Spinal cord injury level influences acute plasma caffeine responses.

Terri Susan Graham-Paulson[1], Thomas Andrew William Paulson[1], Claudio Perret[2], Keith Tolfrey[3], Philip Cordery[3] and Victoria Louise Goosey-Tolfrey[1,*].

[1] Peter Harrison Centre for Disability Sport, School of Sport, Exercise and Health Sciences, Loughborough University, Leicestershire, UNITED KINGDOM.

[2] Swiss Paraplegic Centre, Institute of Sport Medicine, Nottwil, SWITZERLAND.

[3] School of Sport, Exercise and Health Sciences, Loughborough University, Leicestershire, UNITED KINGDOM.

*****Correspondence:

Email: v.l.tolfrey@lboro.ac.uk

Tel.: +44 (0)1509 226386

Address: Peter Harrison Centre for Disability Sport, Loughborough University, School of Sport, Exercise and Health Sciences, Epinal Way, Loughborough, LE113TU, UK

Abstract

Purpose. To investigate the absorption curve and acute effects of caffeine at rest in individuals with no spinal cord injury (SCI), paraplegia (PARA) and tetraplegia (TETRA). **Methods.** Twenty-four healthy males (8 able-bodied (AB), 8 PARA and 8 TETRA) consumed 3 $mg \cdot kg^{-1}$ caffeine anhydrous (CAF) in a fasted state. Plasma caffeine [CAF], glucose, lactate, free-fatty acid [FFA] and catecholamine concentrations were measured during a 150 min rest period. **Results.** Peak [CAF] was greater in TETRA (21.5 µM) compared to AB (12.2 µM) and PARA (15.1 µM), and mean peak [CAF] occurred at 70, 80 and 80 min, respectively. Moderate and large ES were revealed for TETRA compared to PARA and AB (-0.55 and -1.14, respectively) for the total area under the [CAF] versus time

curve. Large inter-individual responses were apparent in 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. Blood lactate concentration reduced over time ($p=0.022$) whereas blood glucose concentration decreased modestly ($p=0.695$), and no difference between groups was seen ($p>0.05$). **Conclusion.** Level of SCI influenced 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 in athletes with an SCI. The results indicate TETRA should trial low doses in training 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.

Keywords: adrenaline; noradrenaline; free fatty acid; ergogenic; wheelchair athletes

Introduction

Supplementation with caffeine (3-6 $mg \cdot kg^{-1}$) can improve long and short-term endurance performance (7,9) in able-bodied (AB) participants. However, there is a paucity of research on the effects of caffeine on exercise performance in physically impaired populations e.g. persons with a spinal cord injury (SCI). While current evidence is equivocal, a beneficial effect of caffeine (4-6 $mg \cdot kg^{-1}$ body mass (BM) in capsule form) on short-term wheelchair propulsion exercise has been reported (5,13). These studies highlighted that there was great inter-individual variability in wheelchair performance responses during a 1500 m time trial, 4 min maximal push and repeated sprints, especially in individuals with an SCI. The authors highlighted the potential for slower caffeine absorption due to delayed gastrointestinal (GI) transit times and prolonged gastric emptying (GE), especially in those with a cervical lesion level (18). Understanding an individual's time to peak caffeine concentration has been shown to have little impact on prolonged AB endurance cycling performance (34) but is likely to be important prior to short-term upper-body exercise (UBE), and may require further consideration in persons with an SCI.

Both metabolic and physiological functions are altered in individuals with an SCI, and the level and completeness of injury has been shown to influence drug pharmacokinetics (15,23). A review of the literature by Mestre et al. (23) indicated that the delayed absorption seen in some individuals with an SCI increased the time to achieve the required therapeutic dose. One drug reportedly affected by delayed GE and decreased GI motility is theophylline (32), which can be used by individuals with an SCI to help treat bradycardia or to promote the recovery of hemidiaphragmatic function. Diminished bioavailability could result in underestimating the load and maintenance dose of theophylline in individuals with tetraplegia (32). As a methylxanthine drug, theophylline has similar pharmacodynamic actions to caffeine (28) and it has also been linked to improved endurance performance (14,22). There

63 is therefore reason to believe that caffeine absorption may also be delayed in persons with an
64 SCI. In disagreement however, Van Soeren et al. (37) suggested that the time to peak caffeine
65 concentration (6 $mg \cdot kg^{-1}$) in individuals with tetraplegia (~47 µM at 40 min (n=6)) did not
66 differ to those of AB individuals. The authors however could not assess the influence of SCI
67 lesion level on caffeine absorption because there was no direct control group and only two
68 individuals with paraplegia. They also did not report individual participant data, which may
69 help to explain inter-individual performance responses. Flueck et al. (4) measured plasma
70 caffeine concentrations (median) at 60 min only in AB individuals (45.1 $\mu mol \cdot L^{-1}$) and
71 individuals with paraplegia (~54 $\mu mol \cdot L^{-1}$) and tetraplegia (66.1 $\mu mol \cdot L^{-1}$). It therefore
72 remains difficult to determine whether the time course of caffeine absorption differs based on
73 an individual's SCI level.

74 Numerous mechanisms of action have been proposed to help explain the beneficial effects of
75 an acute dose of caffeine on exercise performance. Current research suggests the main
76 mechanism at physiological caffeine doses is the blockade of central nervous system (CNS)
77 adenosine receptors, which indirectly ~~effects~~ affects neurotransmitter release (19) to increase
78 arousal, alertness and attention. Individuals with tetraplegia are therefore an interesting study
79 population given the reduced sympathetic activity caudal to the lesion level and associated
80 impaired catecholamine response (27). The study of this population has lent support to the
81 hypothesis that caffeine can have a direct effect on tissues following reports of adrenaline-
82 independent free fatty acid (FFA) mobilisation (37). No study has directly investigated the
83 acute effects of caffeine in a group of individuals with no SCI, paraplegia and tetraplegia.
84 Hence, the current study aimed to explore the time course of caffeine absorption and its
85 effects at rest in these three groups, with the aim of providing safe and accurate
86 recommendations for its use as an ergogenic aid by individuals with an SCI. It wa~~i~~s

hypothesised that caffeine absorption will be delayed in individuals with tetraplegia compared to those with paraplegia and no SCI.

Methods

Participants. Twenty-four ~~healthy~~ recreationally active males (8 able-bodied controls (AB), 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) scale (20). 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 (21). All procedures were approved by the University Ethical Advisory Committee and performed following the Declaration of Helsinki. Participants' characteristics are shown in Table 1.

Procedures. In the days prior to visiting the laboratory, participants maintained their normal dietary and activity patterns (light-moderate intensity 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 and ~~-~~10:~~.~~00~~)~~ after fasting from 21:00 the previous evening~~in a~~following an overnight fast ~~fasted state(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, 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. Participants then consumed cellulose capsules (Bulk Powders, Colchester, UK) containing 3 $mg \cdot kg^{-1}$ BM caffeine anhydrous (My Protein, Northwich, UK), which were filled manually by the investigators to the nearest 0.1 mg. Participants remained rested for 150 min during which a further 9 blood samples were taken. The blood sampling schedule can be seen in Figure 1. After the final blood sample, participants were again asked ~~once more to record~~ whether they experienced any side-effects during the experimental trial.

Blood sampling and analysis. Blood samples were immediately separated into tubes that contained the relevant preservative(s). At every sampling time-point 5 ml blood was added to an EDTA K2 vacutainer for subsequent plasma caffeine concentration ([CAF]) analysis. A 20 µl blood sample was removed and analysed in duplicate for blood lactate ([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 $mg \cdot ml^{-1}$ tetrahydrolipstatin (THL) was added to the tube for [FFA] analysis. All tubes were centrifuged at 1000g for 10 min at 4ºC as previously described (12). Plasma samples were aliquoted into Eppendorfs and stored at -80ºC until analysis.

Plasma [CAF] was analysed using high-performance liquid chromatography (HPLC) as described by Holland et al. (16) 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. 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 (6). 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).

Statistical analyses

Data were analysed using the IBM Statistics Software Package for the Social Sciences (SPSS) version 22 (IBM Corporation, New York, USA). 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. Homegeneity 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 analysis of variance (ANOVA) for group and time were used to examine differences between [FFA], [A], [NA], [Bla] and [GLU].

An analysis of covariance (ANCOVA) was used to examine differences between [CAF], with daily caffeine consumption (low <50 $mg \cdot d^{-1}$, moderate 50-250 $mg \cdot d^{-1}$ and high >250 $mg \cdot d^{-1}$) 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 $p \leqslant 0.05$ and absolute standardised effect sizes (ES) are included to supplement important findings. An ES of 0.2 was considered small, 0.5 moderate and 0.8 large according to Cohen (3). 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 $mg \cdot kg^{-1}$ caffeine (46.4 (6.8), 55.3 (19.8) and 64.1 (6.9) µM, respectively) (4). 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 (4), 90% power, and an α 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).

Results

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 SCI level interaction p =

0.019) (Figure 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). Peak [CAF] in TETRA was significantly greater than AB (p = 0.008) yet non-significantly (p = 0.058), but meaningfully (ES = 0.9) greater than PARA (21.5 ± 7.0, 12.2 ± 2.3 and 15.1 ± 8.1 µM, respectively). Time to peak [CAF] varied greatly between individuals but group means were 80 min for AB and PARA, and 70 min for TETRA. 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 3.74 ± 0.96 µM, PARA 4.62 ± 3.12 µM, and TETRA 6.08 ± 2.15 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), twitching eye (1)) and five participants reported feeling more alert.

Plasma catecholamines (adrenaline and noradrenaline)

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 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).

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).

Plasma FFA, lactate and glucose

Differences in [FFA] were observed over time and between groups, with the latter not reaching significance, but displaying a large effect (ES = 0.80) (main effect time p < 0.0005; main effect group p = 0.054; time by group interaction p = 0.035). Geometric means (95% CI) [FFA] were 26% (-46 to 2%) lower in PARA than AB, but 9% higher in TETRA than AB (-34 to 50%); furthermore, [FFA] were 47% (6 to 103%) higher in TETRA than PARA (-51 to -6%). The interaction indicated that while PARA experienced only a marginal increase in [FFA] from baseline to 150 min (Δ ~0.13 mmol·l^{-1}), AB and TETRA increased to a greater extent over the course of the protocol (Δ ~0.36 and 0.31 mmol·l^{-1}, respectively).

Although the main effect for ~~No significant~~ differences in TAUC-FFA was not significant~~observed~~ ($p = 0.072$), the effect sizes ranged from small ~~yet moderate~~ (AB vs. PARA, ES = 0.47~~, AB vs. TETRA, ES = 0.85~~) to~~and~~ large (AB vs. TETRA, ES = 0.85; 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 $p = 0.065$). ~~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 ($p = 0.983$).

Discussion

The current study is the first to report large inter-individual differences in caffeine absorption within and between groups when separated for level of SCI (AB, PARA and TETRA). Consequently, dosage and timing recommendations provided to individuals with an 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. 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.

Plasma caffeine

Participant's [CAF] increased in all three groups following the ingestion of 3 $mg \cdot kg^{-1}$ 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 $mg \cdot kg^{-1}$ caffeine (5.7, ~15 and 14.6 µM, respectively) (11,33). This

study is the first to investigate the caffeine absorption curve in a group of participants with paraplegia. In agreement with the hypothesis, the PARA results do not differ from the AB responses at 60 min (11.1 ± 7.9 µM) and both groups reached mean peak [CAF] at 80 min. The TETRA responses were significantly greater than AB and the mean peak [CAF] was reached 10 min earlier (70 min). Flueck et al. (4) also reported a higher [CAF] 60 min post-ingestion of ~6 $mg \cdot kg^{-1}$ caffeine in individuals with tetraplegia compared to those with paraplegia (66.1 and 45.1 µM, respectively). Interestingly, Van Soeren et al. (37) also reported a high peak [CAF] of 46.7 ± 5.0 µM in individuals with tetraplegia (n=6) yet this was reached after only 40 min post-ingestion of 6 $mg \cdot kg^{-1}$ caffeine. The current study therefore adds further support to reports of higher [CAF] in TETRA compared to individuals with lower lesion levels and no spinal injury. Furthermore, the data also highlight the large 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 (1). 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 and only lasted for a short duration. The 3 $mg \cdot kg^{-1}$ 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] in TETRA means that the hypothesis of slowed absorption in this population can be rejected. The sharp rise may be due to a number of factors. Firstly, individuals with tetraplegia have a smaller blood volume compared to AB individuals (17) due to atrophy of the musculature and vessels of the lower limbs. 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 (30). The liver is innervated by both sympathetic and parasympathetic nerves, and the sympathetic splanchnic nerves originate from neurons which are located in the spinal column (T7-T12) (38). 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 (30). It has been proposed that abnormal liver function may affect the metabolism and bioavailability of drugs (23,30). The half-life of many drugs can be prolonged in individuals with an SCI who display suboptimal liver function and slow renal clearance (23,30). 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 (36). The half-life of caffeine in healthy individuals is ~4-6 h (1). This may help explain the sharp rise to peak [CAF] 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 previous research (13). It also suggests that individuals with a high lesion level 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.

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 evident in both SCI groups (Figure 2) due to the heterogeneous nature of this population. The equivocal findings regarding the beneficial effects of caffeine during short-term exercise performance (4) 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 9 (L1 lesion; ASIA B) produced a similar curve to the AB participants,

with a peak (albeit larger) 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 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 an athlete with an SCI determines their individual absorption curve to produce individualised dose and timing recommendations. If this is impractical it is recommended that caffeine is provided to individuals with paraplegia earlier to ensure it enters the bloodstream prior to exercise performance. Research into the use of caffeine gum or mouth rinse is emerging yet the evidence of a consistent positive effect is currently limited (26,29). 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 an SCI.

Body mass and habitual caffeine intakes were similar between all three groups, but PARA were significantly older than AB (Table 1). However, previous research has suggested that age is not associated ($p > 0.612$) with C_{max} or time to C_{max} following caffeine ingestion (Skinner et al., 2014) nor does it affect gastric emptying (Kao et al., 1999). Furthermore, no significant correlations were observed between age and C_{max} ($r = 0.07$) or time to C_{max} ($r = -0.11$) within the current cohort.

Plasma catecholamines (adrenaline and noradrenaline)

Resting plasma catecholamine concentrations did not significantly increase over the course of the 150 min protocol in any group (Figure 3). In contrast, Flueck et al. (4) and Van Soeren et al. (37) reported increases in adrenaline in both AB individuals and individuals with

paraplegia, which may in part be due to the larger 6 $mg \cdot kg^{-1}$ 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 nervous system (27,31).

Plasma FFA, lactate and glucose

Mean resting [FFA] increased over time from 0.36 ± 0.19 $mmol \cdot L^{-1}$ at baseline to 0.61 ± 0.25 at 150 min, in agreement with previous research in an AB and SCI population (10,37). In the absence of a catecholamine response, the current results lend further support for a direct effect of caffeine on human tissue, specifically adipocytes. 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 (12,24). It is also unlikely to aid performance during short-term upper-body exercise where participants/athletes predominantly work anaerobically, and therefore utilise carbohydrate as the main substrate.

Baseline [FFA] was higher in TETRA than AB or PARA (Figure 3). The lack of muscle innervation of paralysed lower limbs in individuals with an SCI leads to rapid muscle atrophy and a reduction in resting metabolic rate (25). Alongside poor nutritional choices and a disruption in the secretion of anabolic hormones, these changes can result in an increase in fat mass (35). An expanding fat mass which releases more FFA and a potential reduction in FFA clearance leads to increased plasma [FFA] (2). The [FFA] responses only significantly differed between the two SCI groups (PARA vs. TETRA). One possible explanation for this could be the difference in the group's time since injury (PARA 4.3 ± 4.3 yr and TETRA 12.2 ± 6.3 yr) which has been positively associated with loss of lean tissue and increased fat mass (35). Unfortunately no body composition or respiratory exchange ratio (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 (12,37).

Many studies report an increase in [Bla] during exercise following the ingestion of caffeine, sometimes in the absence of increased workload/speed/power. At rest however, the current data show [Bla] decreased slightly over the course of the 150 min protocol, which is in line with previous data (37). On the other hand, [GLU] decreased modestly (non-significantly) during the current protocol, as previously reported (24) and is unlikely a result of caffeine ingestion.

Conclusion

The current study demonstrates that there is large inter-individual variability in caffeine absorption in individuals with an 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 with paraplegia may consider consuming supplementary caffeine earlier than the 60 min recommended to AB individuals.

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Conflicts of interest

The authors declare no conflict of interest. The results of the present study do not constitute endorsement by ACSM. The authors declare that the results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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Tables

Table 1. Participants' characteristics.

Figures

Figure 1. Schematic of the experimental protocol.

Figure 2. Mean ± SD plasma caffeine concentration following the consumption of 3 mg·kg^{-1} caffeine anhydrous (~~A~~a). Individual data from able-bodied participants (~~B~~b), and participants with paraplegia (~~C~~c) and tetraplegia (~~D~~d) (dotted/bold lines represent individuals with an ASIA A/B classification).

Figure 3. Plasma adrenaline (a), noradrenaline (b), free fatty acid (~~A~~c), lactate (~~B~~d), glucose (~~C~~e)~~, noradrenaline (D) and adrenaline (E)~~ concentrations (mean ± SD) following the consumption of 3 mg·kg^{-1} caffeine anhydrous in able-bodied (AB) individuals and individuals with paraplegia (PARA) and tetraplegia (TETRA). * significant main effect for group; † significant time by group interaction effect.

~~[a]Significantly different to baseline values, [b]significantly different to 60 min, [c]significantly different to 90 min.~~