⁻¹ CAF trials but they did not believe this affected their performance. Average PO was 162, 171, 169 and 175 W following the ingestion of PLA, 2, 4 and 6 mg·kg⁻¹ CAF, respectively (Figure 7.2c). The [Bla] increased throughout all trials and was greater during CAF compared to PLA (Figure 7.2a) but there was no change in [GLU] during any trial (Figure 7.2b). The athlete’s HR was slightly increased in all three CAF trials compared to PLA but this difference was eliminated immediately post-TT.

There was no difference in RPE between trials (Table 7.1). Baseline Felt arousal responses differed between PLA and 4 mg·kg⁻¹ (‘1-low’), and 2 and 6 mg·kg⁻¹ (‘3-moderate’). Arousal increased at each time-point following the ingestion of 4 and 6 mg·kg⁻¹ CAF (Figure 7.3). The athlete was not accurate in predicting which dose had been consumed during each trial. Subjectively the athlete reported feeling more ‘focused’, with an improved ability to ‘refocus’ following the consumption of 2 and 6 mg·kg⁻¹ CAF.
Figure 7.2. (a) Blood glucose and (b) lactate concentrations, and (c) average power output during the 20 km time trial following the consumption of placebo (PLA), 2, 4 and 6 mg·kg\(^{-1}\) caffeine.
Table 7.1. Differentiated (local, central and overall) ratings of perceived exertion (RPE) during the 20 km time trial (TT) following the consumption of placebo (PLA), 2, 4 and 6 mg·kg⁻¹ caffeine.

<table>
<thead>
<tr>
<th></th>
<th>5 km</th>
<th>10 km</th>
<th>15 km</th>
<th>Post-TT</th>
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<tbody>
<tr>
<td>Overall RPE</td>
<td>PLA</td>
<td>15</td>
<td>16</td>
<td>16</td>
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<tr>
<td></td>
<td>2 mg·kg⁻¹</td>
<td>15</td>
<td>15</td>
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<td></td>
<td>4 mg·kg⁻¹</td>
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<td>17</td>
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<td></td>
<td>6 mg·kg⁻¹</td>
<td>15</td>
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<td>17</td>
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<tr>
<td>Central RPE</td>
<td>PLA</td>
<td>16</td>
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<td>16</td>
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<td>2 mg·kg⁻¹</td>
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<td>6 mg·kg⁻¹</td>
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<tr>
<td>Peripheral RPE</td>
<td>PLA</td>
<td>15</td>
<td>16</td>
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<td>2 mg·kg⁻¹</td>
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<td>6 mg·kg⁻¹</td>
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Figure 7.3. Felt arousal responses following the consumption of placebo (PLA), 2, 4 and 6 mg·kg⁻¹ caffeine. TT=time trial.
7.5. Discussion

This case study contributes to the literature exploring the ergogenic effects of caffeine during UBE performance. It is unique in its investigation of an elite male Paralympic triathlete with paraplegia (T7, ASIA A) during endurance TT performance. All three doses (2, 4 and 6 \( \text{mg} \cdot \text{kg}^{-1} \)) improved 20 km TT performance compared to PLA and were likely linked to increased arousal and PO at a given RPE.

7.5.1. Time trial performance

Caffeine improved 20 km TT performance in an elite male Paralympic PT1 triathlete compared to PLA. There was no clear dose response with performance improvements of 2, 1.5 and 2.7\% following the ingestion of 2, 4 and 6 \( \text{mg} \cdot \text{kg}^{-1} \) CAF, respectively. During the first 5 km section average PO was 164, 172, 173 and 184 W, and during the last 5 km section PO was 165, 175, 170 and 170 W following the ingestion of PLA, 2, 4 and 6 \( \text{mg} \cdot \text{kg}^{-1} \) caffeine, respectively. This indicates a distinctly different pacing strategy employed following the ingestion of 2 and 6 \( \text{mg} \cdot \text{kg}^{-1} \) caffeine (two fastest TT times). Following 2 \( \text{mg} \cdot \text{kg}^{-1} \) caffeine the athlete produced a steady PO throughout the TT followed by an end spurt (Figure 7.2c). Whereas, the ingestion of 6 \( \text{mg} \cdot \text{kg}^{-1} \) caffeine resulted in a higher initial PO, a gradual decline and a similar end spurt. The larger caffeine dose increased arousal at each time-point (3, 4, 5), which appears to have resulted in the athlete starting at a higher intensity than in the other trials. This positive pacing strategy must be considered in relation to the triathlon event as a whole but previous research suggests that such a strategy (decreasing from 92 to 73\% maximal 750 m swim TT time) earlier during the swim section is not detrimental to performance compared to both even and negative pacing strategies (Wu et al., 2016). These results support those in Chapter four where 4 \( \text{mg} \cdot \text{kg}^{-1} \) CAF resulted in a greater PO during the first and last 2 km sections of a 10 km TT compared to PLA.

The current triathlete’s DXA results (25.4\%) are also similar to those reported for British male wheelchair athletes (25.0\%; (Goosey-Tolfrey et al., 2016) and International male athletes with a SCI (20.6-25.5\%; Inukai, et al., 2006; Mojtahedi et al., 2009). His 20 km TT time (~36-37 min) was relatively faster than those reported for a 22 km TT by trained handcyclists with a SCI (T2-8) (~45 min) (Fischer et al., 2015). In conjunction with a \( \text{VO}_2 \text{peak} \) of 3.45 l\cdot\text{min}^{-1} \) this reinforces his highly trained or elite status. Chapter four suggested that an individual’s training status may be linked to caffeine’s ability to impact upon TT performance. The current study supports this notion and may be related to changes
in muscle fibre type and oxidative capacity as a consequence of the daily endurance training this triathlete completes (Schantz et al., 1997). It has been suggested that type I fibres are more sensitive to caffeine (Mitsumoto et al., 1990) and hence with potentially more of these available for recruitment compared to lesser trained participants, the caffeine may have been able to influence performance to a greater degree.

It has been noted previously that trained athletes’ muscle and other tissues such as adipocytes and the brain may be more responsive to caffeine (Collomp et al., 1992; Graham, 2001). This has been supported by LeBlanc et al. (1985) who reported caffeine ingestion at rest increased adrenaline, FFAs and resting metabolism to a greater extent in trained than untrained participants. This area of research is currently limited and warrants further investigation. Highly trained athletes may also have the mental discipline to work longer and/or harder to benefit from the stimulus of caffeine (Burke, 2008).

The athlete reported symptoms of spasticity during two experimental trials following CAF. Such symptoms were reported in Chapter five and have been anecdotally reported by athletes with a SCI. The triathlete has a complete SCI but this does not necessarily abolish all neural function below the lesion level. A complete lesion interrupts all signals coming from or going to higher levels of the nervous system, but spinal reflexes can be preserved below the lesion level if spinal nerves remain undamaged (Jacobs & Nash, 2004). Therefore, a sensory stimulus, such as pain in this instance may have led to muscle spasms. The athlete has experienced similar episodes of spasticity during his normal training sessions and it is apparent that the symptoms are often linked to periods of maximal effort such as during the current TT performances. Interestingly, the spasticity was not experienced during the largest dose of 6 mg·kg⁻¹ CAF and importantly the athlete did not believe that it affected performance. Physiological doses of caffeine such as those used in the current study would be insufficient to cause a direct effect on the muscle resulting in spasticity via mechanisms such as increased calcium release from the sarcoplasmic reticulum to reduce the threshold for potentiation (Magkos & Kavouras, 2005).

7.5.2. Blood lactate and glucose

Pre-WU [GLU] ranged between 4.3 and 5.3 mmol·L⁻¹ and [GLU] remained steady or slightly declined during the TT to a minimum of 3.5 mmol·L⁻¹ during PLA (Figure 7.2a). The athlete was not permitted to ingest anything except water and electrolytes during the TT. The decline appears to be smallest following the ingestion of 6 mg·kg⁻¹ CAF which has been seen previously following the same dose at rest and during exercise (Graham et al., 2000).
Adenosine usually contributes to the stimulation of glucose uptake (Raguso et al., 1996) and hence if caffeine acts as a non-selective adenosine receptor antagonist, the rate of disappearance of glucose may be reduced following its ingestion.

The participant’s [Bla] increased throughout each 20 km TT but was greater at 10, 15 and 20 km following the ingestion of 6 mg·kg⁻¹ CAF (Figure 7.2b). This has been reported previously in the literature (Bell & McLellan, 2002; Graham et al., 2000; Greer et al., 2000) and in Chapter four, and is understandable given this trial resulted in the greatest PO and fastest TT performance.

7.5.3. Subjective feelings

Different baseline Felt arousal responses may explain the lack of a dose response to caffeine. The athlete arrived at the laboratory with arousal responses of ‘3-moderate’ at baseline prior to the ingestion of 2 and 6 mg·kg⁻¹ CAF which resulted in faster 20 km TT times than PLA or 4 mg·kg⁻¹ caffeine. The greater arousal responses pre- and post-TT following 2 and 6 mg·kg⁻¹ caffeine may help explain the greater PO during the first (172 and 184 W) and last 5 km (175 and 170 W) sections which ultimately led to faster TT times. The athlete’s RPE responses did not appear to differ between trials but when viewed in conjunction with improved TT times and increased PO, this may indicate an increased PO for a given RPE, which has been reported previously (Astorino et al., 2012) and in Chapter four. Astorino et al. (2012) reported similar RPE, pain and arousal scores following the ingestion of 5 mg·kg⁻¹ caffeine despite improvements in cycling 10 km TT performance.

7.6. Conclusion

Caffeine improved 20 km TT performance in an elite male Paralympic triathlete with paraplegia, which appears to be related to increased arousal and an increased PO for a given RPE. The case study results therefore suggest the athlete could utilise caffeine as an ergogenic aid prior to race performances.

7.7. Practical applications

The triathlete practiced using caffeine during training and race simulations, and following this has now introduced caffeine into his pre-race nutrition strategy. The 20 km TT is the middle discipline of Paralympic triathlon and comprises the largest amount of time on the course (~35-40 min). It follows a 750 m swim (~11-12 min) and precedes a 5 km wheelchair race (13-14 min). Having taken the athlete’s warm-up time into account the athlete now consumes caffeine 20-30 min prior to the race start time. Anecdotally the athlete
has reported feeling focused during races, even when things have not gone to plan e.g. transition errors not under his control. He plans to continue using caffeine in capsule form and is currently trialling a caffeinated isotonic sports drink to help tailor his plan further.
8

General discussion

8.1. Overview of experimental chapters

Given the dearth of evidence regarding NS use by athletes with an impairment and the effectiveness of NS such as caffeine as ergogenic aids in this population, the objectives of the current thesis were:

- To determine the NS habits and perceptions of athletes with a physical or visual impairment, and to establish whether caffeine is a popular NS in this population (Chapter three)
- To examine the influence of caffeine on upper-body i) sprint, ii) short-term, high-intensity and iii) endurance performance (Chapters four, five and seven)
- To explore the acute effects of caffeine in individuals with a SCI to help determine the appropriate dose and timing recommendations for its use as an ergogenic aid (Chapter six)

The main findings from the five experimental chapters of the current thesis are summarised in Table 8.1.

Chapter three provided important evidence that NSs were being used by 58% of athletes with a physical and visual impairment, and that 41% of these athletes followed AB recommendations for dosage and timing. This adherence to AB guidelines may be linked to the 9% that reported negative side-effects as a result of using NS. Athletes with an impairment appear to use similar NS to AB athletes (protein, carbohydrate–electrolyte sports drinks, multivitamins and carbohydrate supplements), for similar reasons (recovery, immunity and energy). As may have been expected, elite athletes were more likely to use NS than those at lower levels of their sport, which may be related to longer training hours and/or access to a
<table>
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<th>Chapter</th>
<th>Modality</th>
<th>Caffeine dose</th>
<th>Population</th>
<th>Performance test</th>
<th>Main finding</th>
</tr>
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</table>
| 3       | n/a      | n/a          | Athletes with a physical or visual impairment (295 males & 104 females) | n/a | - 58% athletes used NS  
- Most used: protein, carbohydrate–electrolyte sports drinks, multivitamins & carbohydrate  
- 5% used caffeine  
- 9% experienced negative side-effects  
- 52% requested more information/education on NS |
| 4       | Cycling & Handcycling | 4 mg·kg\(^{-1}\) | Recreational AB (11 males) | 30 min at 65% \(\dot{VO}_2\) \& 10 km TT | Caffeine resulted in:  
- Improved cycling performance (2.1%)  
- No sig. change in handicycling performance (1.8%)  
- Increased [Bla] post-TT  
- Improved PO for a given RPE |
| 5       | Wheelchair propulsion | 4 mg·kg\(^{-1}\) | Club-level wheelchair sportsmen (12 males) | 20 m sprint 4 min maximal push | Caffeine resulted in:  
- Improved sprint performance  
- Improved one-off bout of 4 min maximal push  
- No change in arousal or RPE |
| 6       | n/a (resting) | 3 mg·kg\(^{-1}\) | AB individuals (8), individuals with PARA (8) & TETRA (8) (males) | n/a | Caffeine resulted in:  
- Different patterns of absorption in AB, PARA & TETRA  
- Greater C\(_{\text{max}}\) in TETRA  
- Large inter-individuality in absorption  
- Increased plasma FFA  
- No change in plasma catecholamine concentrations |
| 7       | Handcycling | 2, 4 & 6 mg·kg\(^{-1}\) | Paralympic PT1 triathlete (1 male) | 20 km TT | Caffeine resulted in:  
- Improved TT performance following all 3 doses  
- Increased [Bla]  
- Increased arousal  
- Improved PO for a given RPE |

Note: AB=able-bodied, C\(_{\text{max}}\)=peak plasma caffeine concentration, FFA=free fatty acids, NS=nutritional supplements, PARA=individuals with paraplegia, PO=power output, RPE=ratings of perceived exertion, TETRA=individuals with tetraplegia and TT=time trial
nutritionist/dietitian, who was reported as the most used and trusted source for NS advice. Beyond any macronutrient providing NS, caffeine was the most popular NS used by athletes with a physical impairment and hence this was chosen as a focus for further research. There is a large body of literature which suggests that caffeine is beneficial during endurance performance in AB individuals and yet the evidence for UBE was equivocal. Chapter four aimed to address the question ‘If caffeine is ergogenic during cycling in AB individuals, is it also ergogenic in the same individuals during handcycling?’ Subsequently, the study employed 11 recreationally active participants to complete a preloaded 10 km cycling and handcycling TT following the ingestion of caffeine (4 mg·kg\(^{-1}\)) or placebo. Caffeine consumption significantly improved cycling but not handcycling performance. Lower RPE were reported during the preload but not post-TT, and higher [Bla] were seen following caffeine compared to placebo. The important finding in Chapter four is that the impact of caffeine on endurance UBE may be related to the participants’ training status. Participants with a handcycling VO\(_2\)\(_\text{peak}\) above the mean improved their handcycling TT performance by 3.2%, whereas those below the mean had a 0.3% reduction. This may be linked to differences between UBE trained and untrained participants’ muscle fibre type distribution, intra and/or extracellular adaptations to UBE, or their ability to perform optimally during maximal testing. Further research regarding the relationship between the ergogenic effects of caffeine and training status is warranted (see section 8.3.2).

Previous research into the effects of caffeine on short-term, high-intensity UBE performance was also varied but Flueck et al. (2014; 2015) reported positive individual responses in wheelchair athletes and individuals with paraplegia. Chapter five therefore employed club level wheelchair sportsmen to investigate caffeine’s effects on short-term, high intensity exercise and 20 m sprint performance. Caffeine (4 mg·kg\(^{-1}\)) improved 20 m sprint and a one-off bout of 4 min maximal push performance. The NS did however fail to improve repeated bouts of 4 min maximal push. Salivary caffeine concentrations pre-warm up (45 min) suggested that this may be inadequate time to develop sufficient caffeine concentrations in some participants with a physical impairment (Figure 5.4). Interestingly, delayed drug pharmacokinetics had previously been noted in individuals with a SCI (Halstead et al., 1985; Mestre et al., 2001) and hence the pattern of caffeine absorption in this population required further investigation.

In contrast, Chapter six observed that C\(_\text{max}\) (3 mg·kg\(^{-1}\)) occurred at 70 min in participants with tetraplegia compared to 80 min in AB participants and participants with
paraplegia. Hence there was no apparent delay in absorption. The $C_{\text{max}}$ in individuals with tetraplegia was significantly higher than the other groups, which may be linked to suboptimal liver function, slow renal clearance (Mestre et al., 2011; Sauerbeck et al., 2015), reduced blood volume and/or increased FM (Abernethy et al., 1985; Kamimori et al., 1987; Skinner et al., 2014). Chapter six also highlighted that the pattern of caffeine absorption differed based on the SCI lesion level and that large inter-individual variation was apparent within and between groups. It was therefore concluded that where possible, an individual’s absorption curve should be assessed prior to making specific dosage and timing recommendations. Where this is not possible, individuals with tetraplegia might consider using a lower dose and all individuals might consider consuming supplementary caffeine earlier than the 60 min recommended prior to short-term exercise performance.

Finally, Chapter seven expanded on the findings of Chapter four that suggested a greater training status may be linked to caffeine’s ability to improve performance during UBE. Chapter seven therefore investigated the influence of caffeine (2, 4 and 6 mg·kg$^{-1}$) on 20 km TT performance by an elite Paralympic triathlete (PT1 ITU category). The case study supported the findings of Chapter four because all three doses of caffeine improved performance in this elite athlete. Improvements may have been linked to increased arousal scores and an improved PO for a given RPE.

8.2. Contribution to scientific understanding and application of findings

Given the lack of evidence in the area of caffeine and UBE, and more specifically in individuals with a physical impairment, this thesis has greatly contributed to scientific understanding. Importantly, the findings are also applicable to the sports nutrition practitioner and athlete.

8.2.1. Nutritional supplement use in individuals with a physical impairment

Prior to the findings of Chapter three there was insufficient evidence regarding the use of NS by athletes with a physical and visual impairment compared to the abundance of AB research in the same area. Only one study had previously investigated the use of food supplements by Paralympic athletes (Tsitsimpikou et al., 2009). Tsitsimpikou and colleagues (2009) collected data from Paralympic athletes at the 2004 Athens Games and hence provided an indication of supplement use at the elite level. The study reported that 27% of athletes declared the use of one or more food supplements (Tsitsimpikou et al., 2009), which was less than the 58% reported in Chapter three. The higher reported NS use may reflect an increase in i) NS use over the previous decade, ii) the popularity and availability of NS,
and/or iii) the training load/demand and pressure placed on modern day athletes with a physical impairment. Chapter three was able to contribute to the understanding of NS use at levels below the elite stage of the Paralympics whereby elite athletes were 1.6 times more likely to use NS than those who competed at a club level. This may be explained by the significantly greater training hours and access to sports nutritionists/dietitians. An important finding was that athletes with a physical impairment wanted more information and education regarding NS and topics such as anti-doping issues, effective NS and what their relative needs are compared to AB athletes. The findings from Chapter three have therefore provided a rationale for further research exploring the effectiveness of popular NS in this population. It has also highlighted the need for more education on both NS and anti-doping issues. The former should be included/mandatory on coaching education courses and any impairment-specific advice should be made available on easily accessed websites such as WADA, IPC and National Governing Bodies of sports. The latter should be easily accessed on the WADA website and should be covered in athlete education sessions at an elite level. Chapter three has greatly enhanced the understanding of the use of NS by athletes with a physical and visual impairment.

8.2.2. Factors influencing caffeine’s ergogenic effects

There are many factors that may influence the ergogenic effects of caffeine during UBE such as genetics, training status, habitual caffeine intake, physical impairment, timing and dose of caffeine, and route of administration. This thesis has contributed greatly to two main factors: i) training status and ii) physical impairment. The combined findings of Chapters four and seven indicate that training status may influence caffeine’s ability to improve performance during UBE due to the UBE-specific training adaptations that occur (see section 8.2.3 and 8.2.4). The results from Chapter six also indicate that individuals with a SCI may need to consider their dosage and timing of caffeine intake more carefully than AB individuals due to high C\text{max} values and slow elimination and clearance rates (see section 8.2.5).

The combined findings of Black et al., (2015) in naive caffeine users, and Chapter four indicate that habitual caffeine intake may not be a large influencing factor on caffeine’s ergogenic ability. No performance improvement was seen in either during UBE and both reported improvements during LBE despite the participants being naive (Black et al., 2015) and habitual (Chapter four) caffeine users. It has also contributed to our understanding of the importance of protocol characteristics. The impact of the preload during both Chapter four
and Black et al., (2015) on peripheral fatigue may have been too great to see performance improvements in recreationally active participants. Exploration of the impact of caffeine on sprint (improvement), short-term endurance (one-off improvement) and endurance TT (no improvement in club level athletes/improvement in elite athlete) performance indicates changes in caffeine’s ability to influence performance depending on the exercise protocol and the participant characteristics. Future studies should consider exercise protocols and participant recruitment carefully and ensure they are as ecologically valid as possible.

8.2.3 Caffeine and endurance UBE in AB participants

Table 2.3 and 2.4 (pg 36-38) show the limited number of studies investigating the effects of caffeine supplementation on UBE, especially during endurance exercise. The double-poling studies contribute to the UBE literature however the findings must be translated to arm-only exercise performance with caution due to the involvement of the trunk and upper leg musculature. Black et al., (2015) was therefore the only study to have investigated the influence of caffeine on endurance exercise during arm-only exercise (asynchronous arm cranking) in the form of a preloaded 10 min performance trial. Caffeine ingestion (6 mg·kg⁻¹) by the male and female naive caffeine users improved cycling but not handcycling performance following a 30 min preload at 60% $\dot{V}O_2\text{peak}$. Chapter four was able to extent the work of Black and colleagues by investigating the use of caffeine prior to a longer-term endurance performance test comprised of a 30 min preload at 65% $\dot{V}O_2\text{peak}$ and a 10 km TT (lasting ~24 min). Chapter four utilised male, habitual caffeine users who are more representative of the general (Tran et al., 2016) and athletic population (Chester & Wojek, 2008). It also employed a synchronous handcycling modality which is applicable to the sports of handcycling and triathlon. Caffeine (4 mg·kg⁻¹) once again improved cycling but not handcycling performance but there were clear inter-individual differences. Chapter four suggested that training status may influence caffeine’s ability to improve performance during arm-only exercise. It agrees with previous literature which has suggested well-trained participants may have the necessary intra and/or extracellular adaptations to training required to improve performance following caffeine consumption (Collomp et al., 1992). Well-trained athletes are also likely to exhibit the motivation to perform optimally during maximal exercise testing. Chapter four contributes further performance data to this field of research.
8.2.4. Caffeine and UBE in individuals with a SCI

Chapters five and seven utilised UBE performance protocols and have contributed to the limited body of caffeine literature utilising participants with physical impairments, and specifically participants with a SCI (Table 2.4). Prior to the current thesis, Flueck et al. (2015; 2014) were the only research group to investigate the use of caffeine in this population. Flueck et al. (2014) reported no significant improvements in 1500 m wheelchair TT in athletes with paraplegia and spina bifida following the ingestion of caffeine. Interestingly, there were 4 out of 9 participants who produced their fastest TT following caffeine. The authors speculated that the elite status of the athletes and therefore the small variance in performance times may have led to a lack of performance improvement and suggested that less trained individuals may benefit more. This is in contrast to Chapters four and seven that suggest a greater training status may increase the likelihood of caffeine’s ability to improve UBE endurance performance in AB participants and an elite athlete with paraplegia. This difference may be related to muscle fibre type distribution. Untrained AB individuals have a greater proportion of type IIb muscle fibres (41%) in the deltoid (a key muscle during handcycling and wheelchair propulsion) compared to trained and untrained individuals with paraplegia (11-15%) (Schantz et al., 1997). Type I fibres appear to dominate the deltoid muscle in individuals with paraplegia (55-59%) (Schantz et al., 1997) and hence there may be a greater likelihood of caffeine improving endurance performance, specifically in well-trained individuals. Chapter seven provided a novel insight into the positive effects of caffeine in an elite athlete with paraplegia during endurance UBE performance. With the suggestion that type I muscle fibres may also be more sensitive to caffeine than type II fibres it might be expected to see more consistent findings in the endurance exercise literature in trained individuals and individuals with a SCI. Further research is required to elucidate why the current body of literature is equivocal.

The beneficial effects of caffeine have also been observed during short-term, maximal exercise in individuals with a physical impairment (Chapter five) and a SCI (Flueck et al., 2015). Flueck and colleagues (2015) also investigated the influence of caffeine on 3 min maximal arm crank performance in AB participants, and participants with paraplegia and tetraplegia. Performance improvements were seen in participants with paraplegia only (Flueck et al., 2015), which may be related to lower type IIa and b muscle fibres in trained individuals with tetraplegia (13 and 4% compared to 32 and 11% in trained individuals with paraplegia, and 17 and 41% in AB) (Schantz et al., 1997). This explanation unfortunately does not hold true for the findings in Chapter five that reported improvements in both 20 m
sprint and a one-off bout of 4 min maximal push performance. The participant group contained seven participants with tetraplegia and five non-SCI participants, and hence a greater variability in muscle fibre type distribution may have been present. Flueck et al. (2015) were surprised not to observe an improvement in the AB participants because a number of UBE performance studies have shown improvements following the ingestion of caffeine (Anderson et al., 2000; Bruce et al., 2000; Skinner et al., 2010). These studies however, employed rowing as the mode of exercise which also involves lower limb and trunk musculature. Furthermore, the aforementioned studies all utilised well-trained competitive oarsmen and women in contrast to the AB participants investigated by Flueck et al. (2015). Hence, as with endurance UBE there may also be an effect of training status and SCI lesion level on caffeine’s influence on short-term, high-intensity UBE performance.

### 8.2.5. Caffeine absorption in individuals with a SCI: effect of lesion level

Halstead et al. (1985) suggested that ingestion of passively absorbed drugs may be delayed in individuals with a SCI, observed as an increase in the time to peak and lag time, and a decrease in the maximum plasma concentrations achieved. The physiological functions that are altered in individuals with a SCI (e.g. delayed GI transit times) mean that assumptions of pharmacokinetics cannot be directly transferred from non-SCI individuals (Mestre et al., 2011). Van Soeren et al. (1996) previously explored caffeine (6 mg·kg⁻¹) absorption in a small number of participants with tetraplegia (n=6) and paraplegia (n=2) at rest. The mean C_max in individuals with tetraplegia was 46.7(5.0) µM after 40 min at rest, which then gradually declined to 25.6(1.4) µM at 180 min without plateauing. The two participants with paraplegia reached C_max of 43.3 and 56.5 µM at 40 min also. The authors therefore concluded that the pattern of caffeine absorption did not differ to that observed in AB individuals. Mohr et al. (1998) reported similar responses in individuals with a SCI in which [CAF] reached 57.3(7.4) µM following 60 min rest. Van Soeren et al. (1996) and Mohr et al. (1998) both investigated caffeine responses in very high caffeine users (1368 and 898 mg/d, respectively), and 4/6 participants were smokers in the former study. Habitual caffeine intake may accelerate caffeine metabolism (Bell & McLellan, 2002; Van Soeren et al., 1993) and it is known to also be accelerated in smokers (Arnaud et al., 1999). Chapter six therefore contributed to the literature by employing a larger sample of individuals with both paraplegia (n=8) and tetraplegia (n=8), and a direct control group (n=8). The participants were low-moderate caffeine users (~220 mg·d⁻¹) and non-smokers to eliminate potential confounding factors. Chapter six presented individual caffeine responses to 3 mg·kg⁻¹ caffeine
at regular time-points to allow further exploration of the pattern of caffeine absorption in individuals with a SCI. *Chapter six* observed a greater $C_{max}$ in individuals with tetraplegia (21.5 µM) compared to AB (12.2 µM) and individuals with paraplegia (15.1 µM), and mean $C_{max}$ occurred at 70, 80 and 80 min, respectively. The large $C_{max}$ reported in individuals with tetraplegia has been seen previously but has occurred earlier at 40 (Van Soeren et al., 1996) and 60 min (Mohr et al., 1998) compared to 70 min in *Chapter six*. The longer time to $C_{max}$ in *Chapter six* may reflect the removal of any potential influence of high habitual caffeine use and smoking on caffeine metabolism. Flueck et al. (2015) also reported a significantly greater [CAF] in individuals with tetraplegia 60 min post-ingestion (64.1(6.9) µM). An individual’s caffeine absorption pattern should therefore be considered when using caffeine as an ergogenic aid, especially for short-term exercise. Individuals with tetraplegia may consider using a lower caffeine dose and individuals may consider consuming caffeine earlier than the 60 min recommended prior to short-term exercise performance.

### 8.3. Future directions

The current thesis has explored the influence of caffeine on UBE performance in recreationally active AB participants and, trained and elite participants with a physical impairment. The findings are therefore applicable to AB sports that involve UBE such as rowing and canoeing, and disability/Paralympic sports such as the wheelchair court sports (rugby, tennis and basketball), wheelchair racing, handcycling, paracanoeing and pararowing. The evidence of caffeine’s effects is inconclusive in either population, and the ergogenic benefit may depend on a number of factors such as SCI lesion level, training status, and intensity and duration of exercise performance. The current thesis has substantially contributed to the field of study however a number of further research questions have arisen that require attention. These will be outlined below.

#### 8.3.1. Caffeine and UBE

The current thesis has proposed a number of factors that may impact upon caffeine’s potential influence on UBE performance such as muscle fibre type distribution, body composition, caffeine absorption and training status. To help explore the magnitude of their influence where feasible, future studies should aim to do the following:

- Measure [CAF] prior to caffeine consumption and prior to exercise testing of participants with a SCI. Any additional time-points would provide greater detail and help to further understand the pattern of the caffeine absorption curve. This data
would also help to exclude impaired absorption/delayed gastrointestinal transit times as a reason for caffeine failing to improve UBE performance.

- Quantify muscle fibre type distribution in the arm musculature of UBE trained individuals with and without a physical impairment. There is currently very little data regarding muscle fibre type distribution and yet it appears it may be an important factor when exploring an individual’s ability to perform UBE with/without caffeine supplementation. Muscle biopsy procedures are invasive for the participant and expensive to conduct however; less invasive procedures such as the measurement of muscle carnosine content via proton magnetic resonance spectroscopy are emerging (Baguet et al., 2011). A larger database would be useful to help explain UBE study findings.

- Report training status, body mass and body composition. Additional participant characteristics would help explore the reasons behind caffeine’s ability to/not to improve UBE performance in individuals with a physical impairment. Level of competition, weekly training hours and fitness markers would help describe training status. A DXA scan would be gold standard to measure body composition in this population (Goosey-Tolfrey et al., 2016; Willems et al., 2016) however, other more accessible and cheaper anthropometric measurements would also be better than providing no data at all.

8.3.2. Caffeine and endurance UBE performance: influence of training status

Previous studies exploring the effects of caffeine on endurance UBE performance have produced varying results and have been observed as an improvement (Chapter seven; Stadheim et al., 2014; 2013) or no significant change (Black et al., 2015; Chapter four). The studies that observed improvements used well-trained athletes, and those that did not used recreationally active participants. Chapter four specifically suggests that training status may be related to caffeine’s ability to improve performance. With only five studies investigating endurance UBE performance and none specifically exploring the impact of training status, further investigation is required.

Handcycling, wheelchair racing or ACE endurance performance protocols should be performed in a laboratory setting to assess caffeine’s impact on performance of UBE in trained individuals with a physical impairment. An extension of the case study in Chapter seven using handcycling and Paralympic triathlon athletes would extend our understanding.
An additional group of recreational handcyclists would increase our understanding further regarding the impact of training status on caffeine’s ability to effect UBE performance.

An alternative method of assessing the impact of training status would be to perform a training study whereby novice participants are tested at baseline and following a period of UBE training (3–4 sessions/wk) following the ingestion of caffeine and placebo. This would require long-term commitment from participants but would provide vital data on the influence of training status on caffeine’s ergogenic properties. Following these findings future studies should explore the influence of caffeine in more practically relevant environments e.g. on the track, road or in the water, because the demands of exercise on an ergometer or treadmill may not adequately replicate those experienced in normal training and competition environments.

8.3.3. Caffeine and UBE performance: influence of SCI lesion level

There appears to be an influence of SCI lesion level on whether caffeine has a beneficial effect on performance. Flueck et al. (2015) reported improvements in 3 min maximal arm crank performance in participants with paraplegia but not AB participants or participants with tetraplegia. Future studies should therefore explore the impact of SCI lesion level during various UBE protocols (sprint, short-term and endurance). Where possible a homogenous group of caffeine responders with complete paraplegia and tetraplegia should initially be tested to assess the influence of SCI lesion level.

The use of a SCI population in research exploring the ergogenic benefits of caffeine would also allow further exploration of its mechanisms of action. Adenosine receptor antagonism increases circulating levels of catecholamines in AB individuals to produce motor-activating and arousing effects (Davis et al., 2003). This influence of caffeine on catecholamine release is not replicated in individuals with tetraplegia or high-level paraplegia due to impaired sympathetic activity. Hence any mechanism of action reliant on circulating catecholamines is unlikely to be responsible for any performance improvements reported in individuals with impaired autonomic function. This may explain the contrasting responses of participants with paraplegia and tetraplegia during the 3 min all-out arm crank test following caffeine (Flueck et al., 2015). However, improvements in short-term, high-intensity UBE performance were seen in Chapter five in individuals with tetraplegia and therefore another mechanism may be responsible. The increase in [FFA] which occurs in individuals with a SCI despite no significant change in catecholamine concentrations (chapter six) indicates a direct effect of caffeine on adipocytes and hence, a potential direct effect on other tissues.
Caffeine is likely to have multiple mechanisms of action and participants with a complete, high-level SCI remain an appealing group to help differentiate between some of these effects due to their impaired autonomic function (Krassioukov & West, 2014).

8.3.4. Caffeine and cognitive/skill performance

Performance outcomes in the wheelchair court sports such as basketball, rugby and tennis are not solely based on physiological parameters. These intermittent sports are partially dependent on motor control, decision making, cognitive function and skill performance (Morgulec-Adamowicz et al., 2011; Vanlandewijck et al., 1999). Skills such as passing, shooting, serving and dribbling are key performance indicators in these sports. Hence the impact of caffeine must be assessed based on its influence on sports performance as a whole, not on individual elements. Caffeine has been shown to improve cognitive function and sport-specific skill performance in AB participants, especially in scenarios where physical or mental fatigue are prominent (Baker et al., 2014). The performance impact of caffeine on cognitive and skill performance must be investigated in UBE-specific sports prior to recommending caffeine to wheelchair sportspersons.

8.3.5. Route of caffeine administration

Given the inter-individual variation in caffeine absorption in individuals with a SCI, further exploration of routes of administration other than capsules is required. Caffeine is available to athletes in many forms such as coffee, sports drinks, gels, capsules and chewing gum. Caffeine in the form of a chewing gum has been shown to deliver the supplement faster than capsules and may indicate absorption via the buccal mucosa (Kamimori et al., 2002). The evidence is currently limited and equivocal on the effects of caffeine gum on exercise performance (Oberlin-Brown et al., 2016 (no improvement in preloaded cycling 20 km TT performance); Paton et al., 2015 (improved mean and sprint performance in a 30 km cycling TT); Ryan et al., 2012 (no improvement in cycling time to exhaustion)) however; given the potential to eliminate the influence of delayed gastrointestinal transit times it warrants further investigation in a population of individuals with a SCI.

8.3.6. Ergogenic effects of other nutritional supplements

The current thesis has shown that the ergogenic benefit of caffeine during various types of exercise in AB individuals may not be directly transferred to individuals with a SCI. The mechanism of action via the CNS should not be altered in individuals with a SCI and yet caffeine does not appear to consistently improve performance in this group. It is reasonable
therefore to assume that other NS may also vary in their ergogenic nature during whole or LBE and UBE performance. Table 2.1 (pp. 27) highlights the limited research in this area with only two studies exploring the use of creatine, one investigating sodium citrate and one assessing the impact of carbohydrate drinks in participants with physical impairments.

8.4. Practitioner reflections

As an applied practitioner’s thesis, the aim was to influence the practice of disability support staff, especially nutritionists/dietitians. The main learning from this thesis is that every athlete must be considered as an individual. As with AB athletes, a practitioner must consider numerous athlete (age, gender, body mass, genetics, training status etc) and sport characteristics (duration and intensity of training and competition, performance indicators for success, the contribution of skill, environmental conditions etc). In disability sport, a practitioner must also consider the impact of the athlete’s physical impairment. The impact of level and completeness of SCI on neurological and physical function is wide-ranging and well-researched. This thesis has shown that something as simple as the caffeine absorption curve displayed by an athlete may also be influenced by level of SCI. Hence a practitioner may need to adjust the dosage, timing and frequency of caffeine consumption in these individuals. Use of available SCI-specific evidence such as in this thesis is important and can be extremely useful however, a practitioner must also understand that the heterogeneity of SCI means that caffeine, and all other NS, should be trialled on an individual basis. The health and well-being of an athlete should always be considered first i.e. does the athlete experience any side-effects from caffeine consumption via food products such as coffee and tea, and is the NS batch-tested? Secondly, is there evidence or a viable mechanism of action for the athlete’s use of caffeine during training or competition? Finally, caffeine should be trialled in a controlled and safe environment alongside quantitative and qualitative data collection to decide whether it should be investigated further as a viable NS to enhance sporting performance.

This thesis has clearly shown that the positive effects of caffeine reported during LBE cannot be directly translated to similar UBE protocols (Chapters four and five). This is likely related to numerous factors including an individual’s UBE-specific training status, whereby those who are highly trained are more likely to see the positive impact of caffeine due to the specific training adaptations acquired and the motivation to perform. A practitioner should therefore consider each athlete and situation separately and not rely on LBE and caffeine.
research. This method of practice should also extend to other NS such as creatine and buffering agents given a lack of impairment-specific research.
References


to able-bodied individuals. *International Journal of Sport Nutrition and Exercise Metabolism*, 25(6), 584-593.


Appendix A: Nutritional supplement questionnaire example

Nutritional Supplement Habits and Perceptions of Athletes with a Disability.

Thank you for choosing to complete this questionnaire, it should only take approximately 15-20 minutes. Please remember that your answers are confidential and we therefore ask you to be as honest as possible.

The following section refers to details about you and your sport.

1. What is your age?

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<th>Age Group</th>
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<tbody>
<tr>
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<td>☐</td>
<td>25-30</td>
<td>☐</td>
<td>31-35</td>
<td>☐</td>
<td>36-40</td>
</tr>
</tbody>
</table>

2. What is your gender?

<table>
<thead>
<tr>
<th>Gender</th>
<th>☐</th>
<th>☐</th>
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</thead>
<tbody>
<tr>
<td>Male</td>
<td>☐</td>
<td>Female</td>
</tr>
</tbody>
</table>

3. What is your nationality?

[Blank]

4. What is your ethnic origin?

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<thead>
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<tbody>
<tr>
<td>White</td>
<td>☐</td>
<td>Black</td>
<td>☐</td>
<td>Asian</td>
<td>☐</td>
<td>Hispanic</td>
</tr>
</tbody>
</table>

5. How much do you weigh? (Please provide units of measurement such as kg, lbs)

<table>
<thead>
<tr>
<th>Weight</th>
<th>☐</th>
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<tbody>
<tr>
<td>Actual (measured in the last 3 months)</td>
<td>☐</td>
<td>Estimated</td>
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</table>

6. What is your height? (Please provide units of measurement such as feet, metres)

<table>
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<tr>
<th>Height</th>
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<tbody>
<tr>
<td>Actual (measured in the last 3 months)</td>
<td>☐</td>
<td>Estimated</td>
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</table>

7. What is your current sport/discipline/event? (Please give as much detail as possible)

[Blank]

8. How many years have you been competing in your current sport?

[Blank]
9. What is the highest level you currently represent in your sport?
  Club ☐
  Regional ☐
  National ☐ If checked, please state which country in the box below.

10. On average, how many hours per week do you train in total? (Please check 1 box)
  0-5 ☐ 6-10 ☐ 11-15 ☐ 16-20 ☐ 21-25 ☐ 26+ ☐

11. What is your disability? (Please give as much detail as possible)

12. What is your sport-specific classification?

The following section refers to your nutritional supplement habits. The term ‘supplements’ refers to any product intended to supplement the diet, provide nutrients and/or enhance performance such as vitamins, minerals, carbohydrate sports drinks/bars, amino acids, herbal remedies, creatine and caffeine etc.

13. How important do you think good nutrition is to sports performance?
  Very important ☐
  Important ☐
  Moderately important ☐
  Of little importance ☐
  Unimportant ☐

14. Do you monitor your hydration status?
  Yes ☐ Please go to Question 14A
  No ☐ Please go to Question 14B

14A. Which of the following methods do you use? (Please check all that apply)
  I use thirst as an indicator of hydration ☐
  I check my urine colour/compare it to a urine/pee chart ☐
  I weigh myself before and after exercise ☐
  A sport scientist/nutritionist/coach measures my hydration status using a machine to measure urine specific gravity or serum osmolality ☐
  Other (Please state in the box below) ☐

14B. Please indicate if there is a reason why you can’t/don’t use any of these methods.
The following section asks about your use of nutritional supplements in the last 6 months. The term ‘supplements’ refers to any product intended to supplement the diet, provide nutrients and/or enhance performance such as vitamins, minerals, carbohydrate sports drinks/ bars, amino acids, herbal remedies, creatine and caffeine etc.

15. Have you used any nutritional supplements in the last 6 months?
   - Yes ☐ Please go to Question 15A, B and C
   - No ☐ Please go to Question 15D

15A. For each sport-specific/ performance-enhancing supplement that you have used in the last 6 months please complete a row in the table below.
Examples of sport-specific/ performance-enhancing supplements include sports drinks, gels, bars, drinks powders, creatine, beta-alanine, caffeine, beetroot juice…

*Do not enter health supplements here; these will be entered in Question 15B
If you have any doubt whether a product is classified as a nutritional supplement then please write it down.

<table>
<thead>
<tr>
<th>Supplement type and brand</th>
<th>How do you take this supplement?</th>
<th>Reason for taking the supplement?</th>
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<tbody>
<tr>
<td></td>
<td>How often? Daily, once a week...</td>
<td>(Please check all that apply)</td>
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<td></td>
<td>When? During a cold/ in the off-season... Or Only on training or rest days</td>
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<tr>
<td></td>
<td>Only for some training? Strength, endurance or skills sessions</td>
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<tr>
<td></td>
<td>Timing? Before, during or after a session</td>
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<tr>
<td></td>
<td>How much? Do you know the dose/ how many grams or pills a day?</td>
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</table>

Example: Powerade ION4 isotonic sports drink
Example: Sip during a cardio session lasting more than 60 min or if I have not eaten in the 3-4 hours before training.
Example: Medical need/ deficiency ☐ Due to an inadequate diet ☐ Support immune system ☐ To provide energy ☒ Increase strength/power ☐ To aid recovery ☐ Because everyone else does ☐ Because I am told to ☐ Other-Hydration/ tastes better than water
Example: Supplement 1
Medical need/ deficiency ☐ Due to an inadequate diet ☐ Support immune system ☐ To provide energy ☐
<table>
<thead>
<tr>
<th>Supplement</th>
<th>Medical need/ deficiency</th>
<th>Due to an inadequate diet</th>
<th>Support immune system</th>
<th>To provide energy</th>
<th>Increase strength/power</th>
<th>To aid recovery</th>
<th>Because everyone else does</th>
<th>Because I am told to</th>
<th>Other (Please state)</th>
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</table>
15B. For each health supplement that you have used in the last 6 months please complete a row in the table below.

Examples of health supplements include vitamins, minerals, herbal remedies, probiotics, omega 3, cranberry extract…

If you have any doubt whether a product is classified as a nutritional supplement then please write it down.

<table>
<thead>
<tr>
<th>Supplement type and brand</th>
<th>How do you take this supplement?</th>
<th>Reason for taking the supplement?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>We are looking for as much detail as possible</td>
<td>(Please check all that apply)</td>
</tr>
<tr>
<td></td>
<td>• <strong>How often?</strong> Daily, once a week...</td>
<td>Medical need/ deficiency</td>
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<td></td>
<td>• <strong>When?</strong> During a cold/ in the off-season... Or Only on training or rest days</td>
<td>Due to an inadequate diet</td>
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<tr>
<td></td>
<td>• <strong>Only for some training?</strong> Strength, endurance or skills sessions</td>
<td>Support immune system</td>
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<tr>
<td></td>
<td>• <strong>Timing?</strong> Before, during or after a session</td>
<td>To provide energy</td>
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<td></td>
<td>• <strong>How much?</strong> Do you know the dose/ how many grams or pills a day?</td>
<td>Increase strength/power</td>
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Supplement 1

<table>
<thead>
<tr>
<th>Medical need/ deficiency</th>
<th>Medical need/ deficiency</th>
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<td>Increase strength/power</td>
<td>Increase strength/power</td>
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<tr>
<td>To aid recovery</td>
<td>To aid recovery</td>
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<tr>
<td>Because everyone else does</td>
<td>Because everyone else does</td>
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<td>Other (Please state)</td>
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<td>Medical need/ deficiency</td>
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<td>Supplement 6</td>
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### Supplement 7

<table>
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<tr>
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<tr>
<td>Support immune system</td>
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<tr>
<td>To provide energy</td>
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</tr>
<tr>
<td>Increase strength/power</td>
<td>☐</td>
</tr>
<tr>
<td>To aid recovery</td>
<td>☐</td>
</tr>
<tr>
<td>Because everyone else does</td>
<td>☐</td>
</tr>
<tr>
<td>Because I am told to</td>
<td>☐</td>
</tr>
<tr>
<td>Other (Please state)</td>
<td>☐</td>
</tr>
</tbody>
</table>

**15C. Where did you obtain/ buy your supplements?** (Please check all that apply)

- Provided by a team sponsor ☐
- Provided by a sports nutritionist/ dietitian ☐
- From a supermarket ☐
- From a health food/ sports shop ☐
- From a pharmacy ☐
- I ordered them on the internet ☐
- Other (Please state in the box below) ☐

**15D. If you don’t use supplements, why not?** (Please check all that apply)

- I do not need them ☐
- They are unhealthy ☐
- I don’t know enough about them ☐
- I am concerned about a positive drugs test ☐
- They are too expensive ☐
- My sport does not allow them ☐
- Taking supplements is like cheating ☐
- Other (Please state in the box below) ☐

**16. Have you taken any supplements by injection in the last 6 months?**

- Yes ☐ Please go to Question 16A
- No ☐ Please continue to Question 17

**16A. Please indicate which supplements you have had injected and why you used them in the box below.**

<table>
<thead>
<tr>
<th>Product</th>
<th>Why?</th>
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<tbody>
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**17. Have you EVER experienced any negative/side-effects from using a supplement? E.g gastrointestinal distress, rapid bowel movements, spasticity, cramps etc**

- Yes ☐ Please go to Question 17A
- No ☐ Please continue to Question 18
17A. Which product(s) did you use and what were the negative/side effects?

<table>
<thead>
<tr>
<th>Product (Please specify brand where possible)</th>
<th>Negative/side-effects</th>
</tr>
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<tbody>
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The following section relates to the sources of information YOU use when considering your nutritional supplement habits.

18. Do you have access to information on anti-doping?
   - Yes ☐
   - No ☐

19. Have you ever attended a workshop/presentation on nutritional supplements and/or anti-doping?
   - Yes ☐ Please go to Question 19A
   - No ☐ Please go to Question 19B

19A. If yes, when did you attend it?

<p>| |</p>
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19B. If no, would you like to?
   - Yes ☐
   - No ☐

20. Would you like more information and education regarding nutritional supplements and anti-doping?
   - Yes ☐ Please go to Question 20A and 20B
   - No ☐ Please continue to Question 21

20A. If yes, how would you prefer to receive this information? (Please check all that apply)
- Workshops ☐
- Presentations ☐
- Leaflets/booklets ☐
- Individual consultation ☐
- Internet ☐
- Other (please state in the box below) ☐

20B. What type of information would be most useful for you regarding nutritional supplements and/or anti-doping? For example effective supplements/doses, doping concerns, the World Anti-Doping Code, how to read product labels, whether your needs are different to able-bodied athletes, other information.

<p>| |</p>
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</table>
21. How do you decide whether a supplement is safe to use? (Please check all that apply)
- It’s says on the label ☐
- I ask a sports nutritionist/ dietitian/ medical professional ☐
- I ask my coach/ teammates ☐
- I check the manufacturer’s website ☐
- I check a website that indicates which products have been tested for banned substances i.e., Informed-Sport ☐
- I do my own research using the internet, books, journals etc ☐
- No supplement is safe ☐
- N/A (I don’t use supplements) ☐
- Other (Please state in the box below) ☐

22. Who/ What do you currently use to help you make a decision about your use of supplements? Please only rank up to 5 responses, 1=Your most used source, 2 = your second most used source, 5=Only used a little/ sometimes. If you only use 2, 3 or 4 sources, only rank 1 down to 2, 3 or 4.

E.g. if you use a physiotherapist most often for information on supplements, write a number 1 in the box opposite and so on, up to a maximum of 5.

Note - The numbers 1, 2, 3, 4 and 5 should only occur once in your answers and therefore some options will be left blank.
Please ask for help if you are at all unsure about this question!

<table>
<thead>
<tr>
<th>Source</th>
<th>Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Training partner/athlete</td>
<td></td>
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<tr>
<td>Coach</td>
<td></td>
</tr>
<tr>
<td>Friends/family</td>
<td></td>
</tr>
<tr>
<td>Physiotherapist</td>
<td></td>
</tr>
<tr>
<td>Sports nutritionist/ dietitian</td>
<td></td>
</tr>
<tr>
<td>Doctor/medical professional</td>
<td></td>
</tr>
<tr>
<td>Supplement/ health food store</td>
<td></td>
</tr>
<tr>
<td>*Books/ magazines</td>
<td></td>
</tr>
<tr>
<td>*Evidence-based/ scientific journals</td>
<td></td>
</tr>
<tr>
<td>*Internet/ websites</td>
<td></td>
</tr>
<tr>
<td>*Other</td>
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</table>

22A. If you checked a box with an *, where possible please indicate which books, magazines, journals, websites or ‘other’ that you use.

23. Do you have access to a sports nutritionist/ dietitian through your sport/ team?
- Yes ☐
- No ☐

24. Have you ever seen a registered sports nutritionist/ dietitian in person for advice?
- Yes ☐Please go to Question 24A
- No ☐Please go to Question 25
24A. How often do you see them?
Very frequently ☐
Frequently ☐
Occasionally ☐
Rarely ☐
Very rarely ☐

25. In your opinion, do you need the same supplements as an able-bodied individual competing in a similar version of your sport?
Yes, I need the same type of supplements ☐
No, I have different nutritional requirements ☐
Yes, I need the same type of supplements but different amounts ☐
Other (Please state in the box below) ☐

26. How do you decide how much of a supplement to take? (Please only check 1 box)
I calculate it based on my body weight ☐
I am told/ given it by the sports nutritionist/ dietitian ☐
I follow the instructions on the label/ manufacturers website ☐
Unsure ☐
N/A – I don’t use supplements ☐
Other (Please state in the box below) ☐

The following section relates to YOUR personal opinions regarding nutritional supplements and anti-doping.

27. Do you think all nutritional supplements that are commercially available on the market have been scientifically tested and are therefore safe to use?
Yes ☐
No ☐

28. Do you think there is a health risk associated with taking supplements?
Yes, all supplements carry a health risk ☐
Some supplements have health risks ☐
No, no supplements carry a health risk ☐
29. Who provides the most trusted source of information on nutritional supplements?
You do not necessarily have to use these sources but you believe they are trustworthy.
Please only rank up to 5 responses, 1 = Your most trusted source, 2 = your second most trusted source and so on. If you only trust 2, 3 or 4 sources, only rank 1 down to 2, 3 or 4.
Note - The numbers 1, 2, 3, 4 and 5 should only occur once in your answers and therefore some options will be left blank.
Please ask for help if you are at all unsure about this question!

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<td>*Internet/websites</td>
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<tr>
<td></td>
<td>*Other</td>
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</tbody>
</table>

29A. If you checked a box with an *, where possible please indicate which books, magazines, journals, websites or ‘other’ that you use.

30. Do you think doping agents have the potential to improve sports performance?
   Yes ☐
   No ☐

31. If you would definitely not be caught, would you risk your health for any performance gains that may come with taking doping agents?
   Yes ☐
   No ☐
   Maybe ☐

32. Which (if any) of the prohibited substances/methods do you believe has the greatest potential to improve performance in your sport? (This is not saying you would use it, just that you believe it would aid performance in your sport). (Please only check 1 box).
   Stimulants e.g. amphetamines ☐
   Anabolic-androgenic steroids e.g. nandrolone ☐
   Diuretics and masking agents to prevent detection ☐
   Blood doping e.g. EPO, blood reinfusion ☐
   Peptide hormones, growth factors and related substances ☐
   Beta-2 agonists e.g. clenbuterol ☐
   Hormone and metabolic modulators ☐
   Anorectics and weight loss agents e.g. sibutramine ☐
   Boosting ☐
32A. How/ why do you believe this type of doping would improve your sports performance?

Please indicate to what extent you agree or disagree with the following statements:

33. ‘The more supplements I take, the better I will perform’.
   - Strongly disagree □
   - Disagree □
   - Neither agree nor disagree □
   - Agree □
   - Strongly agree □

34. ‘Taking supplements gives me the competitive edge I need to win’.
   - Strongly disagree □
   - Disagree □
   - Neither agree nor disagree □
   - Agree □
   - Strongly agree □

35. ‘I feel under pressure to use supplements’.
   - Strongly disagree □
   - Disagree □
   - Neither agree nor disagree □
   - Agree □
   - Strongly agree □

36. ‘Exercise increases the need for supplements’.
   - Strongly disagree □
   - Disagree □
   - Neither agree nor disagree □
   - Agree □
   - Strongly agree □

37. ‘There is a risk of consuming a banned substance when taking a supplement’.
   - Strongly disagree □
   - Disagree □
   - Neither agree nor disagree □
   - Agree □
   - Strongly agree □
38. ‘I feel pressured to take nutritional supplements because my competitors/ opponents do’

| Strongly disagree | ☐ |
| Disagree         | ☐ |
| Neither agree nor disagree | ☐ |
| Agree            | ☐ |
| Strongly agree   | ☐ |

If you would like to receive feedback on the study results please write your email address in the box below.

Thank you for taking the time to complete this questionnaire, we greatly appreciate your assistance in helping us to further understand the nutritional supplement habits of disabled athletes.

Please don’t hesitate to contact us if you have any questions regarding the questionnaire or the overall study.
Appendix B: Caffeine Enzyme-linked immunosorbent assay (ELISA) technique for saliva

Sample collection
All saliva samples were collected via the passive dribble method into a sterile tube. Samples were weighed to the nearest 10 mg. Saliva volume was estimated assuming saliva density to be 1.00 g/ml, and saliva flow rate was calculated from saliva volume and collection time. Saliva samples were transferred into Eppendorfs and centrifuged at 12,000 rpm for 3 min in a high speed microcentrifuge. The supernatant was removed and frozen at -80°C until analysis.

Sample analysis
Salivary caffeine concentration was determined using a commercially available ELISA kit. For more detailed instructions for the assay please refer to the manufacturer’s instructions: Caffeine ELISA kit Cat No.: DEIA6842, Creative Diagnostics, Shirley, New York, USA.
Briefly, the ELISA consisted of the following steps:

- Samples were thawed completely
- Samples were re-spun at 1300 rpm for 10 min and the supernatant was pipetted into an appropriately labelled Eppendorf.
- Saliva samples and standard samples of a known concentration were pipetted into a 96 well plate pre-coated with the specific capture antibody for antibody for the protein being measured.
- During an incubation period, any protein within the saliva is bound by the immobilised antibody in the well.
- The unbound substances are washed away prior to a second detection anti-body being added to each well, followed by a further incubation period.
- The wash step is repeated to remove any unbound anti-body reagent, and a substrate and amplifier solution is added to the wells to bind to the anti-body-sample complex. This step initiates a reaction and causes a colour change in the sample.

Finally, the reaction is stopped and the absorbance of each well is measured using a micro plate reader (Opsys MR, Dynex Technologies, Chantilly, VA). Sample concentrations are determined by relation to a standard curve generated by plotting the absorbance of the standard samples against the standard’s known concentration.
Appendix C: Reverse phase high-performance liquid chromatography (HPLC) methodology for caffeine analysis

Plasma [CAF] was analysed using HPLC as described by Holland et al. (1991) with two minor modifications; prior to injection onto the HPLC column each sample was individually filtered (Mini-UniPrep syringeless filters, Fisher Scientific, UK) and no guard column was used. The method produced a coefficient of variation (CV) of 1.06% (range 0.24-1.45%). Briefly, the HPLC caffeine analysis consisted of the following steps:

**Caffeine sample preparation:**
- 250 μL plasma was added to 250 μL 0.8 M perchloric acid (Sigma-Aldrich, UK).
- Sample was mixed thoroughly using a vortex (30 s).
- Proteins were removed by centrifugation at 14000g at room temperature for 4 min.
- 350 μL supernatant was removed and 27 μL of 4 M sodium hydroxide (Fisher, UK) was added to produce a sample with a pH of ~5.0.
- Sample was mixed thoroughly using a vortex (30 s).
- 100 μL deproteinised sample was filtered using syringeless filters (Sigma-Aldrich, UK) ready for direct injection onto the HPLC column.

**Caffeine sample analysis:**
- Sample injected by autoinjector and eluted isocratically with the elution buffer (15 mM potassium phosphate (Sigma-Aldrich, UK) (pH 4.9)-methanol (Fisher, UK) (85:15, v/v) for 20 min.
- Column flushed with acetonitrile:water (80:20, v,v) for 5 min and the reequilibrated with the elution buffer for 5 min.
- Flow rate was constant at 1.75 ml/min at ambient temperatures (21-24°C).
- Eluted peaks were detected by ultraviolet absorbance at 274 nm and peak areas were used for quantitation using an eight-point standard curve.