Altered attentional control strategies but spared executive functioning in chronic cannabis users

Amy T. Nusbauma,⁎, Paul Whitneya, Carrie Cuttlera,⁎,b, Alexander Spradlinba, John M. Hinsona, Ryan J. McLaughlina,b,c

Abstract
Background: Cannabis use has increased rapidly in recent decades. The increase in cannabis use makes it important to understand the potential influence of chronic use on attentional control and other executive functions (EFs). Because cannabis is often used to reduce stress, and because stress can constrain attentional control and EFs, the primary goal of this study was to determine the joint effect of acute stress and chronic cannabis use on specific EFs.

Methods: Thirty-nine cannabis users and 40 non-users were assigned to either a stress or no stress version of the Maastricht Acute Stress Test. Participants then completed two cognitive tasks that involve EFs: (1) task switching, and (2) a novel Flexible Attentional Control Task. These two tasks provided assessments of vigilant attention, inhibitory control, top-down attentional control, and cognitive flexibility. Salivary cortisol was assessed throughout the study.

Results: Reaction time indices showed an interaction between stress and cannabis use on top-down attentional control (p = 0.036, n² = 0.059). Follow-up tests showed that cannabis users relied less on top-down attentional control than did non-users in the no stress version. Despite not relying on top-down control, the cannabis users showed no overall performance deficits on the tasks.

Conclusions: Chronic cannabis users performed cognitive tasks involving EFs as well as non-users while not employing cognitive control processes that are typical for such tasks. These results indicate alterations in cognitive processing in cannabis users, but such alterations do not necessarily lead to global performance deficits.

1. Introduction

Cannabis is the most commonly used illicit drug in the United States (Center for Behavioral Health Statistics and Quality, 2015), and chronic use is prevalent, particularly among young adults (Haberstick et al., 2014). With increasing ease of access due to legalization in many American states, chronic use of cannabis has the potential to influence many activities of daily living, such as those that involve organization and direction of goals and work performance. Because of this potential influence, it is important to better understand the effects of chronic cannabis use on cognitive processes related to attentional control and other executive functions (EFs) that are involved in the regulation of behavior generally and that are directly affected by substance use behavior (Giancola and Tarter, 1999; Verdejo-García et al., 2006; Pentz et al., 2016).

When evaluating effects of cannabis use on cognition, consideration should be given to factors that motivate cannabis use. One of the most common reasons given for cannabis use is stress reduction. Motives related to managing stress have often been linked to both frequency of cannabis use and dependence (McKay et al., 1992; Chabrol et al., 2004; Hyman and Sinha, 2009). Acute stress has been found to increase cannabis cravings in some studies, particularly cravings to use cannabis for coping purposes (Buckner et al., 2016). Thus, for many people, stress appears to play a role in both initiation and maintenance of chronic use. Additionally, recent work has shown a blunted stress response in chronic cannabis users, as assessed by subjective stress ratings and salivary cortisol (Cuttler et al., 2017). Although there is substantial interest in the literature on the effects of cannabis use (e.g., Pope et al., 2001; Pattij et al., 2008; Fontes et al., 2011) and stress (Starcke et al., 2016; Shields et al., 2016; Robinson et al., 2015) on EFs, there have...
been no experiments directly examining possible interactive effects of cannabis use and stress on attentional control or other EFs.

When EFs are diminished, such as in substance dependent individuals (Tanabe et al., 2007), those with traumatic brain injuries (Mangeot et al., 2002), and some older adults (Dodge et al., 2011), the inability to engage in goal-directed behavior can impair social relationships, decision making in risky contexts, and creative problem solving (Mangeot et al., 2002; Roca et al., 2010; Tanabe et al., 2007). Despite a common assumption that chronic cannabis use is detrimental to EFs, evidence is equivocal (e.g., Bryod et al., 2016; Pope et al., 2001). The lack of consistent association between cannabis use and EFs may stem from the fact that EFs are a collection of at least partly dissociable functions that include attentional control, cognitive flexibility, and inhibition (e.g., Stuss and Alexander, 2007; Miyake et al., 2000). Different tasks used to study EFs load on different abilities and these abilities can be sensitive to different factors (e.g., Clarke et al., 2005; Phillips et al., 2002; Shields et al., 2015).

A recent review on the effects of cannabis use on cognition established that attentional control is one of the functions most consistently decreased by both acute and chronic cannabis use (Bryod et al., 2016), but there are insufficient data to draw definitive conclusions (Bryod et al., 2016; Volkow et al., 2016). Similarly, detrimental effects of chronic cannabis use have been reported for cognitive flexibility, an executive function involved in shifting strategies as the environmental context changes (Lane et al., 2007; Fontes et al., 2011). However, other studies report finding no differences between chronic users and non-users on measures such as attentional control (Pope et al., 2001), cognitive flexibility, and memory span (Fisk and Montgomery, 2008), and one study examining medical marijuana users before and after initiation of use showed improvement on some EF measures (Gruber et al., 2016).

Evidence for effects of acute stress on EFs is also inconsistent. Working memory efficiency, inhibitory control, and top-down attentional control have all been reported to decrease under stressful conditions (Luethi et al., 2009; Starcke et al., 2016; Singer et al., 2014). Moreover, in some cases, acute stress decreased self-reported ability to use attentional control in a goal-directed manner (Putman et al., 2014). However, acute stress has been reported to impair cognitive flexibility (Alexander et al., 2007; Hillier et al., 2006; Plessow et al., 2011), enhance cognitive flexibility (e.g., Delahaye et al., 2015), or have no effect (Dierolf et al., 2016). Thus, while stress can act as a detriment to some forms of cognition, it can also facilitate or have no influence depending on the specific tasks employed.

In the current study, we employed a pair of tasks that are designed to assess multiple, distinct EF indices (vigilant attention, inhibitory control, top-down attentional control, and cognitive flexibility) within a short temporal window. We used this approach to evaluate the extent to which chronic cannabis use and stress interact to produce deficits in specific domains of EF. In this study, we evaluated two distinct possibilities. First, chronic cannabis use may interact with acute stress to exacerbate impairments in various EFs. Alternatively, acute stress may differentially impact chronic cannabis users and non-users to produce different types of effects on EFs in these two groups. Given the recent finding that chronic cannabis use is associated with decreased reactivity to acute stress (Cutler et al., 2017), chronic cannabis use could dampen the stress response that ordinarily impairs performance of some EFs. Thus, we predicted that this blunted stress response in chronic cannabis users would confer an advantage over non-users in aspects of EF that are particularly vulnerable to the deleterious effects of acute stress.

2. Method

2.1. Participants

Participants were first screened for psychological disorders, the use of psychoactive medications, medical and neurological conditions, concussions, head injury involving a loss of consciousness for more than two minutes, learning disabilities, heavy drinking (defined as alcohol use four or more days per week), and non-cannabis illicit drug use in the past six months.

When EFs are diminished, such as in substance dependent individuals (Tanabe et al., 2007), those with traumatic brain injuries (Mangeot et al., 2002), and some older adults (Dodge et al., 2011), the inability to engage in goal-directed behavior can impair social relationships, decision making in risky contexts, and creative problem solving (Mangeot et al., 2002; Roca et al., 2010; Tanabe et al., 2007). Despite a common assumption that chronic cannabis use is detrimental to EFs, evidence is equivocal (e.g., Bryod et al., 2016; Pope et al., 2001). The lack of consistent association between cannabis use and EFs may stem from the fact that EFs are a collection of at least partly dissociable functions that include attentional control, cognitive flexibility, and inhibition (e.g., Stuss and Alexander, 2007; Miyake et al., 2000). Different tasks used to study EFs load on different abilities and these abilities can be sensitive to different factors (e.g., Clarke et al., 2005; Phillips et al., 2002; Shields et al., 2015).

A recent review on the effects of cannabis use on cognition established that attentional control is one of the functions most consistently decreased by both acute and chronic cannabis use (Bryod et al., 2016), but there are insufficient data to draw definitive conclusions (Bryod et al., 2016; Volkow et al., 2016). Similarly, detrimental effects of chronic cannabis use have been reported for cognitive flexibility, an executive function involved in shifting strategies as the environmental context changes (Lane et al., 2007; Fontes et al., 2011). However, other studies report finding no differences between chronic users and non-users on measures such as attentional control (Pope et al., 2001), cognitive flexibility, and memory span (Fisk and Montgomery, 2008), and one study examining medical marijuana users before and after initiation of use showed improvement on some EF measures (Gruber et al., 2016).

Evidence for effects of acute stress on EFs is also inconsistent. Working memory efficiency, inhibitory control, and top-down attentional control have all been reported to decrease under stressful conditions (Luethi et al., 2009; Starcke et al., 2016; Singer et al., 2014). Moreover, in some cases, acute stress decreased self-reported ability to use attentional control in a goal-directed manner (Putman et al., 2014). However, acute stress has been reported to impair cognitive flexibility (Alexander et al., 2007; Hillier et al., 2006; Plessow et al., 2011), enhance cognitive flexibility (e.g., Delahaye et al., 2015), or have no effect (Dierolf et al., 2016). Thus, while stress can act as a detriment to some forms of cognition, it can also facilitate or have no influence depending on the specific tasks employed.

In the current study, we employed a pair of tasks that are designed to assess multiple, distinct EF indices (vigilant attention, inhibitory control, top-down attentional control, and cognitive flexibility) within a short temporal window. We used this approach to evaluate the extent to which chronic cannabis use and stress interact to produce deficits in specific domains of EF. In this study, we evaluated two distinct possibilities. First, chronic cannabis use may interact with acute stress to exacerbate impairments in various EFs. Alternatively, acute stress may differentially impact chronic cannabis users and non-users to produce different types of effects on EFs in these two groups. Given the recent finding that chronic cannabis use is associated with decreased reactivity to acute stress (Cutler et al., 2017), chronic cannabis use could dampen the stress response that ordinarily impairs performance of some EFs. Thus, we predicted that this blunted stress response in chronic cannabis users would confer an advantage over non-users in aspects of EF that are particularly vulnerable to the deleterious effects of acute stress.

2. Method

2.1. Participants

Participants were first screened for psychological disorders, the use of psychoactive medications, medical and neurological conditions,
In the No Stress version of the task, participants were required to alternate between five trials of submerging their hand in lukewarm water (\(M = 92.7^\circ F, SD = 3.9\)) for equal lengths of time and repeatedly counting from 1 to 25. Additionally, those in the No Stress version were not recorded, nor were errors corrected by the experimenter.

### 2.2.3. Stress measurement

Objective stress responses to the MAST were evaluated by measuring the concentration of cortisol in saliva samples. To collect saliva, participants were first instructed to rinse their mouths with water for one minute. They were then given Salivettes (Sarstedt, Germany) to provide their samples. Participants were instructed to tip the swab into their mouths directly and to chew on the swab for one minute. Next, they spit the swab directly back into the container without touching it. Samples were immediately labeled and stored at \(-20^\circ C\) until analysis. Salivary cortisol concentrations were assessed in duplicates using enzyme-linked immunosorbent assay kits (Salimetrics, State College, PA). The limit of detection was 0.01 \(\mu g/dl\) and the intra-assay coefficient of variance was 5.67%.

### 2.2.4. Stroop-like task switching

In Stroop-like task switching (Fig. 1), participants used a given rule to respond to a stimulus by left- or right-clicking on a mouse (Baldo et al., 1998). They first saw the rule (either “word” or “arrow”) and then an image with the word right or the word left written inside of an arrow pointing either right or left. The rule indicated what part of the image determined the correct response. For example, if the rule was “arrow” and the image had an arrow pointing to the left, a left mouse click would be the correct response. Consistent trials were those in which the word and arrow indicated the same response (the word “left” with a left-pointing arrow). Inconsistent trials were those in which the word and arrow indicated different responses. “Switch” trials were trials in which the rule had switched from the previous trial. If the rule had not switched, it was considered a “no-switch” trial. This switching occurred every two trials. There were 144 trials in this task.

In this task, cognitive flexibility was defined as the ability to switch the rule being followed, operationalized as the difference in reaction time (RT) between switch and no-switch trials. A positive difference score indicated poor cognitive flexibility. Inhibitory control was defined as the ability to inhibit the incorrect response option, operationalized as the difference in RT between inconsistent and consistent trials (Table 2). A positive difference score indicated poor inhibitory control.

### 2.2.5. Flexible attentional control task (FACT)

In the FACT (Fig. 2), participants were instructed to respond with a left mouse click to a smiling emoticon and a right mouse click to a frowning emoticon. Prior to the presentation of the target stimuli, participants viewed a cue of either the word “friend” or “foe”, which they were previously told could help them know what stimulus is coming next, but which would not always be correct. The interval between the cue and the stimulus was jittered between one and five seconds. There were also trials that did not have a cue prior to presentation of the stimulus (no cue trials). In the beginning of the task, the cue was highly predictive of the stimulus to come (i.e., a “friend” cue means that a smiling stimulus will appear 67% of the time). Thus, individuals could rely on the cues to speed up their response to the stimulus. The use of frequently valid cues to improve performance is a highly reliable effect (e.g., Posner, 1980; Summerfield and de Lange, 2014).

After 84 trials, the cue validity changed so that the cue was no longer predictive of the upcoming stimulus (no cue trials). In the beginning of the task, the cue was highly predictive of the stimulus to come (i.e., a “friend” cue means that a smiling stimulus will appear 67% of the time). Thus, individuals could rely on the cues to speed up their response to the stimulus. The use of frequently valid cues to improve performance is a highly reliable effect (e.g., Posner, 1980; Summerfield and de Lange, 2014).

After 84 trials, the cue validity changed so that the cue was no longer predictive of the upcoming stimulus (no cue trials). In the beginning of the task, the cue was highly predictive of the stimulus to come (i.e., a “friend” cue means that a smiling stimulus will appear 67% of the time). Thus, individuals could rely on the cues to speed up their response to the stimulus. The use of frequently valid cues to improve performance is a highly reliable effect (e.g., Posner, 1980; Summerfield and de Lange, 2014).

After 84 trials, the cue validity changed so that the cue was no longer predictive of the upcoming stimulus (no cue trials). In the beginning of the task, the cue was highly predictive of the stimulus to come (i.e., a “friend” cue means that a smiling stimulus will appear 67% of the time). Thus, individuals could rely on the cues to speed up their response to the stimulus. The use of frequently valid cues to improve performance is a highly reliable effect (e.g., Posner, 1980; Summerfield and de Lange, 2014).

After 84 trials, the cue validity changed so that the cue was no longer predictive of the upcoming stimulus (no cue trials). In the beginning of the task, the cue was highly predictive of the stimulus to come (i.e., a “friend” cue means that a smiling stimulus will appear 67% of the time). Thus, individuals could rely on the cues to speed up their response to the stimulus. The use of frequently valid cues to improve performance is a highly reliable effect (e.g., Posner, 1980; Summerfield and de Lange, 2014).

After 84 trials, the cue validity changed so that the cue was no longer predictive of the upcoming stimulus (no cue trials). In the beginning of the task, the cue was highly predictive of the stimulus to come (i.e., a “friend” cue means that a smiling stimulus will appear 67% of the time). Thus, individuals could rely on the cues to speed up their response to the stimulus. The use of frequently valid cues to improve performance is a highly reliable effect (e.g., Posner, 1980; Summerfield and de Lange, 2014).

After 84 trials, the cue validity changed so that the cue was no longer predictive of the upcoming stimulus (no cue trials). In the beginning of the task, the cue was highly predictive of the stimulus to come (i.e., a “friend” cue means that a smiling stimulus will appear 67% of the time). Thus, individuals could rely on the cues to speed up their response to the stimulus. The use of frequently valid cues to improve performance is a highly reliable effect (e.g., Posner, 1980; Summerfield and de Lange, 2014).

After 84 trials, the cue validity changed so that the cue was no longer predictive of the upcoming stimulus (no cue trials). In the beginning of the task, the cue was highly predictive of the stimulus to come (i.e., a “friend” cue means that a smiling stimulus will appear 67% of the time). Thus, individuals could rely on the cues to speed up their response to the stimulus. The use of frequently valid cues to improve performance is a highly reliable effect (e.g., Posner, 1980; Summerfield and de Lange, 2014).

After 84 trials, the cue validity changed so that the cue was no longer predictive of the upcoming stimulus (no cue trials). In the beginning of the task, the cue was highly predictive of the stimulus to come (i.e., a “friend” cue means that a smiling stimulus will appear 67% of the time). Thus, individuals could rely on the cues to speed up their response to the stimulus. The use of frequently valid cues to improve performance is a highly reliable effect (e.g., Posner, 1980; Summerfield and de Lange, 2014).

### Table 2

Accuracy on EF measures.

<table>
<thead>
<tr>
<th></th>
<th>Stroop-like task switching</th>
<th>Cannabis User group</th>
<th>Cannabis Non-user group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stress</td>
<td>No Stress</td>
<td>Stress</td>
</tr>
<tr>
<td>Consistent/No Switch</td>
<td>98.6%</td>
<td>99.0%</td>
<td>98.7%</td>
</tr>
<tr>
<td>Inconsistent/No Switch</td>
<td>84.2%</td>
<td>90.3%</td>
<td>87.8%</td>
</tr>
<tr>
<td>Consistent/Switch</td>
<td>98.7%</td>
<td>99.2%</td>
<td>99.5%</td>
</tr>
<tr>
<td>Inconsistent/Switch</td>
<td>80.0%</td>
<td>87.6%</td>
<td>83.7%</td>
</tr>
<tr>
<td>FACT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valid cues pre-contingency shift</td>
<td>94.5%</td>
<td>95.5%</td>
<td>96.9%</td>
</tr>
<tr>
<td>Invalid cues pre-contingency shift</td>
<td>90.0%</td>
<td>90.7%</td>
<td>97.2%</td>
</tr>
<tr>
<td>Valid cues post-contingency shift</td>
<td>92.1%</td>
<td>97.0%</td>
<td>91.5%</td>
</tr>
<tr>
<td>Invalid cues post-contingency shift</td>
<td>91.4%</td>
<td>93.8%</td>
<td>92.2%</td>
</tr>
</tbody>
</table>

Note: All tests to evaluate potential group differences in these variables were non-significant. Results presented are \(M (SD)\).

---

**Figure 1.** Schematic for one trial of Stroop-like task switching.

**Figure 2.** Schematic for one trial of the FACT.
learning (e.g., Izquierdo et al., 2017).

2.3. Procedure

Prior to entering the lab, participants were asked to sit and wait for 10 min to dissipate any residual stress from traveling. Participants then provided informed consent and filled out the DFAQ-CU. After rinsing out their mouths, participants provided their first saliva sample to assess baseline cortisol. Next, they were randomly assigned to complete either the Stress or No Stress version of the MAST. After the MAST, the second saliva sample was obtained.

Participants then completed the FACT and Stroop-like task switching (Baldo et al., 1998), with the order counterbalanced across individuals. Following each cognitive task, a saliva sample was obtained. After the second task, a urine sample was collected and participants were debriefed.

2.4. Data analysis

For all analyses, stress version and cannabis use group were between-subjects factors and sex and task order were covariates. Cortisol reactivity was assessed as a change in cortisol from baseline to the time point between the two cognitive tasks. An analysis of covariance (ANCOVA) was performed with cortisol reactivity as the dependent measure. For both Stroop-like task switching and the FACT, overall accuracy rates were high (94.4% and 93.2%, respectively) and uniform across conditions (Table 2). Thus, all behavioral analyses were conducted on RT for correct response trials. A multivariate analysis of covariance across conditions (Table 2). Thus, all behavioral analyses were conducted on RT for correct response trials. A multivariate analysis of covariance (MANCOVA) was used for both tasks. For Stroop-like task switching, inhibitory control and cognitive flexibility were dependent measures; for the FACT, vigilant attention, top-down attentional control, and cognitive flexibility were dependent measures (see Table 3). Consistent with standard practices for RT tasks (e.g., Henderson et al., 2012), trials on which RTs were less than 200 milliseconds (ms) or greater than 3 standard deviations above the mean were excluded, which accounted for 1.8% of trials in Stroop-like task switching and 1.7% of trials in the FACT.

3. Results

3.1. Stress response

As previously reported in Cuttler et al. (2017), there were no baseline differences in cortisol levels between groups and there was a significant cannabis x stress interaction on cortisol reactivity immediately after the MAST manipulation, which revealed blunted stress reactivity in cannabis users. There was a significant main effect of stress on cortisol reactivity after the first cognitive task, $F(1, 73) = 28.695$, $p < 0.001$, $\eta_p^2 = 0.282$, indicating that the stress manipulation was successful (Fig. 3). Further, there were trends indicating continued decreased stress reactivity in cannabis users following the first cognitive task. Specifically, there was a trend toward a main effect of cannabis use on cortisol change, $F(1, 73) = 3.138$, $p = 0.081$, $\eta_p^2 = 0.041$.

3.2. Cognitive performance

3.2.1. Stroop-like task switching

Consistent with previous research on task switching using this specific task (e.g., Aarts et al., 2008), paired-samples t-tests indicated that, across all groups, participants took longer to respond to inconsistent as compared to consistent trials, and for no-switch as compared to switch trials (see Table 3).

There were no significant multivariate effects for stress, Wilks’ $\lambda = 0.991$, $F(2, 72) = 0.321$, $p = 0.726$, $\eta_p^2 = 0.009$, or cannabis use, Wilks’ $\lambda = 0.957$, $F(2, 72) = 1.619$, $p = 0.205$, $\eta_p^2 = 0.043$. Similarly, there were no significant between-subjects effects of either stress or cannabis use on inhibitory control, $F(1, 73) = 0.223$, $p = 0.879$, $\eta_p^2 = 0.000$; $F = 1.996$, $p = 0.162$, $\eta_p^2 = 0.027$, respectively, or cognitive flexibility, $F(1, 73) = 0.629$, $p = 0.430$, $\eta_p^2 = 0.009$; $F = 1.281$, $p = 0.262$, $\eta_p^2 = 0.017$, respectively.

3.2.2. FACT

As anticipated, participants took longer to respond to invalid as compared to valid trials in the first part of the task, and this difference was reduced after contingencies shifted and trials were mostly invalid (Table 2).

There were no significant multivariate effects for stress, Wilks’ $\lambda = 0.983$, $F(3, 71) = 0.415$, $p = 0.743$, $\eta_p^2 = 0.017$, or cannabis use, Wilks’ $\lambda = 0.934$, $F(3, 71) = 1.661$, $p = 0.183$, $\eta_p^2 = 0.066$. In the univariate analyses, there were no significant between-subjects effects of either stress or cannabis use on vigilant attention. However, there was a significant interaction between stress version and cannabis use on initial employment of top-down attentional control, $F(1,73) = 4.569$, $p = 0.036$, $\eta_p^2 = 0.059$ (see Fig. 4). Follow-up ANCOVAs showed that there was an effect of cannabis use on top-down attentional control in the No Stress version, $F(1,36) = 5.736$, $p = 0.022$, $\eta_p^2 = 0.137$, but not in the Stress version, $F(1,35) = 0.018$, $p = 0.894$, $\eta_p^2 = 0.001$.

There was also a main effect of cannabis use on cognitive flexibility, $F(1,73) = 5.051$, $p = 0.028$, $\eta_p^2 = 0.065$ (Fig. 5). Cannabis users did not shift their attentional control strategy ($M = −1.45$ ms) after the contingencies switched, while non-users did ($M = 28.33$ ms). Overall the data indicate that cannabis users made little use of top-down attentional control when cues were valid, and thus there was no need to shift away from a top-down strategy when cues were no longer valid.

A surprising result was the absence of differences in overall task performance between cannabis users and non-users, despite group differences in specific EF indices. That is, raw RT to each trial type (Fig. 6) did not vary as a function of cannabis user group – a repeated measures analysis of covariance with block (pre-/post-contingency shift) and validity (valid/invalid) as repeated measures showed non-significant effects of stress version $F(1,73) = 1.748$, $p = 0.190$, $\eta_p^2 = 0.023$, and cannabis use, $F(1,73) = 0.076$, $p = 0.784$, $\eta_p^2 = 0.001$. Thus, while cannabis use altered top-down attentional control and cognitive

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Overall performance on EF measures.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dependent variable</strong></td>
<td><strong>Operational definition</strong></td>
</tr>
<tr>
<td>Inhibitory control</td>
<td>Lower reaction time (RT) for consistent vs. inconsistent trials</td>
</tr>
<tr>
<td>Cognitive flexibility</td>
<td>Lower RT for no switch vs. switch trials</td>
</tr>
<tr>
<td>FACT</td>
<td></td>
</tr>
<tr>
<td>Vigilant attention</td>
<td>RT to trials with no proceeding cue</td>
</tr>
<tr>
<td>Top-down attentional control</td>
<td>Lower RT for valid vs. invalid trials pre-contingency shift</td>
</tr>
<tr>
<td>Cognitive flexibility</td>
<td>Lower RT for valid vs. invalid trials pre-contingency shift, as compared to post-shift</td>
</tr>
</tbody>
</table>
Cognitive flexibility in cannabis users, it did not impede their overall performance, which was comparable to cannabis non-users.

4. Discussion

This study is the first to examine whether chronic cannabis use and acute stress interact in influencing EFs. EFs were assessed using Stroop-like task switching (Baldo et al., 1998), as well as the newly developed FACT. Together, these tasks provided an assessment of four dissociable EFs: vigilant attention, inhibitory control, top-down attentional control, and cognitive flexibility. Among the many abilities in the literature that fit into the category of EFs, these four represent distinct functions studied across a wide range of contexts and populations (e.g., Kofman et al., 2006; Starcke et al., 2016; Shields et al., 2015; Diamond, 2013).

One potential implication of the recent finding that cannabis users have dampened reactivity to acute stress (Cuttler et al., 2017) is that chronic cannabis users might have an advantage over non-users under conditions of acute stress. Instead, we found no overall effect of stress on measures of EF. While several previous studies have indicated that stress negatively impacts a variety of EFs (e.g., Luethi et al., 2009; Starcke et al., 2016; Sänger et al., 2014), there are also some exceptions (e.g., Kofman et al., 2006; Delahaye et al., 2015; Dierolf et al., 2016). These differences across studies may be due to the specific measures of EFs used, the timing of stress measurements, and/or the stressor employed. For example, the test batteries used in Luethi et al. (2009) and in Starcke et al. (2016) were longer, lasting one hour and 45 min respectively, and both found negative results of stress on EFs. In contrast, the task batteries used in Dierolf et al. (2016) and Sänger et al. (2014) were both shorter, at around 30 min and 15 min respectively, but found opposing results. Therefore, it is possible that the effects of stress on EFs are less reliable at shorter durations.

The MAST has been shown to be particularly efficacious at inducing a stress response (Smeets et al., 2012) and this was corroborated by the significant increase in salivary cortisol observed in control participants. However, as indicated above, it is possible that the time point at which we examined the effects of stress on EFs did not properly coincide with the time course of the effects of stress on the brain. For instance, although plasma cortisol levels in the body peak at roughly 20–30 min post-stress onset, their levels in the brain do not peak until an hour or later (Bouchez et al., 2012). Moreover, the effects of glucocorticoids typically involve transcriptional events that can often take hours to manifest (McEwen and Sapolsky, 1995) and thus, our test battery may have also been administered prior to reaching maximal effects of cortisol on the brain. Additionally, optimal release of catecholamines such as dopamine and norepinephrine is required for many facets of EF and are especially sensitive to acute stress exposure (see Arnsten, 1998; Ramos and Arnsten, 2007 for reviews). In contrast with cortisol, these catecholamines represent the first wave of the stress response, rising almost instantaneously and dissipating shortly thereafter (Bouchez et al., 2012). Therefore, the time at which these tests were administered may have also been discordant with the surge in catecholamines that is known to impair EF.

What is clear from the present data is that regardless of stress condition there is a difference between cannabis users and non-users in the use of top-down attentional control. Specifically, chronic cannabis users exhibited reduced reliance on top-down control even when cues were predictive of targets. The striking and unexpected finding was that decreased reliance on top-down control in cannabis users did not lead to overall performance impairment compared to non-users. This result suggests that cannabis users are adopting a qualitatively different form of attentional control that compensates for the absence of top-down control.

Although the use of valid cues to improve speed and accuracy of responding to targets is a robust phenomenon (e.g., Posner, 1980), there are several conditions that reduce the use of top-down control, including positive mood (Fröber and Dreisbach, 2012) and exposure to nicotine (Vossel et al., 2008). However, it is typical for decreased top-down control to be accompanied by poorer overall performance. In our
data, lower reliance on cues did not increase RT or decrease accuracy. One possible explanation for this finding is that chronic cannabis users may be unable to employ top-down control effectively, perhaps due to working memory deficits that have previously been linked to top-down control (see Redick, 2014). Nonetheless, because their use is long-term chronic users may have developed compensatory mechanisms. Thus, when in a situation where top-down control is advantageous, they can use a stimulus-driven strategy and still perform appropriately.

Our results align with previous studies showing different, but not detrimental, performance in chronic cannabis users on some cognitive tasks. Prior studies have indicated neurobiological alterations in chronic cannabis users and our results extend this finding to functional alterations in cognition. For instance, Harding et al. (2012) showed that chronic cannabis users had similar behavioral performance on a cognitive control task; however, fMRI data showed that they had increased connectivity between the prefrontal cortex and the occipitoparietal cortex, which the authors attributed to a compensatory mechanism (Harding et al., 2012). A similar result has been obtained with inhibitory control, where cannabis users had equivalent behavioral performance but increased blood oxygen level dependent response, particularly in dorsolateral prefrontal and parietal areas (Tapert et al., 2007). Further, Hester et al. (2009) found a selective behavioral effect of cannabis use, whereby users had equivalent inhibitory control but worse error monitoring, the latter of which was associated with hypovascularity in the anterior cingulate cortex and right insula. Together, these studies indicate that chronic cannabis users engage compensatory neurobiological mechanisms that involve alternate strategies to achieve comparable cognitive task performance.

Within the FACT, chronic cannabis users did not flexibly shift attentional control strategies because they did not initially adopt top-down control. Therefore, they did not benefit from a task environment in which valid cues provided an advantage, but, consequently, did not suffer from the change in cue validity. As with other measures of cognitive flexibility (e.g., reversal learning), the FACT can only measure flexibility to the extent that participants initially perform in an expected manner. That is, flexibility can only be assessed if a participant initially employs a top-down strategy. Because cannabis users did not initially rely on cues to guide performance we were unable to evaluate their ability to switch to a different strategy when task contingencies changed. However, cannabis users showed comparable switch costs as the control participants, suggesting no differences in cognitive flexibility as defined by the measures used herein. Future research is needed to determine any limitations on flexibility associated with chronic cannabis use because, like EF measures in general, differences can be due to the operationalization of cognitive flexibility (Dajani and Uddin, 2015).

It should be emphasized that while a selective effect of cannabis use on attentional control was found, no differences in performance were found for inhibitory control, vigilant attention, or cognitive flexibility. This result, along with a lack of overall performance differences, lends further support to the theory that alterations in cognitive performance in chronic cannabis users are not inherently deficits, nor are differences global in nature. Recent work by Gruber et al. (2016) has suggested that chronic medical marijuana use may even improve performance on EF tasks, though it is plausible that their results are driven by a decrease in pain and an increase in sleep quality in their participants. Still, their work supports the finding that chronic cannabis use is not inherently detrimental to cognition. Research with animal models has also found that chronic cannabis exposure in adults did not negatively affect cognition, as assessed by recognition memory (Schneider and Koch, 2003). Furthermore, it is not uncommon in studies of EFs to find inconsistent effects across the variable of interest, due to EFs being distinct abilities (e.g., Shields et al., 2016). This has been demonstrated specifically with cannabis use as well, e.g., reviews by Broyd et al. (2016), Mizrahi et al. (2017), and Crean et al. (2011a) found mixed results of chronic cannabis use for cognitive functions such as inhibition, working memory, and verbal fluency.

A few qualifications in our findings should be noted. First, the sample of cannabis users in this study was well-educated, with all but five having completed at least some college education. Therefore, findings from this sample may reflect a subset of cannabis users that are high functioning in general. Future research should determine whether the educational background of cannabis users contributes to ability to compensate for stress and task demands. Future research should also attempt to examine potential sex by cannabis interactions in the EFs examined here as there is a small body of research indicating that the effects of cannabis on cognition may vary as a function of sex (Cutler et al., 2016). Second, while we screened for heavy alcohol use we did not formally measure frequency or quantity of alcohol use as part of the study procedure and therefore it is possible that there are differences in the alcohol use patterns of cannabis users and non-users. Third, the FACT is a newly developed task designed to provide measures of EFs over a narrow time window. Future studies should attempt to confirm our findings with other measures of attentional control. In addition, although we did not measure catecholamine levels in the current study, it is possible that differential recruitment of catecholamines could have contributed to the altered attentional control strategies observed in chronic cannabis users. This will be especially important to examine in future studies given that chronic cannabis use is known to blunt the sympathetic response to stress (Benowitz and Jones, 1977).

Another limitation concerns the period of abstinence for the cannabis users. While we required participants to abstain from using cannabis on the day of testing and we excluded participants who reported using on the day of testing, it is possible there was residual THC that could have altered cognitive performance. Future studies should attempt to replicate these findings after a more prolonged period of abstinence, particularly given that some cognitive functions may recover with prolonged abstinence (e.g., Broyd et al., 2016) or even become more pronounced (Crean et al., 2011b). Finally, we did not collect data on the cannabis use motives for the participants within our study. While many people who use cannabis report using for stress coping purposes (e.g., Hyman and Sinha, 2009), we are unable to confirm that this was true in our sample.

5. Conclusions

The present study is the first to examine potential interactions between cannabis use and acute stress on EFs. Stress did not influence EFs in either group, but chronic cannabis use selectively altered attentional control while not affecting inhibitory control, vigilant attention, or cognitive flexibility. The results demonstrating equivalent overall task performance despite a decreased reliance on top-down attentional control contribute to a growing body of literature showing that cannabis users may adopt different strategies to achieve comparable cognitive performance.

Role of funding source

This work was supported by Washington State University’s Dedicated Marijuana Account. The funder had no role in the study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

Contributors

ATN contributed to data collection, data analysis, writing the first draft of the manuscript, and editing of the manuscript. PW and CC contributed to funding acquisition, data analysis, and editing of the manuscript. AS contributed to data collection and editing of the manuscript. JMH and RJM contributed to funding acquisition and editing of the manuscript. All authors contributed to the design of the
study and approve the final draft of the manuscript.

Conflict of interest
None.

Acknowledgement
We thank Anthony Berger for running the cortisol assays.

References
Hyman, S.M., Sinha, R., 2009. Stress-related factors in cannabis use and misuse: im-
lications for prevention and treatment. J. Subst. Abuse Treat. 36, 400–413.
Neurosci. 2.
Plessow, F., Fischer, R., Kirschbaum, C., Gescheke, T., 2011. Inflexibly focused under stress: acute psychosocial stress increases shielding of action goals at the expense of reduced cognitive flexibility with increasing time lag to the stressor. J. Cognit.
Neurosci. 23, 3218–3227.
Starcke, K., Wiesen, C., Troszczy, P., Brand, M., 2016. Effects of acute laboratory stress on