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A Metacognition-Based Approach to Improve HIV-associated Neurocognitive Disorders
among Substance Users

A dissertation submitted in partial satisfaction of the
requirements for the degree of Doctor in Philosophy

in

Clinical Psychology

by

Kaitlin Blackstone Casaletto

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2016

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2016

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PEER-REVIEWED PUBLICATIONS:

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3. Montoya, J.L., Gouaux, B., Rooney, A., **Casaletto, K.B.**, Grant, I., Moore, D.J. (2015, April, oral presentation). Predictors of antiretroviral adherence among active methamphetamine users with HIV. *Society of Behavioral Medicine*, San Antonio, TX.
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5. **Casaletto, K.B.**, Tulskey, D. & Heaton, R.K. (2015, February, symposium). Uncorrected versus Demographically-adjusted scores on the NIH Toolbox Cognition Battery: What is the difference? *International Neuropsychological Society Conference*, Denver, CO.
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- McCutchan, J.A., Collier, A. C., Marra, C.M., Clifford, D.B., Gelman, B.B., McArthur, J.C., Morgello, S., Simpson, D.M., Abramson, I., Garnst, A., Fennema-Notestine, C., Smith, D.M., Grant, I. for the CHARTER Group (2014, July). Neurocognitive change in the era of HIV combination antiretroviral therapy: A longitudinal CHARTER study. *International AIDS Conference*, Melbourne, Australia.
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- improves antiretroviral dose timing among HIV+ persons with bipolar disorder. *Society for Behavioral Medicine Conference*, San Francisco, CA.
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 23. **Blackstone, K.**, Weber, E., Moore, D.J., Grant, I. Woods, S.P. & the HNRP Group (2013, November; oral presentation). Self-predictions of prospective memory performance in HIV infection: Evidence of a meta-memory deficit. *National Academy of Neuropsychology*, San Diego, CA.
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ABSTRACT OF THE DISSERTATION

A Metacognition-Based Approach to Improve HIV-associated Neurocognitive Disorders
among Substance Users

by

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Rationale: The neurotoxic effects of comorbid HIV infection and substance use disorders (HIV/SUD) preferentially impact the fronto-striatal regions of the brain, leading to increased disruption of higher-order executive functions. Poor insight into such neurocognitive deficits (impaired metacognition) tracks with executive dysfunction and is associated with errors in everyday life. We evaluated the efficacy of a brief Metacognitive Training module for neurorehabilitation of HIV/SUD individuals.

Design: A between-subjects, randomized design was used to examine the effectiveness of Metacognitive Training among HIV/SUD individuals with current executive dysfunction. To determine the efficacy of the Metacognitive Training compared to an

executive strategy (Goal Management Training, GMT), 90 HIV/SUD participants were randomized to: 1) active control (n=30); 2) executive strategy only (i.e., GMT; n=30); or 3) Metacognitive Training plus executive strategy (Meta+GMT; n=30). Following the study condition, participants completed a complex instrumental activities of daily living (IADL) task (Everyday Multitasking Test, “Everyday MT”); additionally, in-vivo metacognitive abilities regarding IADL task performance were evaluated.

Results: There was an increasing tendency for better Everyday MT performances across study conditions (Control≤GMT≤Meta+GMT) that approached significance ($p < 0.08$). Pairwise differences indicated the GMT or Meta+GMT trainings demonstrated small ($d = 0.20-0.24$) benefits in Everyday MT performance compared to the control condition ($p < 0.11$). HIV/SUD individuals who completed the GMT (in addition to the Meta or not) had significant, medium-sized enhancements in Everyday MT performances compared the control condition ($p < 0.05$; $d = 0.38-0.41$); the effect of these enhancements became even larger among those who had poorer dual-tasking capacities prior to training and completed the GMT ($p < 0.04$; $d = 0.83-1.04$). Regarding metacognition, although there was no significant study group effect on Global Metacognition, Online Awareness (one of the two components of global abilities) showed a significant positive trend across training condition (Control≤GMT≤Meta+GMT; $p = 0.04$). Among the skills comprising Online Awareness, a tendency toward more elaborate Task Appraisals was observed among HIV/SUD individuals who completed either the GMT or Meta+GMT (versus control; $p < 0.07$, $d = 0.21-0.27$). Those who completed the GMT (in addition to the Meta or alone) demonstrated medium, significant benefits of GMT on Task Appraisals compared to the control condition ($p = 0.01$; $d = 0.50$).

Conclusions: Our experimental design demonstrated meaningful benefits of a brief GMT executive strategy for everyday multitasking and metacognition among HIV/SUD

individuals. Ours are among the first findings supporting a compensatory neurorehabilitation tool in HIV+ individuals and/or substance users.

INTRODUCTION

Drug and alcohol dependence is one of the most prevalent comorbidities in HIV infection (HIV+) and has been associated with some of the most significant HIV epidemics worldwide (Altice, Kamarulzaman, Soriano, Schechter, & Friedland, 2010). HIV+ substance users have a higher frequency of medical (e.g., cardiovascular disease), psychiatric (e.g., major depressive disorder), and neurocognitive disorders that result in greater mortality and morbidity than their age-matched peers (Lewden, 2010). Regarding the latter condition, indeed HIV-associated neurocognitive disorders (HAND) are disproportionately frequent among HIV+ drug users compared to non-users, with up to 60% evidencing at least mild-to-moderate levels of impairment in both the early and chronic stages of the disease (e.g., Rippeth et al., 2004; Weber, Morgan, et al., 2013). Despite the established relationship between such neurocognitive deficits and declines in daily functioning in these populations (e.g., unemployment and medication nonadherence; Blackstone, Iudicello, et al., 2013; Blackstone et al., 2013; Heaton et al., 2004; Henry, Minassian, & Perry, 2010; Hinkin et al., 2004), there are no empirically validated techniques to address these impairments and their everyday life consequences among HIV/SUD persons. Therefore, this dissertation project aims to evaluate the efficacy of a targeted neuroremediation technique in order to improve quality of life and reduce the economic burden in this high-risk population.

HIV-1 Infection: Impact on the Brain, Neurocognition, and Everyday Functioning

HIV-1 infection is a highly neurotropic lentivirus, which preferentially affects the fronto-striato-thalamo-cortical circuits of the brain (Langford, Hurford, Hashimoto, Digicaylioglu, & Masliah, 2005). HIV crosses the blood brain barrier (BBB) via infected monocytes and lymphocytes (Kanmogne et al., 2007); once in the brain

parenchyma, HIV disrupts neural systems via both direct infection of microglia and macrophages as well as indirect neurotoxic inflammatory cascades (e.g., release of cytokines and chemokines within the neural tissue; Kaul, Garden, & Lipton, 2001). Neuroimaging studies have illustrated HIV-associated CNS atrophy and disruptions in white matter integrity as well as functional alterations in cortical (e.g., prefrontal) and subcortical (e.g., basal ganglia) regions, all of which are associated with behaviorally observed neurocognitive impairments (e.g., Kuper et al., 2011; Melrose, Tinaz, Castelo, Courtney, & Stern, 2008; Pfefferbaum, Rosenbloom, Adalsteinsson, & Sullivan, 2007). Furthermore, postmortem studies indicate that reduced dendritic and synaptic complexity are directly related to antemortem neurocognitive functioning in individuals with HIV (Cherner et al., 2002; Moore et al., 2006; Masliah et al., 1997).

Importantly, despite advances of combination antiretroviral therapies (cART), up to 50% of HIV+ individuals demonstrate persistent mild-to-moderate neurocognitive impairments (e.g., Heaton et al., 2010). Commensurate with the fronto-striato-thalamic predilection of HIV infection in the CNS, HIV-associated neurocognitive disorders (HAND) are most commonly characterized by deficits in episodic memory, executive functions, and working memory (Heaton et al., 2011), sparing other cognitive functions, such as naming abilities, simple attention, and somatosensory functions (Heaton et al., 1995). Interestingly, from an historical perspective, the current neurocognitive difficulties observed demonstrate a somewhat different profile than that of the pre-cART era in which HIV-associated deficits were more consistently characterized by additional difficulties in psychomotor skills, verbal fluency, and speed of information processing (Heaton et al., 2011).

Of particular relevance to this study, neurocognitive impairments (especially those affecting executive functioning) is reliably associated with everyday functioning

declines in this population. Despite the observed prevalence of largely “mild” impairments, up to 60% of individuals with HIV-associated impairment demonstrate difficulties on functional outcomes (e.g., Heaton et al., 2004). The functional impairments following HIV-associated neurocognitive impairment are largely observed on complex daily activities (e.g., medication and financial management; Thames et al., 2011) while difficulties on basic living activities (e.g., dressing, bathing) are less commonly seen and more strongly associated with physical symptoms associated with advanced HIV disease progression (Blackstone, Iudicello, et al., 2013). Higher-level neurocognitive deficits in executive functions, attention, and memory are consistently associated with greater antiretroviral therapy (ART) nonadherence (Hinkin et al., 2002; Woods et al., 2009), while HIV-associated declines in processing speed and executive functions are predictive of increased driving accidents (Marcotte et al., 2004) and unemployment (e.g., Cattie, Doyle, Weber, Grant, & Woods, 2012), respectively. Given the established ecological impact of such HIV-associated neurocognitive impairments, the neuroAIDS field is currently well positioned to begin exploring and developing neuroremediation techniques that may begin to improve HAND in everyday life.

Substance Use: Impact on the Brain, Neurocognition, and Everyday Functioning

Although specific substances of abuse may preferentially affect some neural substrates greater than others, the common underlying network most adversely affected by drug addiction are the dopamine-modulated frontostriatal systems (Koob & Volkow, 2010). Specific brain regions have been linked to the shared behavioral elements of addiction; for example, the dopamine-rich ventral tegmental area and ventral striatum may be a focal point for the binge/intoxication stage, while the cingulate, dorsolateral prefrontal and inferior frontal cortices appear to be the disrupted systems leading to poor

inhibitory control (Koob & Volkow, 2010). Therefore, the evolving transition from substance use to sustained abuse or dependence may involve a series of neuroadaptations stemming from the acute effects in the mesolimbic dopamine system to longer term changes in the striatum, orbitofrontal cortex, and ultimately, the amygdala and prefrontal cortex (Bjork, Grant, & Hommer, 2003; Koob & Volkow, 2010). Chronic substance use, therefore, increases the risk for injury to brain structure and function through several pathways. For instance, in the context of stimulant use, methamphetamine has been shown to result in catecholamine system neurotoxicity with losses in dopamine and serotonin transporters, depletion of dopamine and serotonin levels, and destruction of dopamine terminals, plus changes in brain volume especially in the basal ganglia, nucleus accumbens, cingulate, and parietal lobes (McCann et al., 1998; Davidson, Gow, Lee, & Ellinwood, 2001; Wilson et al., 1996); similarly, cocaine-related decreases in connectivity with the midbrain were found to interfere with striatal activation and deactivation signals (Tomasi et al., 2010), and brain volume loss in the prefrontal and insular cortices are consistently documented (e.g., Ersche et al., 2011). Even histories of alcohol dependence are associated with decreased gray and white matter volumes, the adverse effect of which appears to be particularly potentiated among individuals with other comorbid substance use (i.e., cocaine; Bjork et al., 2003).

Importantly, these disturbed neural networks are associated with significant disruption of neurocognitive processes, ranging from impairments in basic attention to episodic memory. Although the prominence of such impairments may vary by proximity to acute use (e.g., intoxication effects), the most long-standing and significant neurocognitive impairment that is also a common thread across substances of use is executive dysfunction (Verdejo-Garcia & Perez-Garcia, 2007). From a developmental perspective, youth at risk for substance use disorders exhibit a higher prevalence of

deficits in executive functioning compared to those with average substance use risk, even prior to drug exposure (Tarter et al., 1999), which is negatively associated with frontal systems activation (McNamee et al., 2008). Therefore, not only may individuals with substance use disorders (SUD) be particularly predisposed to have frontal systems disruption, but also there is a body of evidence supporting the adverse effect of substance use on executive dysfunction (Sullivan, Rosenbloom, Lim, & Pfefferbaum, 2000). Indeed, executive dysfunction is a hallmark of problematic substance use, in which disrupted inhibitory control prevents moderation of use and promotes continued use despite harmful consequences (Goldstein & Volkow, 2002; Koob & Volkow, 2010; Lubman, Yucel, & Pantelis, 2004); these discontrol symptoms emerge in the context of ongoing substance-related frontal systems neurotoxicity, which promulgate networks of impulsivity and risky decision-making. For instance, significant rapid discounting of delayed hypothetical rewards is consistently evidenced across various substances, including alcohol and marijuana (Kollins, 2003), cocaine (Coffey, Gudleski, Saladin, & Brady, 2003), and methamphetamine (Hoffman et al., 2006) use. Although not as face evident as impaired delayed gratification and inhibitory processes, deficits in other aspects of frontally-mediated skills are also observed, including impaired set-shifting, working memory, and abstract thinking (Albein-Urios, Martinez-Gonzalez, Lozano, Clark, & Verdejo-Garcia, 2012; Fernandez-Serrano, Perales, Moreno-Lopez, Perez-Garcia, & Verdejo-Garcia, 2012; Scott et al., 2007; Sullivan et al., 1993)

This constellation of dysexecutive symptoms has important downstream implications for the day-to-day lives of substance abusers. Not surprisingly, executive function deficits are consistently associated with poorer IADL capacities in the laboratory (e.g., medication and financial management) among substance users (e.g., Henry et al., 2010). Of note, however, these SUD-related neurocognitive deficits also appear to have

a critical impact on manifest daily functioning. For instance, alcohol-related deficits in problem-solving, set-shifting, and inhibition are among the strongest predictors of poorer educational achievement, occupational outcomes, and quality of life (Sullivan et al., 2000). Additionally, in the context of methamphetamine abuse, users were significantly less likely to be employed than non-users, which was associated with specific frontally-mediated deficits in working memory, executive functions, and verbal fluency, among others (Weber et al., 2012). Lastly, although the cognitive mechanisms are not fully elucidated, the literature consistently reports a strong association between neurocognitive impairment and worse treatment retention among marijuana, cocaine, and mixed SUD individuals; specifically, Patkar and colleagues (2004) found that greater self-reported impulsivity and sensation seeking were associated with fewer days in treatment and increased dropout rates among individuals with cocaine dependence. These latter findings may support that executive-mediated processes (e.g., impulsivity, disinhibition) may be directly contributing to poorer treatment compliance and outcomes among substance users. Taken together, these studies suggest an important role of SUD-associated neurocognitive impairment in decreased everyday functioning abilities, and suggest that such deficits may be mediated by frontal systems dysfunction.

Comorbid HIV Infection and Substance Use: Impact on the Brain, Neurocognition, and Everyday Functioning

Both HIV infection and substance use independently impair CNS functioning, and together may result in a “double hit” to the brain. There may be several mechanisms by which substance use can potentiate HIV-associated neural dysfunction. First, from a broad prospective, dopamine is the primary neurochemical system modulated in drug use, especially methamphetamine and cocaine, and is also implicated in the

pathogenesis of HIV. Specifically, HIV-related proteins (e.g., gp120) impair dopamine transporter functions resulting in increased dopaminergic levels early in the disease (Purohit, Rapaka, Shurtleff, 2011). In combination with exogenous increases of dopamine during substance use, this accumulated synaptic dopamine may then activate adjacent microglia resulting in increased HIV replication and inflammatory responses (e.g., chemokine release; Purohit, Rapaka, & Shurtleff, 2011). Additionally, such heightened levels of dopamine in the brain may trigger neurotoxic responses in which apoptosis of dopaminergic cells results in overall degradation of these networks among HIV+ substance users (Purohit et al., 2011). Indeed, there is evidence of significant disruption in the dopamine transporter systems (e.g., reductions in available dopamine transporters) among HIV infected methamphetamine and cocaine users, which are associated with poorer subsequent neurocognitive performances (e.g., Chang et al., 2008).

From a structural standpoint, both chronic alcohol and methamphetamine use are independently associated with increased permeability of the blood brain barrier (BBB), and this is exacerbated in the context of HIV infection (Liang et al., 2008; Shiu, Barbier, Di Cello, Choi, & Stins, 2007). This degradation of the BBB allows for greater numbers of HIV-infected leukocytes to transport into the brain, and furthermore, HIV-induced damage of the BBB may also allow for increased concentration of drugs into the CNS (Kousik, Napier, & Carvey, 2012). Indirectly, cross-amplification of the cellular effects of HIV-associated Tat expression by methamphetamine, opioids, and/or alcohol has been shown to exhibit an enhanced pro-inflammatory response leading to greater neurotoxicity among HIV+ substance users (i.e., via pro-inflammatory cytokine cascades; Flora et al., 2003; Meyerhoff, 2001; Zou et al., 2011). These multiple pathways of neurobiological alterations therefore result in significant adverse effects on

neuronal integrity in this high-risk population. For example, in the context of methamphetamine use, magnetic resonance spectroscopy demonstrated additive abnormal metabolite levels in frontal white and gray matter and the basal ganglia, compared to either condition alone (Chang, Ernst, Speck, & Grob, 2005), suggesting that amphetamines may potentiate the CNS effects of HIV.

Not surprisingly, given their deleterious neural impact at the neurocognitive level, HIV infection and substance use disorders (SUD) result in an increased prevalence of deficits (Carey et al., 2006; Hinkin et al., 2004; Rippeth et al., 2004; Martin et al., 2004). Of note, given the propensity of both HIV infection and SUD to independently affect the fronto-striato-thalamo-cortical circuits, these brain areas appear to be particularly vulnerable in these dually affected populations leading to primary deficits in executive functions, learning, memory, and motor skills (e.g., Chang et al., 2008; Rippeth et al., 2004). For example, considering methamphetamine, use during the early and acute stages of HIV infection is independently associated with neurocognitive impairment (Weber, Morgan, et al., 2013), and is additionally an independent predictor of cognitive decline in chronic infection (Heaton et al., 2015), with the additive effects of methamphetamine and HIV resulting in up to 60% global impairment (Rippeth et al., 2004). Similarly, past alcohol abuse has demonstrated a synergistic and cocaine an additive adverse effect on cognition in the context of HIV infection, resulting in worse executive functioning, auditory processing, episodic memory, and reaction times, than either condition on its own (Chang et al., 2008; Green, Saveanu, & Bornstein, 2004). Taken together, substance use does appear to confer an increased risk of neurocognitive dysfunction among HIV+ individuals.

Although neurocognitive impairment is independently associated with poorer everyday outcomes in both singly affected populations (e.g., Heaton et al., 2004; Henry

et al., 2010), few studies have explored the dual impact of HIV infection and SUD use on real world functioning. In those that have, however, dually affected individuals consistently exhibited the greatest prevalence of everyday functioning difficulties. For example, in a recent study, Blackstone and colleagues (2013) found that 69% of HIV+ methamphetamine users met criteria for global functional dependence (compared to 29% in a neurologically healthy, but higher risk comparison group (i.e., elevated rates of major depression, 25%, and other lifetime substance use disorders, 29%, than the general population)), with unemployment reported in up to 83% of dually affected individuals. Additionally, both alcohol and drug use appear to be associated with decreased access to and use of HIV treatment, as well as increased risk for antiretroviral nonadherence (e.g., Altice et al., 2010; Hinkin et al., 2007; Palepu, Horton, Tibbetts, Meli, & Samet, 2004), which have critical implications for HIV disease management in this population (e.g., viral rebound, development of disease-resistant strains). Importantly, active substance use has been also linked to a higher likelihood of engaging in risky HIV transmission behaviors. For example, Purcell and colleagues (2001) demonstrated that HIV+ individuals who reported drinking or using drugs before or during sex were significantly more likely to report having unprotected sex with casual partners. Given the significant adverse health outcomes following substance use in the context of HIV infection, both directly via disease-mediated neurobiological changes and downstream via cognitive impairments and nonadherence, individuals with HIV/SUD represent a critical high-need target for neuroremediation. Yet, despite these clear risk factors and the economic burden associated with HIV/SUD (e.g., unemployment, SUD use treatment, poorly controlled HIV disease), no empirically validated techniques exist to treat HAND among SUD users.

Metacognition

Metacognition (i.e., “thinking about thinking”) involves the conscious knowledge of cognitive processes as well as the ability to monitor and regulate one’s ongoing activities while engaging in a task (Toglia & Kirk, 2000). The current study is guided by Toglia and Kirk’s (2000) model of metacognition, which posits that “metacognitive knowledge” (i.e., knowledge of the task demands and one’s own abilities) directly interacts with “online awareness” (i.e., ability to monitor and apply one’s knowledge during task performance) to comprise metacognitive functioning (Figure 1).

Metacognitive knowledge is the perception of one’s cognitive abilities, knowledge of the cognitive strategies appropriate for the given task, and knowledge about the task characteristics, whereas online awareness refers to individuals’ task appraisal, self-monitoring (including appropriate application of cognitive strategies), and self-evaluation during performance. As such, performances in any one metacognitive domain may both directly and indirectly impact the functioning of another domain (e.g., increased knowledge of one’s cognitive strengths and weaknesses may increase online application of cognitive strategies during task performance).

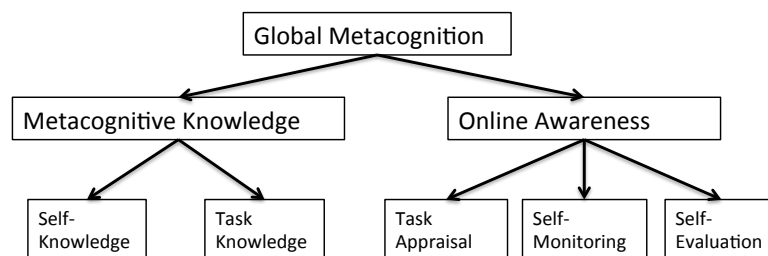


Figure 1. Adapted version of Toglia and Kirk’s (2000) Model of Metacognition subdivided into the hypothesized domains.

In everyday life, metacognition is thus critical for decision-making, troubleshooting, strategy selection, and performance of non-routine activities (Fernandez-Duque, Baird, & Posner, 2000). As such, impaired capacity for such

cognitive introspection may pose fundamental problems when engaging in daily activities. For example, an individual who is unaware of an executive functions deficit (e.g., difficulty completing multistep tasks such as medication adherence) may not prepare appropriate compensatory strategies (e.g., write down pill calculations for dispensing) to ensure success on the given task. To further illustrate, in the context of neurorehabilitation, deficits in metacognitive abilities are associated with poorer outcomes and motivation for treatment (e.g., setting unattainable goals; Prigatano & Wong, 1999) and dependent functioning outside of the rehabilitation setting (e.g., poor vocational attainment; Fleming & Strong, 1999; Sherer et al., 1998; Trudel, Tryon, & Purdum, 1998). This combination of effects may then preclude successful community reentry and re-employment following rehabilitation, thereby leading to increased familial and societal burden (e.g., Wehman et al., 1990).

Importantly in the context of the current study, metacognition is commonly impaired following injury to the prefrontal systems (Kelley et al., 2002; Stuss, 2011) and is associated with integrity of executive functions (Fernandez-Duque et al., 2000; Lysaker et al., 2008). At the neural level, imaging studies converge on the medial prefrontal cortex (mPFC; i.e., Brodmann's area (BA) 10) as the primary common area underlying self-reflective thinking abilities (e.g., Johnson et al., 2006; Kelley et al., 2002; Mitchell, Macrae, & Banaji, 2006). Specifically, a recent meta-analysis posits a model in which the ventral mPFC may be responsible for identifying relevant "self" information whereas the dorsal mPFC may be responsible for evaluative processes and decision-making during self- and other-referential tasks (van der Meer, Costafreda, Aleman, & David, 2010). Not surprisingly, given its neural basis, metacognition is a distinct, but associated process with other executive functions (e.g., Fernandez-Duque et al., 2000; Stuss, 2011). Specifically, when breaking down the components of executive functions

that may play a role in metacognition, a recent study involving participants with schizophrenia illustrated that awareness of one's own thoughts and feelings were more strongly associated with tests of cognitive flexibility, whereas recognizing the needs of others was more closely tied to tests of inhibitory control (Lysaker et al., 2008). Additionally, increased perseverative responses have been associated with denial of cognitive difficulties (Young, Davila, & Scher, 1993). Taken together, these studies converge to indicate that the mPFC, and particularly flexible problem-solving abilities, may critically contribute to metacognitive abilities.

Given the neural and cognitive systems impacted by HIV infection and substance use, metacognition may be a particularly vulnerable process among dually affected individuals. Although metacognition has not been examined in the context of dually affected individuals, it has been reported that up to 50% of individuals with HIV infection evidence difficulties recognizing their cognitive limitations (e.g., Hinkin et al., 1996). For example, several studies indicate that self-reports of neurocognitive difficulties are not significantly associated with objective performance in HIV infection across a variety of cognitive domains (e.g., memory, global neurocognition, prospective memory), though these reports are consistently related to greater affective distress (Hinkin et al., 1996; van Gorp et al., 1991; Moore et al., 1997; Blackstone et al., 2012; Juengst, Skidmore, Pramuka, McCue, & Becker, 2012). Of note, greater disturbances in metacognition (i.e., increased discrepancy between reported and observed neurocognitive abilities) may be associated with worse HIV-associated neurocognitive impairment (Blackstone, Weber, Moore, Grant, & Woods, 2014; Juengst et al., 2012) and HIV-related metacognitive difficulties appear to be present even in cases of mild neurocognitive impairment (e.g., asymptomatic neurocognitive disorder; Chiao et al., 2013). Of ecological relevance, such difficulties in cognitive awareness have been linked to poorer everyday functioning

outcomes among individuals with HIV (i.e., ART nonadherence; Blackstone, Woods, Weber, Grant, & Moore, 2013).

Metacognition has received less attention as a construct in substance use; however, impaired insight into problematic behaviors is indeed a common characteristic of addiction (Brevers et al., 2014). For example, both imprecise positive (e.g., “Using will improve my mood”) and negative (e.g., “My using persists no matter how I try to control it”) self-beliefs regarding substance use have been found to predict severity of actual use (Spada, Caselli, Nikcevic, & Wells, 2015). Additionally, there are a handful of studies that have directly examined insight into thinking abilities (i.e., metacognition) among substance users. Specifically, chronic alcoholics and individuals with methamphetamine dependence have been shown to demonstrate a meta-memory deficit, such that alcoholics rated their memory capacities as comparable to controls though demonstrated objective impairment (i.e., overconfidence), while methamphetamine users both over- and under-estimated current levels of memory functioning compared to controls (Casaletto et al., 2015; Le Berre et al., 2010). Importantly, these disruptions in meta-memory were also associated with deficits in frontal systems (i.e., executive functioning), as well as reduced independence on functional activities of daily living (Casaletto et al., 2015; Le Berre et al., 2010). Similarly, Balconi and colleagues (2014) recently showed that cocaine users demonstrated unrealistic representations of their abilities on a decision-making task (Iowa Gambling Task) compared to controls, and that increased reward sensitivity among the cocaine users drove the observed behavioral deficits. Finally, in the broader context of addictive behaviors, pathological gamblers also showed a disconnection between confidence in their ability to perform a grammar-learning paradigm versus actual performance, whereas controls had a significant correlation between perceived confidence and abilities (Brevers et al., 2014).

In sum, there indeed appears to be a disruption of metacognition among substance users that is importantly related to frontal systems dysfunction and poorer daily functioning outcomes. Taken together with the awareness deficits observed in the HIV literature, HIV+ substance users may be particularly at risk for disturbed metacognition. Improving metacognition among these individuals may therefore be a critical target to both alleviate everyday functioning declines via reduced errors in daily functioning and enhance treatment outcomes via improved motivation and accuracy of cognitive abilities. Targeted rehabilitation of metacognition, a non-traditional, ecologically translational cognitive ability, may additionally demonstrate generalized improvements across neurocognitive domains, especially executive dysfunction, as well as provide a compensatory strategy that may be applied across functional contexts for HIV/SUD individuals.

Cognitive Rehabilitation in HIV Infection and Substance Use

Although the field of neuropsychology has greatly advanced our understanding of the neurobehavioral consequences following brain insult, evidence supporting the rehabilitation and treatment of such deficits has been modest thus far (Sullivan & Tapert, 2013). More recently, cognitive rehabilitation has gained empirical traction as developments of novel approaches to enhance functioning following brain injury are being advanced. Briefly, these rehabilitation approaches fall broadly into two categories: restorative and compensatory. Restorative approaches rely largely on principles of neuroplasticity and utilize repeated practice of a specific cognitive skill or skill-set in order to enhance effective neural organization and improve abilities (Wykes & Spaulding, 2011). By contrast, compensatory strategies do not necessarily aim to directly change underlying cognitive deficits, and instead try to improve functioning by

supporting the damaged cognitive processes largely via reliance on intact processes (e.g., chunking procedures, cueing reminders; Twamley, Jeste, & Bellack, 2003).

Researchers have additionally begun to theorize that integration of both restorative and compensatory approaches may further enhance the efficacy of the rehabilitation process (Huckans et al., 2013; Weber, Blackstone, & Woods, 2013).

From a pharmacological standpoint in HIV infection, although recent studies suggest a positive impact of cARTs on more severe HIV-associated neurocognitive impairments (Cysique, Waters, & Brew, 2011; Letendre et al., 2004; Shiramizu et al., 2012), mild-to-moderate impairments still persist in a large percent of infected individuals. Moreover, the literature validating pharmacological treatment of neurocognitive disorders is still in its infancy and is in need of well-designed randomized clinical trials in order to better understand the role of these treatments for cognition (e.g., Cysique et al., 2011). Relatedly, non-ARV pharmacological treatments of HAND have produced largely mixed results for cognitive improvement. For example, although Sacktor et al. (2001) found improvements in verbal memory and psychomotor speed in 14 HIV+ individuals following transdermal application of selegiline, Schifitto et al. (2009) were unable to replicate these positive outcomes in a larger, longitudinal study (i.e., 3 and 6 months following initiation of selegiline treatment). Additionally of importance, exclusive pharmacological treatment of HAND may prove complicated due to the inherent difficulties with medication adherence that are associated with neurocognitive impairment in this population (e.g., Hinkin et al., 2002).

On the other hand, however, only three studies to date have been published exploring cognitive and behavioral approaches to improve HAND. All three of these studies employed computerized, restorative approaches for cognitive remediation and demonstrated at least some positive effects on neurocognitive impairments in HIV (e.g.,

improved processing speed), thus illustrating promising early evidence for the potential efficacy such approaches to improve HAND moving forward (Becker et al., 2012; Boivin et al., 2010; Vance, Fazeli, Ross, Wadley, & Ball, 2012). However, given some methodological (e.g., lack of utilization of HAND as inclusion criteria, lack of active control comparison group) and statistical (e.g., uncontrolled practice effects) limitations in these early studies, further development and testing of cognitive rehabilitation approaches in the context of HIV is needed.

Similarly, despite the prevalence of SUD-associated neurocognitive impairments and the evidence of their impact on daily functioning and treatment outcomes (e.g., Henry et al., 2010), very few studies have explored neurorehabilitation treatments for these individuals. Pharmacological approaches to improve SUD-associated neurocognitive deficits have been sparse and evidenced mixed results; for example, among non-treatment seeking chronic methamphetamine users, modafinil appeared to improve encoding abilities (Ghahremani et al., 2011), whereas rivastigmine showed no discernable affect on cognition (Kalechstein et al., 2011). Regarding behavioral techniques, a recent randomized clinical trial examined the efficacy of a CBT-based treatment both with and without adjunctive computerized cognitive rehabilitation program to improve attention, executive functions, and memory training among abstinent alcohol users (Rupp, Kemmler, Kurz, Hinterhuber, & Fleischhacker, 2012). The authors found that the cognitive rehabilitation training showed medium effect size improvements in divided attention/working memory, delayed recall, alertness, and visual-spatial construction compared to the CBT-only training, as well as decreased affective distress and cravings by the end of the treatment period (4 weeks; Rupp et al., 2012). Of relevance to our study, Alfonso and colleagues (2011) recently examined Goal Management Training (GMT, an executive-based compensatory strategy) plus

mindfulness-based meditation in a cohort of polysubstance users during a 7-week program. Compared to a treatment as usual group, users who received GMT plus mindfulness meditation showed improved working memory, response inhibition, and decision-making performances following treatment. This literature therefore suggests that cognitive and behavioral approaches to neurocognitive impairment associated with substance use may be feasible and effective in these populations, especially as an adjunctive to substance use treatments; however, further research is clearly needed to better address the requirements and efficacy of treatment techniques among HIV+ substance users.

Metacognitive Training as a Neurorehabilitation Approach

Despite the ecological relevance of metacognition as a component of HAND and the significant social, economic, and healthcare costs of HAND among substance users, no study to date has targeted metacognitive deficits as a vehicle for IADL rehabilitation in the context of SUD- or HIV-associated impairments. Metacognitive training is an approach that promotes identification of individuals' cognitive strengths and weaknesses as may be applicable to the task at hand (typically via psychoeducation and therapeutic feedback) as well as appropriate selection of cognitive strategies to compensate for these difficulties in the context of ongoing performance (Lucas & Fleming, 2005). In this manner, metacognitive training may represent both restorative (i.e., training to improve metacognition via neural reorganization) and compensatory (i.e., application of appropriate strategy during online task performance) approaches to cognitive rehabilitation. Similarly, this training represents a 'top-down' remediation approach targeting the monitoring and application of higher-level control processes to improve behavior; such 'top-down' techniques may show greater sustainability and

generalizability from one training context to another compared to more basic ‘bottom up’ approaches (e.g., motor training; Cicerone & Tupper, 1991). Additionally, training in metacognitive skills may be desirable over a pharmacological treatment because it is a skills-based technique, which may provide greater sustainability across time (i.e., less susceptible to drug tolerance effects) as well as circumvent potential negative aspects of pharmacological treatment (e.g., medication side effects, suboptimal medication adherence). Importantly, metacognitive training has been used to improve IADL performance in other clinical populations with executive dysfunction (e.g., TBI; Goverover, Johnston, Tolia, & Deluca, 2007; Lucas & Fleming, 2005) and has shown efficacy in improving both cognitive and functional outcomes. For example, Goverover and colleagues (2007) employed a metacognitive training intervention with ten individuals with moderate-to-severe TBI, and found improved awareness during IADL performance and actual improved IADL performance in the laboratory. Additionally, Ownsworth and colleagues (2006; 2010) have employed a metacognitive training in several single case study designs of individuals with TBI and demonstrated decreased errors and increased self-checking behaviors on performance-based IADL tasks (e.g., cooking). Therefore, the current study aims to examine the efficacy of a brief metacognitive training to improve in-vivo metacognitive abilities as well as subsequent performance on an IADL task. This neurorehabilitation technique may have a wide range of implications across multiple everyday functioning contexts for HIV/SUD individuals and may be applicable for implementation in a variety of novel contexts.

Multitasking

The current study selected everyday multitasking as the primary IADL outcome to examine following metacognitive training in HIV/SUD individuals. In part, multitasking

was selected due to its potential vulnerability (i.e., reliance on fronto-striatal systems) following HIV infection and SUD, and its ecological relevance in participants' everyday lives. Multitasking represents the ability to select and maintain higher-order internal goals while subgoals are being processed and performed (e.g., Dreher, Koechlin, Tierney, & Grafman, 2008). As such, multitasking appears to require a discrete "cognitive system" that is conceptualized to be related, but disparate from traditional cognitive domains. For example, in a study aimed at exploring the cognitive processes underlying multitasking, Burgess et al. (2000) identified three constructs: retrospective memory, planning, and prospective memory, each of which is associated with dissociable fundamental neural bases. Additionally, although multitasking is associated with executive abilities, multitasking deficits are observed despite intact performance on commonly employed tests of executive functions (e.g., Roca et al., 2011; Shallice & Burgess, 1991). Therefore, multitasking may draw upon several neurocognitive systems, including executive functions (e.g., planning, set-shifting), memory (e.g., retrospective and prospective memory), and working memory (e.g., maintaining goals in mind), in which case deficits in any one area may disrupt overall successful multitasking performance in everyday life. Importantly, multitasking is ubiquitous in almost all real life tasks (e.g., cooking, shopping), and it is clear that the ability to orient behavior toward an internal plan of central goals (versus simply responding to the environment) is critical in everyday functioning. However, despite the omnipresence of multitasking in daily life, there is a well-established cost of declines in performance when completing multiple tasks simultaneously; that is, even among healthy individuals, completing two or more tasks at once reliably compromises performance on one or more of the tasks regardless of task complexity or modality (i.e., performance deterioration is observed when competing tasks do not overlap sensory or motor output systems; e.g., Dux et al., 2009).

Therefore, given the complexity of multitasking for cognitively intact individuals and its reliance on a network of cognitive systems affected by HIV and SUD (e.g., executive functions, memory), and yet its ubiquity in everyday life, multitasking may represent a particularly vulnerable, and important area of functioning among HIV/SUD individuals.

At the neural level, multitasking abilities are associated with integrity of prefrontal areas (Shallice & Burgess, 1991), particularly Brodmann's Area (BA) 10 (i.e., frontopolar cortex; Burgess et al., 2000; Dreher et al., 2008; Roca et al., 2011). Lesion studies indicate that patients with damage to BA 10 show deficits in multitasking performance whereas patients with non-BA 10 frontal lesions do not, and that volume of damage to BA 10 is correlated with degree of performance impairment (Dreher et al., 2008; Roca et al., 2011). Of note, more recently, striatal brain regions have been implicated to support multitasking performance. Thoma and colleagues (2008) found that vascular lesions in the basal ganglia (but not those in the cerebellum) were associated with poor dual-task performance. Given the overlap between the neural correlates underlying multitasking abilities and those preferentially affected by HIV infection and substance use (i.e., fronto-striatal), difficulties in multitasking functioning may be hypothesized in dually affected individuals.

Although executive dysfunction is well documented among substance users, there are very few studies examining multitasking, per say, in this population. In the one study we found, Verdejo-Garcia and colleagues (2007) demonstrated that polysubstance users indeed performed more poorly than healthy controls on a performance-based multitasking task (i.e., Modified Six Elements Test); importantly, these multitasking deficits were strongly associated with problems in everyday frontal systems behaviors, as well. Additionally, several studies have demonstrated an adverse effect of alcohol and/or cannabis administration on cognitive dual-tasking abilities. That is,

disproportionate decrements in both speed and accuracy of computerized dual task performances (e.g., respond to a tone during an ongoing visual task) are observed following drug administration, among both users and non-users (Marks & MacAvoy, 1989; Maylor, Rabbitt, James, & Kerr, 1990).

On the other hand, several studies have begun to delineate the effect of HIV infection on the ability to perform simultaneous tasks. In laboratory-based dual task paradigms, individuals with HIV infection exhibit poorer performances compared to seronegative comparison participants (Castellon, Hinkin, & Myers, 2000; Hinkin, Castellon, & Hardy, 2000; Cole et al., 2007). Of note, such HIV-related decrements in dual-task performance also have been associated neurobehavioral disturbances (i.e., apathy, irritability; Castellon et al., 2000; Hinkin et al., 2000) and executive dysfunction (Cole et al., 2007), implicating specificity of the frontostriatal circuits affected by HIV infection, as well as greater disease severity (i.e., AIDS diagnosis; Hinkin et al., 2000). Additionally, a performance-based IADL task of multitasking abilities, the Multitasking Test (Scott et al., 2011), was recently developed in the context of HIV infection and is proposed for use in this current study. The Multitasking Test parameters are modeled after the Six Elements Test (Shallice & Burgess, 1991), but draw content from the Functional Impact Study (Heaton et al., 2004) and the UCSD Performance-based Skills Assessment (Patterson, Goldman, McKibbin, Hughs, & Jeste, 2001); in this manner, the Multitasking Test requires participants to complete multiple everyday tasks concurrently (e.g., cooking, medication management; see *Methods: Multitasking Test* below for more details). Scott and colleagues (2011) found that HIV+ individuals exhibited worse overall task performance (i.e., total points scored), fewer simultaneous task attempts, and increased errors (e.g., omissions) compared to seronegative controls on this test, and that these deficits were predictive of self-reported declines in instrumental activities of

daily living independent of depression or global neurocognitive impairment. Taken together, these studies strongly implicate the adverse role of HIV infection, and likely substance use, on multitasking abilities. Therefore, given the doubly impacted neural and neurocognitive processes in HIV/SUD individuals and their ecological relevance, multitasking may represent an especially important cognitive target for remediation via metacognitive training in this high-risk group.

Specific Aims and Hypotheses (see Figure 2)

Specific aim. Evaluate the efficacy of a brief Metacognitive Training plus Goal Management Training strategy (Meta+GMT) module for neurocognitive rehabilitation in HIV/SUD individuals with executive dysfunction.

Hypothesis 1. There will be a stair-step effect, such that HIV/SUD individuals receiving the Meta+GMT will perform the best, those receiving only the GMT strategy will have somewhat worse performance, and those receiving the no treatment active control intervention will perform the worst on the Everyday Multitasking Test (e.g., fewer steps completed).

Hypothesis 2. Meta+GMT will significantly improve multiple aspects of metacognition (i.e., awareness of IADL Multitasking Test performance) compared to HIV/SUD individuals who receive the GMT strategy only, who will additionally perform better than participants in the active control.

Exploratory aim. Examine the effects of relevant HIV/SUD clinical covariates on the response to the Metacognitive and Goal Management Trainings (i.e., in-vivo metacognition and Multitasking Test performance), including demographic (e.g., age), HIV disease (e.g., plasma viral load, nadir CD4), SUD characteristics (e.g., recency of

use), neurocognition (e.g., severity of executive dysfunction) and comorbid psychiatric factors (e.g., lifetime and current major depression).

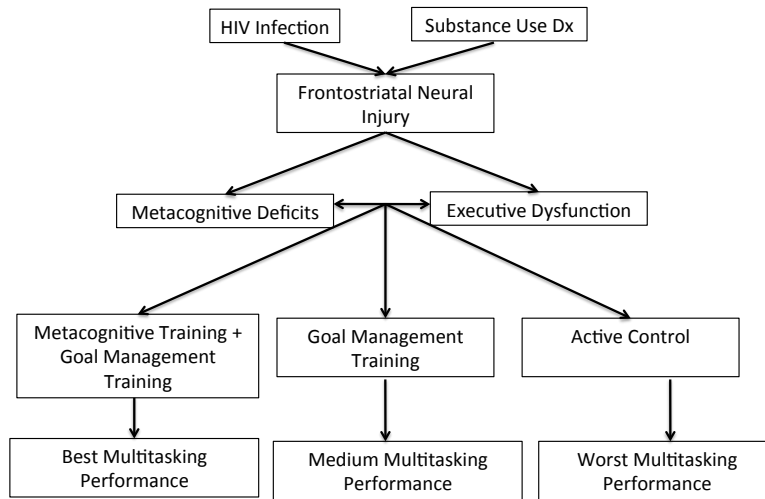


Figure 2. Conceptual impact of HIV infection and substance use disorders (SUD) on metacognition and executive functions and the relative benefit of Goal Management Training and Metacognitive Training for Everyday Multitasking Test performance.

METHODS

Participants

Prior to the primary study implementation, we assessed a pilot sample of 6 HIV-infected individuals without executive functioning deficits but with current episodic memory dysfunction and any histories of substance abuse or dependence between the ages of 18-60 in order to guide development of the metacognitive training. We chose to select HIV+ participants with *memory* (rather than executive) dysfunction for the pilot study in order to not draw eligible participants from our primary participant pool. In the primary study, to test the efficacy of a brief Metacognitive Training plus Goal Management Training Strategy (Meta+GMT) on Multitasking Test performance and metacognitive abilities, a sample of 90 HIV-infected individuals with a diagnosis of a lifetime substance use disorder and current executive dysfunction between the ages of 18-60 were selected. Participants were largely drawn from the parent NIH-funded grants and centers within the HNRP [e.g., Translational Methamphetamine AIDS Research Center (TMARC; I. Grant - NIDA P50DA026306); Individualized Texting for Adherence Building in Methamphetamine (iTAB-M; D.J. Moore – NIDA R34DA31058); HIV Neurobehavioral Research Center (HNRC; R.K. Heaton; NIMH P30MH062512)]. We chose to examine our paradigm in the context of HIV infection, SUD, and executive dysfunction, because of the public health significance of this high-risk group (e.g., high HIV transmission risk). Additionally, limiting the cohort to HIV/SUD individuals with executive function deficits provides specificity and allows us to identify a potential mechanism by which metacognitive training may function; it also allows for standardization of the metacognitive training itself (see *Meta+GMT Training* below).

Participant Characterization and Inclusion/Exclusion Criteria

HIV serostatus was determined via enzyme-linked immunosorbent assay (ELISA) and a confirmatory Western Blot. In regards to substance use, participants needed to meet lifetime criteria for any substance abuse or dependence (i.e., any of the following substances alone or in combination: alcohol, cocaine, methamphetamine, cannabis, and/or opioid) according to the Diagnostic and Statistical Manual 4th ed. (DSM-IV). DSM-IV diagnoses of substance abuse and dependence were determined by a structured and well-validated clinical interview (Composite International Diagnostic Interview [CIDI]). “Executive dysfunction” was determined via impairment on any of the following neurocognitive domains at participants’ prior parent study visit: Abstract Reasoning/Cognitive Flexibility, Working Memory, and/or Verbal Fluency. An average Domain Deficit Score >0.50 (Carey et al., 2004) approach was applied to indicate “impairment.” All prior parent study visits were conducted within two years of current evaluation; for participants with parent visits greater than 18 months old, executive domains that evidenced dysfunction were reassessed to confirm current impairment status.

Participants who tested positive for alcohol on a Breathalyzer or evidenced behavior consistent with current, acute intoxication based on examiner evaluation on the day of testing were rescheduled for another day. Participants were not excluded on the basis of positive urine toxicology screens; we chose these latter criteria in order to enhance the generalizability of our findings (e.g., implications for how the trainings may apply to participants based on how they present in “real life” situations) and to increase the available participant selection pool. Finally, we excluded participants with psychosis unrelated to SUD (e.g., schizophrenia), or neurological conditions that might influence

cognitive functioning (e.g., traumatic brain injury with loss of consciousness > 30 min, stroke, seizure disorders).

Design

In order to guide development and refinement of the study procedures, 6 HIV+ substance users with current memory dysfunction were piloted on all tasks prior to study implementation (i.e., NIH Toolbox Cognition Battery, Metacognitive Training, Goal Management Training strategy, and Multitasking Test; see below for more details). Feedback was gathered from pilot participants with an emphasis regarding the feasibility and perception of the trainings; revisions were incorporated prior to implementation of the primary study. In the primary study, we employed blinded randomization to assign HIV/SUD participants to the Metacognitive Training plus Goal Management Training strategy arm (Meta+GMT; n=30), Goal Management Training strategy only arm (GMT; n=30), or active control condition (n=30). Study arm randomization was conducted via sequential treatment assignment balancing for prognostic factors, including demographics (age, education, sex, race/ethnicity) and severity of executive dysfunction (i.e., average deficit score across Abstract Reasoning/Cognitive Flexibility, Working Memory, and Verbal Fluency tests; Pocock & Simon, 1975). We chose to utilize a between-subjects randomized-controlled trial design versus a within-subjects pre- and post-training assessment design in order to increase the feasibility (time limitations in a dissertation project) and decrease participant dropout between evaluations. Participants received the study assessments and trainings in the following order (see below for more detailed descriptions): 1) NIH Toolbox Cognition Battery; 2) Meta+GMT, GMT only, or Active Control Condition; and 3) Everyday Multitasking Test.

Procedures

All potential participants signed IRB-approved TMARC/HNRP study consents, which included language confirming their willingness to be approached by Ms. Casaletto for participation in the current study. Additionally, we obtained written informed consent specific to this study from all enrolled participants.

Current Neuropsychological Assessment

Prior to training, all participants completed a brief neuropsychological battery, including the NIH Toolbox Fluid Cognition Battery, Tower of London – Drexel Version (ToL^{DX}; Culbertson, 2001), and Test of Everyday Attention (TEA) – Telephone Search Dual Task (Robertson, Ward, Ridgeway, Nimmo-Smith, 1994). The NIH Toolbox Fluid Cognition Battery is a 25-minute computerized evaluation consisting of five tests covering five cognitive domains ranked most important for health, success in school and work, and independent daily functioning: 1) executive functions (Flanker Inhibitory Control and Attention Test and Dimensional Change Card Sort Test), 2) episodic memory (Picture Sequence Memory Test), 3) processing speed (Pattern Comparison Processing Speed Test), 4) working memory (List Sorting Working Memory Test), and 5) attention (Flanker Inhibitory Control and Attention Test). The ToL^{DX} is a test of cognitive planning abilities, in which participants must replicate a target structure by sequentially moving three distinctly colored balls across three pegs. The ToL^{DX} provides several different scores representing distinct aspects of an individual's planning abilities (e.g., total moves, total correct designs, number of rule violations) and has been shown to sensitively identify differences in planning and problem-solving (Unterrainer & Owen, 2006). In the TEA - Telephone Search Dual Task, participants must search a simulated telephone directory for key symbols while simultaneously counting strings of tones

presented on an audio recorder. This measure provides an indicator of participants' divided attention, or dual tasking abilities.

Executive Dysfunction Awareness

All participants completed the self-report version of the Frontal Systems Behavior Scale (FrSBe) prior to completing a training condition. The FrSBe is a 46-item behavior rating scale that provides a quantitative measurement of perceived behavioral and/or cognitive disturbances related to damaged frontal systems. A Total score and three subscales are provided: apathy (e.g., *sit around and do nothing*), disinhibition (e.g., *talk out of turn; interrupt others*), and executive dysfunction (e.g., *cannot do two things at once, poor problem-solver*). Each item is rated on a 6-point Likert-type scale between 1 (*almost never*) to 5 (*almost always*), with higher scores indicating greater reported behavioral disturbances. Although the FrSBe allows for comparison of pre- and post-injury responses, we only utilized responses regarding current perceived behaviors (i.e., post-injury). Total and subscale scores were converted into demographically adjusted T-scores, with a cut-point of $T \geq 65$ indicating clinically elevated levels of reported symptoms.

Given that all HIV/SUD participants in the current study met criteria for objective frontal systems dysfunction (i.e., executive dysfunction), absence of reported symptoms may be an indicator of poor awareness of one's frontal systems/neurocognitive functioning. Therefore, we interpreted low FrSBe scores as an indicator of poor metacognitive accuracy.

Diet, Sleep, and Exercise

Given the emerging evidence regarding the important impact of physical activity and health on the brain (e.g., Dufour et al., 2013), a clinician-administered questionnaire was administered to determine participants' diet (food categories consumed in the past

24 hours; e.g., fruits/vegetables), sleep (hours in the past 72 hours), and exercise (hours of mild, moderate, and/or strenuous exercise in the past 72 hours).

Metacognitive Training plus Goal Management Training strategy (Meta+GMT)

Condition

Each HIV/SUD participant randomized into the Metacognitive Training plus Goal Management Training strategy (Meta+GMT) study arm (n=30) completed a 20-minute metacognitive feedback and GMT exercise prior to administration of the Everyday Multitasking Test (Everyday MT). The Meta+GMT exercise was developed to target both metacognitive domains of Toggia and Kirk's (2000) model, Metacognitive Knowledge (via the metacognitive feedback) and Online Awareness (via GMT).

1) In the Metacognitive Feedback component (5-10 minutes), participants were provided information regarding their specific executive functions impairment(s) (starting, stopping, switching, and/or holding things in mind; Callahan, 2009; Miyake et al., 2000). The training included lay-language definitions of what executive functions are and how executive dysfunction is known to affect performance in everyday life and on the Everyday MT (e.g., increased likelihood for omission errors; Scott et al., 2011). Importantly, this feedback was framed to illustrate how this information may improve Everyday MT performance (e.g., emphasize that recognition of these difficulties may help participants to reduce these errors during performance). This component directly targeted Metacognitive Knowledge by increasing participant knowledge regarding one's abilities (i.e., an existing cognitive weakness) and task knowledge (i.e., how cognitive abilities may impact Everyday MT performance).

2) In the Goal Management Training (GMT) component (10 minutes), participants were provided with a GMT as an executive strategy to use during Everyday MT performance (see the Appendix for detailed information regarding GMT). In brief, GMT

was chosen because it is one of the few cognitive rehabilitation strategies targeting executive dysfunction that has been empirically validated using randomized controlled study designs (Levine et al., 2000). Additionally, GMT was designed for implementation in naturalistic settings so it is an ideal strategy to use on a performance-based IADL task (Levine et al., 2000). Of note, the GMT implemented in the current study was a novel, abbreviated version of the training originally described by Levine et al. (2000); the original GMT has only been deployed as a multi-week training across IADL domains. Details regarding the GMT are provided in the Appendix. In brief, GMT utilizes goal lists to direct behavior in response to either external or internal demands. The five stages of goal monitoring outlined by GMT include, 1) Stop (before beginning a new task), 2) Define (the task goal), 3) List (the steps needed to complete that task), 4) Learn (how you will complete the steps), and 5) Check (ensure behaviors are goal-directed/on-task). Participants were trained on a brief, single-session GMT as adapted for the Everyday Multitasking Test (see Table 1). Corrective feedback was provided throughout GMT instruction in order to ensure comprehension of the information.

Table 1. Application of Goal Management Training to the Multitasking Test.

	Goal Management Training	Everyday Multitasking Test (MT) Application
Stage 1	Orient and alert to task	Participants were trained to “Stop and Think” when beginning a new task or engaging in task switch (e.g., cooking to medication management)
Stage 2	Goal setting	Participants defined the goals of MT (e.g., to complete as much of the 4 tasks as possible in the 12-minute time limit)
Stages 3 & 4	List and learn steps	Participants paraphrased steps of each task into his own words to enhance learning (MT instructions were available as a guide)
Stage 5	Checking	Participant instructed to cross out each completed step from the MT instructions sheet during task performance

Goal Management Training (GMT) only Condition

Thirty HIV/SUD participants were randomized to receive the Goal Management Training (GMT) strategy only. In this condition, participants received a brief (5-10 minute) psychoeducation regarding HIV infection, substance use and their effect on the brain, followed by the GMT strategy as delineated above (10 minutes). Given that the Meta+GMT condition was a 15-20-minute session, we added the psychoeducational component to the GMT only training in order to control for any time- or attention-based effects. Participants in this condition did not receive neurocognitive feedback regarding their executive dysfunction.

Active Control Condition

Finally, 30 HIV/SUD participants were randomly assigned to the active control (no treatment) arm. In the control condition, participants were provided the same brief (5-10 minute) HIV and SUD psychoeducation as those in the GMT only condition, and then were subsequently trained to create paper origami structures for 10 minutes prior to taking the Everyday MT. Thus, participants in this condition did not receive either feedback regarding their executive dysfunction or training on the executive GMT strategy. However, by training participants to create paper origami, we provided a time-equivalent condition that controlled for the verbal learning, face-to-face interaction with examiner, and following directions skills involved in the other trainings, as well as accounted for the training of a novel skill.

Assessment of Instrumental Activity of Daily Living (IADL): Everyday Multitasking Test

A validated performance-based Everyday Multitasking Test (Everyday MT) was implemented to measure IADL functioning abilities in the laboratory. In the Everyday MT, individuals were required to complete as much of four separate tasks as possible within

a 12-minute time limit (Scott et al., 2011). The four tasks included: 1) Cooking a Meal; 2) Advanced Finances (e.g., paying bills); 3) Medication Management (e.g., pill dispensing); and 4) Telephone Communication. This task was developed for and has been validated in HIV-infected individuals (Scott et al., 2011). The Everyday MT shows good discriminative validity between HIV-infected individuals versus seronegative controls, construct validity with standard neuropsychological measures (e.g., executive functions), predictive validity (i.e., performance was uniquely predictive of IADL dependence beyond global neurocognitive functioning and depression), and good variability with little floor or ceiling effects (reported range: 8-43 out of 0-60 total possible points) among HIV+ individuals (Scott et al., 2011). We chose the Everyday MT because it is a complex, unstructured task that requires the integration of multiple cognitive systems, which is reflective of most true everyday functioning environments thereby providing ecological validity for our paradigm. There are several outcome variables that can be derived from the Everyday MT: 1) total steps completed; 2) number of errors; 3) number of task switches; 4) number of simultaneous task engagements; and 5) number of tasks attempted.

Assessment of Metacognition: Metacognitive Measures

Each domain of metacognition as outlined by Toggia and Kirk (2000) was measured in the context of the Everyday Multitasking Test (see Table 2 for an outline of measures per metacognitive domain).

Metacognitive knowledge includes both task knowledge and self-knowledge. All participants were given the same Everyday MT instructions and therefore had the same baseline knowledge of the task. Comprehension of the Everyday MT instructions was assessed by a brief self-report questionnaire and additional prior task knowledge was measured via the Everyday Functioning Questionnaire, which ascertains familiarity

and prior experience with the four multitasking tasks (i.e., cooking, finances, medication management, and telephone communication). Self-knowledge was measured via accuracy of one's prediction of Everyday MT performance (i.e., subtraction of objective Everyday MT score from predicted Everyday MT performance) as well as a Multitasking Abilities Questionnaire (i.e., perceived frequency and ability to perform multitasking tasks in everyday life; e.g., prepare a meal while talking on the telephone).

Online awareness includes ongoing task appraisal, self-monitoring, and self-evaluation during task performance. Task appraisal was measured via verbal formulations of the plan by which the participant anticipates completing the task. The plan was scored for elaborateness according to established criteria (e.g., number of executable steps, order and rules for steps; Kliegel, McDaniel, & Einstein, 2000). Self-monitoring was measured via number of error corrections completed on the Everyday MT (more corrections indicates stronger self-monitoring). Finally, self-evaluation was assessed via accuracy of Everyday MT performance post-diction (i.e., subtraction of objective Everyday MT score from post-diction of perceived Everyday MT performance).

Table 2. Measures of metacognition by domain.

Metacognitive Domain	Measure
METACOGNITIVE KNOWLEDGE	
Task Knowledge	Everyday Functioning Questionnaire ^c MT Instructions Comprehension Questionnaire ^a
Self Knowledge	Planning Abilities Questionnaire ^c MT performance prediction accuracy ^a
ONLINE AWARENESS	
Task appraisal	Verbal plan formulation ^a
Self-Monitoring	MT error corrections ^b
Self-Evaluation	MT performance post-diction accuracy ^c
^a Measured after the training, but before Everyday Multitasking Test (MT) performance.	
^b Measured during MT task performance.	
^c Measured after the training and after MT task performance.	

Existing Neuromedical and Psychiatric Data

The basic medical and neuropsychiatric characterization of this cohort was drawn from the existing data from linked HNRP visits (within 2 years; median=149 days). Specifically, we drew an array of important neuromedical information, including: 1) current and nadir CD4 counts; 2) CDC HIV staging; 3) HIV RNA measured in plasma; 4) estimated duration of HIV infection; 5) current ART regimen; and 7) other important neuromedical factors, such as hepatitis C co-infection. In addition, all participants underwent a comprehensive psychiatric research evaluation, which provided: 1) DSM-IV diagnoses of current and lifetime substance use (e.g., alcohol, methamphetamine) and mood (e.g., major depression) based on the CIDI; 2) substance use quantification (e.g., onset, recency, duration, quantity, and frequency) of all drugs of abuse based on a semi-structured time-line follow-back interview; 3) current affective distress as measured by the Profile of Mood States, which includes scales assessing depression, anxiety, fatigue, and vigor, and Beck Depression Inventory-II; and 4) Lawton & Brody's Instrumental Activities of Daily Living Questionnaire, a self-report measure of functional decline as assessed in multiple domains (e.g., shopping, medication management).

Data Analyses

Hypothesis 1. Everyday Multitasking Test Performance: Control < GMT only < Meta+GMT.

A series of omnibus Jonckheere-Terpsta (J-T) tests were conducted to determine monotonic positive trends across the study conditions on metrics of Everyday Multitasking Test (Everyday MT) performances (i.e., total errors, task switches, simultaneous task engagements, number of tasks attempted, overall points earned). The J-T test for ordered alternatives tests the null hypothesis that the medians for the study conditions were the same, against an alternative hypothesis that the medians were

ordered in magnitude (i.e., $\text{Control} \leq \text{GMT} \leq \text{Meta+GMT}$; Siegal, 1988). Follow-up one-way Wilcoxon tests with false discovery rate adjusted p-values examined pairwise study condition differences on the Everyday MT. For all nonparametric pairwise comparisons, Cliff's d was calculated to determine effect sizes, which is an appropriate statistical metric for nonparametric data (Cliff, 1993). Cliff's d ranges from -1 to +1 and reflects the probability that values for one group (e.g., GMT) are larger than values for another group (e.g., control). The magnitude of the values may be interpreted as follows: $d < 0.15$ "negligible," $d < 0.33$ "small," $d < 0.47$ "medium", otherwise "large" (Romano, 2006).

Given the comparability observed between the GMT and Meta+GMT conditions, these groups were collapsed in order to more closely examine the effect of GMT (i.e., "All GMT"). The sufficiently large sample sizes ($n's \geq 30$) and decreased number of groups (i.e., 2 groups) in these analyses, allowed for parametric statistical testing. Subsequently, a series of one-way t-tests were conducted to determine differences between the All GMT versus active control groups on Everyday MT performances, followed by Cohen's d effect sizes (appropriate for parametric analyses). Additionally, we aimed to determine the efficacy of GMT (versus control) for Everyday MT performances relative to HIV/SUD individuals' cognitive dual-tasking abilities prior to training. A series of interaction linear regression models were conducted with study condition (Control vs. All GMT), dual task performance (TEA-Dual Task raw score), and their interaction (Condition*dual task) predicting Everyday MT performances. Post-hoc one-way t-tests were conducted to follow-up on significant interaction models in order to determine directionality of effects.

Hypothesis 2. Metacognition: $\text{Control} < \text{GMT only} < \text{Meta+GMT}$.

In order to examine the in-vivo components of metacognition comparably across the same metric, we created sample-based z-scores (i.e., individual participant score vs.

the cohort's average score) for each metacognitive measure (see Table 2 for Metacognitive Measures). The measures that comprise each of the metacognitive domains were then averaged together to create the primary metacognitive summary scores (e.g., Metacognitive Knowledge, Online Awareness, Global Metacognition).

Parallel analyses to those conducted for the Everyday MT outcomes were calculated on each of the metacognition outcomes. Specifically, a series of omnibus J-T tests were conducted to test possible “stair-step” trends across the study conditions on each of the metacognitive scores (Siegal, 1988). Pairwise one-way Wilcoxon tests with false discovery rate adjusted p-values were then calculated in order to determine individual group differences. Cliff's d was calculated to determine pairwise effect sizes between study groups (see Hypothesis 1 above for rationale and interpretation of Cliff's d effect sizes; Cliff, 1993).

Given comparability on the metacognitive outcomes between the GMT only and Meta+GMT conditions, these two groups were, again, collapsed in order to more closely examine the effects of GMT (i.e., “All GMT”). One-way t-tests were then conducted to determine the efficacy of All GMT versus control condition on the metacognitive scales. Finally, a series of interaction linear regression models were developed in order to determine the efficacy of GMT at differing levels of metacognition (i.e., higher FrSBe total score as an indicator of more accurate metacognition). Specifically, study condition (Control vs. All GMT), FrSBe total score, and their interaction (Condition*FrSBe) were entered into the models predicting each of the metacognitive scales.

Exploratory Aim. *Examine the effects of relevant HIV/SUD clinical covariates on the response to the Metacognitive and Goal Management Trainings (i.e., in-vivo metacognition and Multitasking Test performance), including demographic (e.g., age),*

HIV disease (e.g., plasma viral load), SUD characteristics (e.g., recency of use), and comorbid psychiatric factors (e.g., major depression).

Given that only the GMT demonstrated significant beneficial effects (in the context of the Metacognitive Training or not), follow-up exploratory analyses were conducted examining the extent to which individual-level characteristics may moderate the effect of All GMT (versus control). Only those outcomes that demonstrated small-to-medium effects of GMT were examined (i.e., Everyday MT task switches, simultaneous task engagements, tasks attempted, total points; and Metacognitive task appraisals). A series of separate interaction linear regression models were conducted with study condition (Control vs. All GMT), clinical covariate of interest, and their interaction (Condition*clinical covariate) on each of the Everyday MT outcomes of interest and metacognitive task appraisals. Models were developed for the following clinical variables of interest: demographics (i.e., age, education, sex, race), sleep, exercise, substance use (i.e., lifetime alcohol, cocaine, methamphetamine, cannabis or opioid use disorders examined separately, and any substance use in the last year), HIV disease (i.e., nadir CD4 count and plasma HIV viral load), mood (i.e., lifetime major depressive disorder and Beck Depression Inventory-II), and everyday functioning (i.e., employment, ADL declines, PAOFI cognitive symptoms). Significant interaction models were followed-up with post-hoc one-way t-tests to determine directionality of effects.

Missing Data. There were no missing data on either of the primary study outcome measures (i.e., Everyday MT or metacognition); however, some missing data occurred on several of the accompanying self-report measures (i.e., individual items missing on FrSBe and self-reported Everyday Multitasking Abilities). Given that the missing data were minimal and only on two self-report measures, we calculated each

missing individual's mean on the particular scale (e.g., FrSBe Executive Functions scale) and imputed that value in order to compute total scores on the measures.

RESULTS

Pilot Study

Six HIV+ individuals with lifetime histories of substance use disorders (SUD; alcohol, cocaine, cannabis, inhalant, amphetamine) completed one of the three study conditions (n=2 per study condition: Active Control, Goal Management Training (GMT), or Metacognitive Training + GMT (Meta+GMT)). Participant feedback indicated high levels of overall satisfaction and perceived helpfulness of the study trainings (Likert scale 0=*Not at all Satisfactory/Helpful* to 5=*Very much Satisfactory/Helpful*; Satisfaction=5.0 and Helpfulness=4.1). A structured, open-ended feedback discussion occurred at the end of each pilot session. Several suggestions were noted during these discussions that were subsequently included in the final study methodology, including: 1) fewer words on the PowerPoint presentation trainings; 2) increased interaction with the participant during the trainings (e.g., integrated questions/opportunities for participants to share their experiences); and 3) clarification of the Everyday Multitasking Test stimulus cards.

Main Study Participants

A total of 90 HIV+ participants with substance use disorders (HIV/SUD) and current executive dysfunction completed the study, meeting the enrollment goal of n=30 per study arm (i.e., Active Control, Goal Management Training (GMT), or Metacognitive Training + GMT (Meta+GMT)). Data regarding comprehensive neuromedical, neuropsychiatric, and neuropsychological factors were linked from participants' prior parent study visit at the HNRP (median days since last parent study visit=149 (61, 325.5), range 0-730 days). See Table 3 for participant descriptive information by study condition. There were no significant differences across demographic (e.g., age, education), HIV disease characteristics (e.g., nadir CD4, HIV viral load), neuropsychiatric or substance use (e.g., lifetime histories or current diagnoses of

methamphetamine use disorders, major depressive disorder), or neuropsychological (e.g., executive dysfunction, global neurocognitive impairment) background factors across the three study arms (all $p>0.15$; see Table 3). On average, participants were about 50-years-old, slightly more than high school educated, majority male, and about half identified as White. In the whole sample, the most common lifetime substances of abuse/dependence were alcohol (72.1%), methamphetamine (58.1%), and cocaine (38.9%). Interestingly, only 18.1% of the sample met criteria for any current substance abuse or dependence; however, 27.8% of the sample screened positive for some substance on urine toxicology on the day of evaluation for the present study (13.3% urine toxicology positive for methamphetamine). Of those that had a positive urine toxicology, 20.8% also had a current substance use disorder (versus 16.9% ($n=10$) of the participants were urine toxicology negative met criteria for a current SUD). Notably, positive urine toxicology at evaluation did not differ by study arm and was not associated with any of the study outcomes (i.e., Everyday Multitasking or Metacognition; $p>0.13$). In terms of other psychiatric functioning, a large majority of the sample met DSM-IV criteria for lifetime histories of major depressive disorder (MDD; 70.9%), with only a small subset meeting criteria at their last study visit (18.1%), and participants' report of current depression symptomology was minimal-to-mild (BDI-II=13.6, $SD=11.9$).

From a neurocognitive standpoint, the HIV/SUD sample demonstrated low average performances as a group on the NIHTB-CB Fluid Composite on the day of evaluation (Fluid T-score=47.9, $SD=10.7$, range=19.6-71.4). Neuropsychological (NP) data from their last study visit indicated that abstract reasoning/cognitive flexibility was the most commonly impaired area of executive functioning (49.4% impaired), followed by verbal fluency (39.0% impaired), and then working memory (37.5%). Overall, 65.5% of

the sample demonstrated global neurocognitive impairment (Global Deficit Score ≥ 0.5) on the gold standard comprehensive battery.

In terms of daily functioning, only 19.8% of the sample was employed, and on average, participants reported current declines in 1.8 (SD=2.0) instrumental ADL (e.g., medication management) and 0.6 (SD=0.9) basic ADL (e.g., grooming) areas. Additionally, participants reported an average 6.3 (SD=7.3) significant cognitive symptoms in daily life (Patient's Assessment of Own Functioning) and 42.7% noted globally elevated frontal systems symptoms (Frontal Systems of Behavior Evaluation Total Score $T \geq 65$).

Table 3. Clinico-demographic characteristics of sample across study arms.

	Active Control (n=30)	Goal Management Training (GMT) (n=30)	Metacognitive Training + GMT (n=30)	p-value
<i>Demographics</i>				
Age, y	47.8 (11.6)	50.1 (10.1)	50.6 (9.2)	0.56
Education, y	13.1 (2.9)	13.5 (2.1)	12.9 (2.8)	0.69
Sex (% M)	86.7% (26)	90.0% (27)	90.0% (27)	0.89
Race (% White)	56.7% (17)	53.3% (16)	56.7% (17)	0.64
Strenuous Exercise (any past 72h, % Y)	50.0% (15)	46.7% (14)	33.3% (10)	0.38
Sleep (hrs past 72h)	21.7 (6.1)	21.7 (5.2)	21.5 (4.9)	0.99
<i>HIV and Neuropsychiatric</i>				
% U-Tox Positive at Evaluation	36.7% (11)	26.7% (8)	20.0% (6)	0.35
LT Alcohol Diagnosis	75.0% (21)	62.1% (18)	79.3% (23)	0.31
LT Meth Diagnosis	60.7% (17)	44.8% (13)	69.0% (20)	0.17
LT Cocaine Diagnosis	46.4% (13)	34.5% (10)	32.1% (9)	0.49
LT Cannabis Diagnosis	39.3% (11) 14.3% (4)	41.4% (12) 6.9% (2)	35.2% (10) 17.9% (5)	0.91 0.45
LT Opioid Diagnosis				
LT Polysub Diagnosis	63.3% (19)	60.0% (18)	70.0% (21)	0.71
Any Current Substance Use Diagnosis	18.5% (5)	14.3% (4)	21.4% (6)	0.78
Nadir CD4	155 (29, 344.5)	134 (39.5, 269)	182 (15.5, 407)	0.41
Current CD4	588.5 (404, 857)	489 (278.3, 642)	552 (307, 867)	0.26
% AIDS	66.7% (18)	64.3% (18)	55.2% (2)	0.64
Est Duration HIV, y	13.1 (20.8)	15.5 (8.0)	11.0 (7.9)	0.50

Table 3, continued

	Active Control (n=30)	Goal Management Training (GMT) (n=30)	Metacognitive Training + GMT (n=30)	p-value
% VL Detectable (plasma)	28.6% (6)	38.9% (7)	20.8% (5)	0.44
% On ART	85.2% (23)	92.9% (26)	82.1% (23)	0.48
% VL Detect on ART (plasma)	23.5% (4)	31.3% (5)	15.8% (3)	0.56
Lifetime MDD	67.9% (19)	69.0% (20)	75.9% (22)	0.77
Current MDD	18.5% (5)	10.7% (3)	25.0% (7)	0.38
Beck Depression Inventory-II	16.3 (11.2)	10.8 (10.8)	13.9 (13.4)	0.27
<i>Neurocognitive</i>				
TEA Dual Srch Decr (ss)	9.7 (4.5)	10.0 (3.9)	10.9 (4.2)	0.52
TEA Dual Srch Decr raw % below median(<1.165)	46.7% (14)	53.3% (16)	50.0% (16)	0.88
Tower of London				
Total Moves (SS)	93.9 (19.9)	95.5 (20.3)	95.2 (17.6)	0.94
Rule Violations (raw)	1.7 (1.9)	2.1 (2.3)	1.6 (1.8)	0.66
NIH Toolbox, T-scores				
DCCS	50.4 (8.7)	49.4 (11.5)	51.0 (10.0)	0.84
Flanker	47.5 (9.8)	49.5 (12.1)	50.8 (10.7)	0.50
List Sorting	45.6 (8.9)	47.1 (8.8)	47.0 (9.1)	0.76
Pattern Comp	46.4 (12.8)	48.4 (13.2)	47.2 (13.0)	0.85
Picture Seq Mem	47.0 (11.7)	47.6 (9.8)	48.7 (10.6)	0.83
Fluid Composite (%T<45)	42.9% (12)	44.4% (12)	35.7% (10)	0.78
Comprehensive Neuropsychological Battery (prior parent study visit)				
% Reasoning/ Flexibility Impairment	50.0% (14)	48.3% (14)	50.0% (15)	0.99
% Working Memory Impairment	32.0% (8)	33.3% (9)	46.4% (13)	0.48
% Verbal Fluency Impairment	42.3% (11)	33.3% (9)	41.4% (12)	0.76
% Global NP Impairment	64.3% (18)	58.6% (17)	73.3% (22)	0.49
Global NP Mean T	43.3 (7.3)	43.7 (5.3)	42.9 (7.0)	0.89
<i>Functional</i>				
Cognitive Symptoms (PAOFI)	7.7 (8.8)	4.7 (4.8)	6.4 (7.6)	0.31
ADL Declines	2.6 (2.7)	1.9 (2.4)	2.7 (2.8)	0.53
% Unemployed	74.1% (20)	81.5% (22)	85.2% (23)	0.58
Karnofsky Score	87.1 (12.7)	89.1 (11.1)	88.1 (11.2)	0.86
FrSBE % T≥65, curr				
Apathy	53.3% (16)	26.7% (8)	34.5% (10)	0.10
Disinhibition	43.3% (13)	36.7% (11)	37.9% (11)	0.85
Executive	50.0% (15)	43.3% (13)	37.9% (11)	0.65
Total	46.7% (14)	40.0% (12)	41.4% (12)	0.86

Table 3, continued. **Note.** U-tox Positive=urine toxicology positive; LT=Lifetime abuse or dependence diagnosis; AIDS=Acquired Immune Deficiency Syndrome; ART=antiretroviral; VL=viral load; MDD=Major Depressive Disorder; TEA Dual Srch Decr=Test of Everyday Attention Dual Search Decrement; SS=Standard Score (M=100, SD=15); ss=scaled score (M=10, SD=3); DCCS=Dimensional Change Card Sorting test; Pattern comp=Pattern Comparison test; Picture Seq Mem=Picture Sequence Memory test; NP=neuropsychological; PAOFI=Patient's Assessment of Own Functioning; ADL=Activities of Daily Living; FrSBE=Frontal Systems Behavior Evaluation.

Everyday Multitasking Test (Everyday MT)

Control vs. GMT vs. Meta+GMT. Omnibus Jonckheere-Terpstra (J-T) tests indicated trends toward increasing task switches ($J^*=1.44$, $p=0.07$), simultaneous task engagements ($J^*=1.41$, $p=0.08$), and tasks attempted ($J^*=1.4$, $p=0.08$) on the Everyday MT across the study conditions (i.e., monotonic trend $\text{Control} \leq \text{GMT} \leq \text{Meta+GMT}$; Figure 3), though these omnibus models did not reach statistical significance at $\alpha=0.05$. There were no study group differences on total errors ($J^*=0.49$, $p=0.31$) or total points earned ($J^*=0.84$, $p=0.20$). Follow-up pairwise one-way Wilcoxon tests with false discovery rate (FDR) adjusted p-values demonstrated small effect sizes that approached significance ($0.05 < p < 0.11$) between the control group versus GMT group, as well as the control versus Meta+GMT groups. HIV/SUD individuals in the control group demonstrated fewer task switches (vs. GMT $z=1.45$, Adj. $p=0.11$, Cliff's $D=0.22$; vs. Meta+GMT $z=1.44$, Adj. $p=0.11$, $D=0.21$), simultaneous task engagements (vs. GMT $z=1.5$, Adj. $p=0.11$, Cliff's $D=0.23$; vs. Meta+GMT $z=1.4$, Adj. $p=0.11$, $D=0.21$), and tasks attempted (vs. GMT Cliff's $z=1.52$, Adj. $p=0.11$, $D=0.24$; vs. Meta+GMT $z=1.41$, $p=0.11$, $D=0.20$) compared to either of the active groups. Of note, the pairwise effect sizes of the GMT and Meta+GMT training (versus the control group) on Everyday MT performances were comparable (i.e., GMT vs. control $D=0.22$ - 0.24 and Meta+GMT vs. control $D=0.20$ - 0.21). Additionally, when comparing Everyday MT performances between HIV/SUD individuals who completed the GMT versus those who completed Meta+GMT condition, there was

no significant effect of the Meta+GMT beyond GMT only (GMT vs. Meta+GMT; Cliff's D= -0.14 to -0.01). In other words, HIV/SUD participants who received only the GMT or the Meta+GMT trainings did not demonstrate any meaningful differences on the Everyday MT test, but both performed marginally better than those who received the control condition. Therefore, it appeared that GMT (not Meta) may be driving the modestly enhanced performances on Everyday MT.

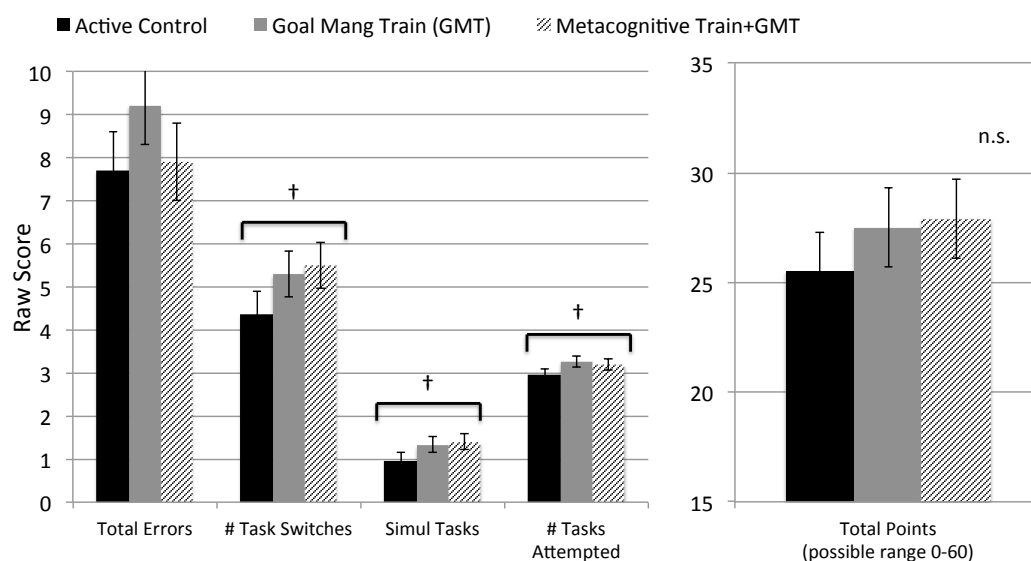


Figure 3. HIV/SUD participants' performances on the Everyday Multitasking Test following study training condition. †Omnibus Jonckheere-Terpstra Test $p=0.07$; Bars=Mean, SE.

Control vs. All GMT. Given that no significant difference was observed between the GMT and Meta+GMT cohorts, we collapsed these two study conditions ("All GMT"; $n=60$) in order to examine the effect of GMT on the Everyday MT with greater power. One-way T-tests demonstrated small-to-medium effects, such that those HIV/SUD individuals who received the GMT (as part of the Meta training or not) tended to engage

in more task switches ($t=1.6$, $p=0.06$, Cohen's $d=0.36$), simultaneous tasks ($t=1.8$, $p=0.04$, $d=0.41$), task attempts ($t=1.7$, $p=0.04$, $d=0.38$), and to a lesser extent, earned more total points on the Everyday MT ($t=1.0$, $p=0.16$, $d=0.22$) compared to controls (Figure 4). The number of total errors on the Everyday MT did not differ between groups ($t=0.80$, one-way $p=0.79$, $d=-0.10$).

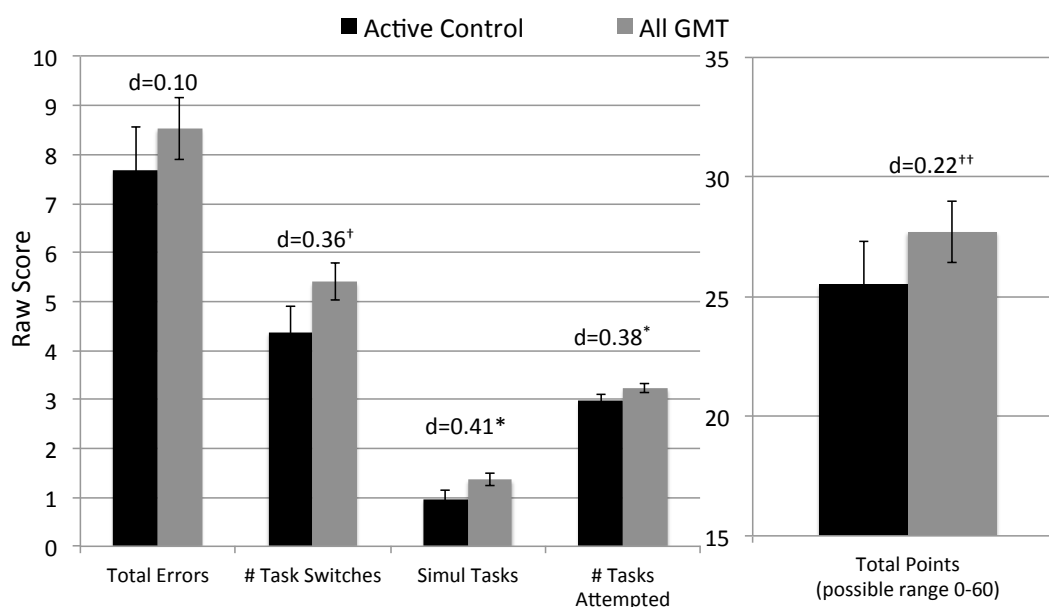


Figure 4. Performances on the Everyday Multitasking Test comparing HIV/SUD participants who completed the active control and those who completed the Goal Management Training (as part of the Metacognitive Training or not). One-way t-test $^*p=0.04$, $^{\dagger}p=0.06$, $^{\dagger\dagger}p=0.16$; Bars=Mean, SE; d =Cohen's d .

Control vs. All GMT: Interaction models. In order to determine the utility of GMT for Everyday MT as a function of dual tasking capacity, we conducted a series of interaction models with study condition (control vs. All GMT), raw dual task performance (TEA-Telephone Search Dual Task), and their interaction (condition*dual task) as

predictors of Everyday MT performances (i.e., task switches, simultaneous task engagements, tasks attempted, total points). Significant omnibus multivariable models with significant interaction terms were found for Everyday MT task switches ($F(3,86)=2.7$, $p=0.05$; condition*dual task $b=-0.11$, $p=0.04$), tasks attempted ($F(3,86)=3.9$, $p=0.01$; condition*dual task $b=-0.02$, $p<0.01$), and total points ($F(3,86)=3.8$, $p=0.01$; condition*dual task $b=-0.40$, $p=0.03$; Table 4). The model predicting simultaneous task engagements approached, but did not reach significance ($F(3,86)=2.4$, $p=0.07$; condition*dual task $b=-0.02$, $p=0.21$). Follow-up analyses using a median split on raw dual task performances (<1.165) found that HIV/SUD individuals with low dual task abilities before the training performed more task switches (one-way $t=2.6$, $p=0.006$, Cohen's $d=0.83$), attempted more tasks (one-way $t=3.1$, $p=0.002$, Cohen's $d=1.04$), and tended to complete more points (one-way $t=1.4$, $p=0.08$, Cohen's $d=0.35$) when in the All GMT condition compared to the control condition (Figure 5). In other words, HIV/SUD individuals with poorer dual tasking abilities prior to training benefitted the most from the GMT strategy on the Everyday MT.

Table 4. Interaction models demonstrating the significant benefit of Goal Management Training (GMT) among HIV/SUD individuals with poor dual tasking abilities on Everyday Multitasking Test performances.

Variable	Model	Parameter (unstandardized beta)	P-value	95% CI
Task Switches				
Adjusted R^2	0.05			
F	2.68		0.05	
Condition (Control vs. All GMT)		-0.66	0.04	-1.3, -0.02
Dual Task (raw)		-0.12	0.02	-0.22, -0.01
Condition*Dual Task		-0.11	0.04	-0.21, -0.002

Table 4, continued

Tasks Attempted				
Adjusted R ²	0.09			
F	3.93		0.01	
Condition (Control vs. All GMT)	-0.17		0.02	-0.32, -0.02
Dual Task (raw)	-0.03		0.02	-0.06, -0.006
Condition*Dual Task	-0.03		<0.01	-0.06, -0.01
Simultaneous Task Engagements				
Adjusted R ²	0.05			
F	2.42		0.07	
Condition (Control vs. All GMT)	-0.24		0.04	-0.46, -0.01
Dual Task (raw)	-0.03		0.11	-0.07, 0.07
Condition*Dual Task	-0.02		0.21	-0.06, 0.01
Total Points				
Adjusted R ²	0.08			
F	3.80		0.01	
Condition (Control vs. All GMT)	-1.69		0.12	-3.8, 0.44
Dual Task (raw)	-0.49		<0.01	-0.84, -0.14
Condition*Dual Task	-0.40		0.03	-0.75, -0.05

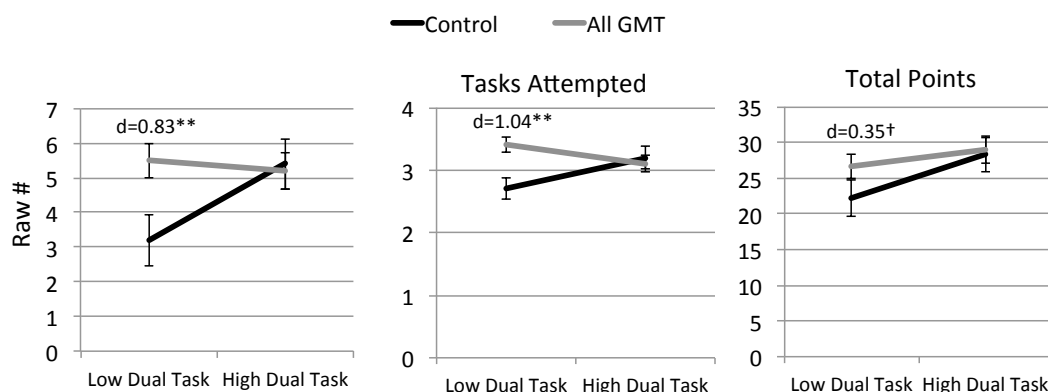


Figure 5. HIV/SUD individuals with poor dual tasking abilities benefitted most from Goal Management Training on Everyday Multitasking Test performances. One-way t-test $^{**}p<0.01$, $^{\dagger}p=0.08$; d =Cohen's d .

Metacognition

Control vs. GMT vs. Meta+GMT. Omnibus J-T models were conducted to determine the effect of study condition on metacognitive processes. There was no significant study group effect on Global Metacognition ($J^*=0.67$, $p=0.25$); however, when examining the two constructs that comprise Global Metacognition (i.e., Metacognitive Knowledge and Online Awareness), Online Awareness showed a significant positive trend across the study conditions (Control $\leq$ GMT $\leq$ Meta+GMT; $J^*1.7$, $p=0.04$), while the Metacognitive Knowledge model was not significant ($J^*=-1.12$, $p=0.87$; Figure 6). Pairwise one-way Wilcoxon analyses with FDR adjusted p-values indicated that HIV/SUD individuals in the Meta+GMT condition demonstrated null, but small-to-medium positive effect on Online Awareness compared to those in the control condition ($z=1.77$, $p=0.11$, Cliff's $D=0.27$).

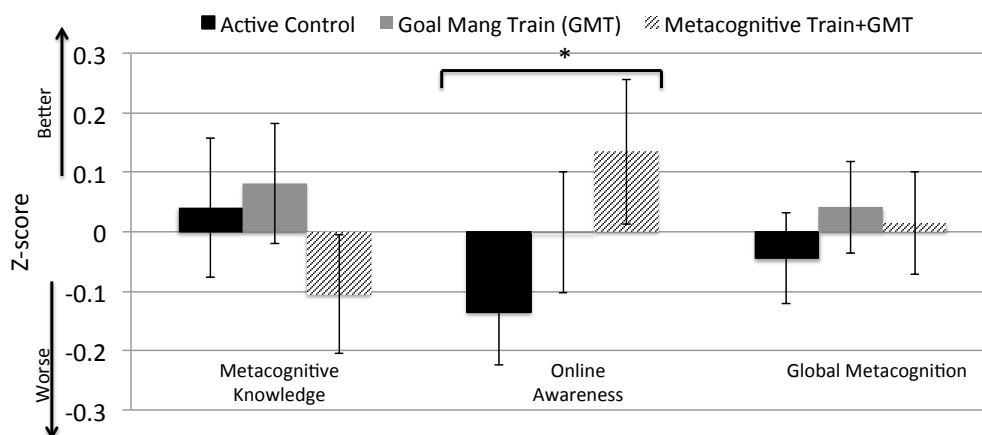


Figure 6. Major domains of in-vivo metacognitive performances by study condition; Online Awareness demonstrates a significant increasing positive trend across study arms. *Omnibus Jonckheere-Terpstra Test $p=0.04$; Bars=Mean, SE.

We additionally conducted J-T models to examine which component(s) of Online Awareness (i.e., Task Appraisals, Self-Monitoring, Self-Evaluation) may be driving this study group effect. Only the model for Task Appraisals approached significance with an increasing trend across study conditions (Control $\leq$ GMT $\leq$ Meta+GMT; $J^*=1.4$, $p=0.08$; Figure 7). One-way Wilcoxon pairwise analyses indicated that the control group tended to have less elaborate Task Appraisals compared to the GMT only or Meta+GMT conditions (vs. GMT $z=1.7$, FDR Adj. $p=0.07$, Cliff's $D=0.21$; vs. Meta+GMT $z=1.96$, FDR Adj. $p=0.07$, Cliff's $D=0.27$). The GMT and Meta+GMT study groups did not differ from one another on Task Appraisals ($z=0.26$, FDR Adj. $p=0.40$, Cliff's $D=-0.003$), and showed comparable effects when compared to the control group. In sum, similar to the pattern of results on Everyday MT, HIV/SUD individuals who completed the GMT or Meta+GMT trainings demonstrated better metacognitive abilities than individuals in the control condition, but comparable metacognitive abilities to one another.

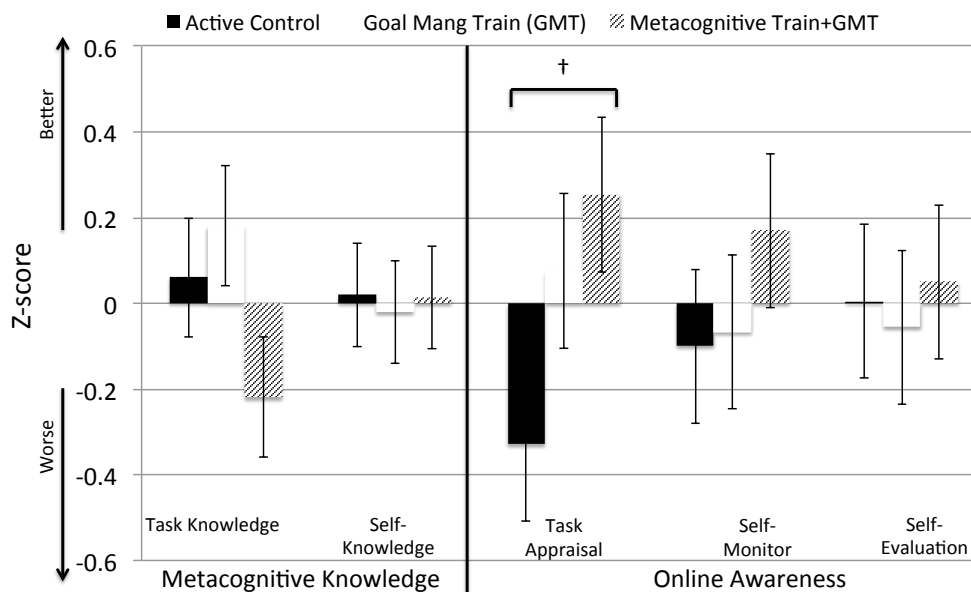


Figure 7. Among the measuring comprising metacognition, Task Appraisal demonstrates a trend for increasing elaboration across study conditions. †Omnibus Jonckheere-Terpstra Test $p=0.07$; Bars=Mean, SE.

Control vs. All GMT. Given that the effect on metacognition appeared to be driven by GMT (regardless of receiving the Meta training), we collapsed the latter two groups (“All GMT”) in order to increase power and more closely examine the effect of GMT on metacognitive processes. One-way t-tests indicated that there were no study group differences on Global Metacognition ($t=0.82$, $p=0.21$). However, there was a study group effect that approached significance again for Online Awareness abilities, one of the two constructs that comprise Global Metacognition. HIV/SUD individuals who completed the GMT (as part of the Metacognitive Training or not) tended to demonstrate better Online Awareness with medium effect sizes compared to those in the control condition ($t=1.64$, $p=0.052$, Cohen’s $d=0.37$; Figure 8). Parallel to the results reported above, the positive impact of GMT for Online Awareness appeared to be driven by more elaborate Task Appraisals (not Self-Monitoring or Self-Evaluation) in HIV/SUD individuals who received the GMT compared to controls ($t=2.25$, $p=0.01$, Cohen’s $d=0.50$; Figure 9).

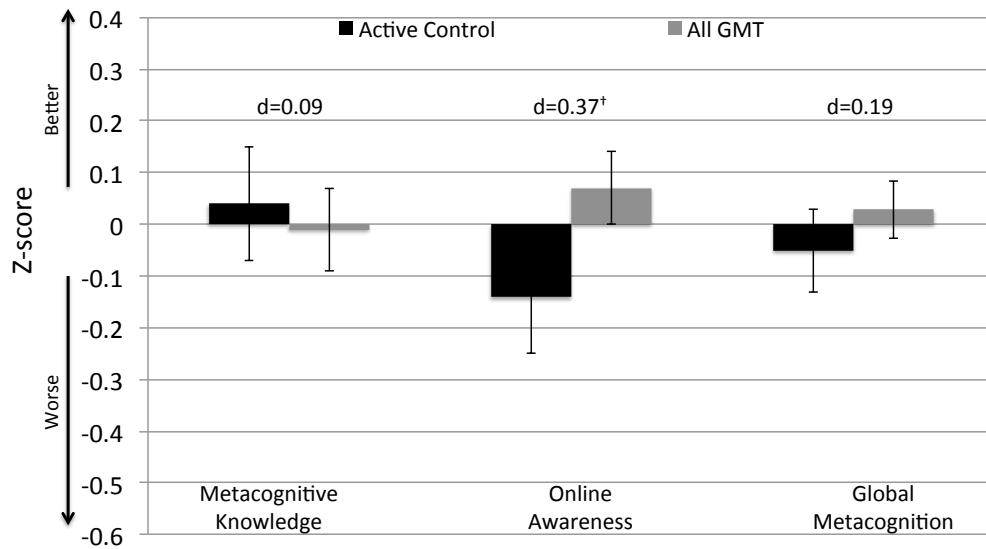


Figure 8. Goal Management Training (GMT; as part of the Metacognitive Training or not) demonstrates a small-to-medium benefit for Online Awareness among HIV/SUD individuals compared to those who received the control condition. [†]One-way t-test $p=0.052$; Bars=Mean, SE, d =Cohen's d .

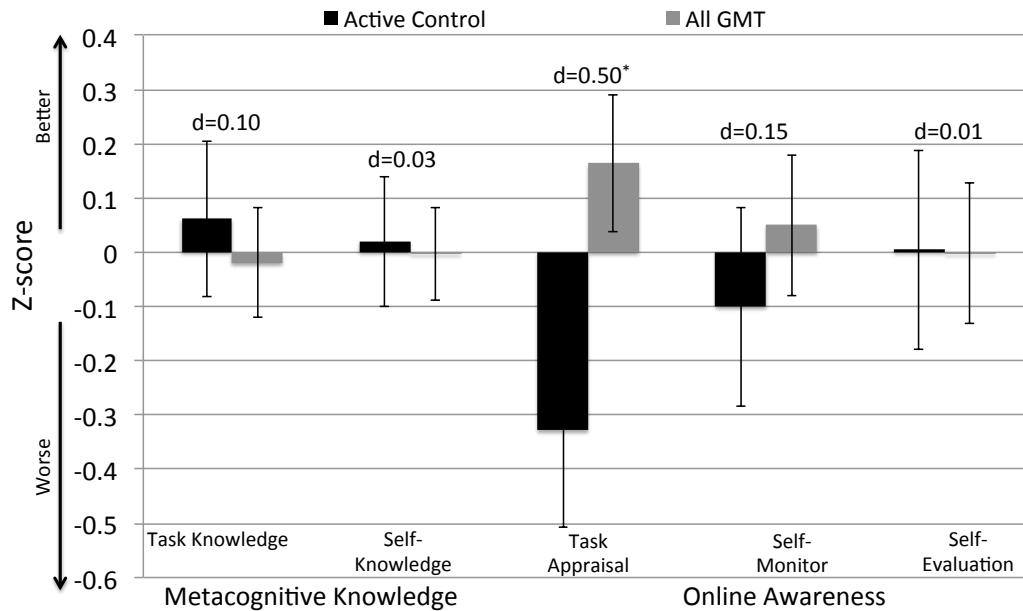


Figure 9. Goal Management Training (GMT; as part of the Metacognitive Training or not) resulted in more elaborate Task Appraisals among HIV/SUD individuals than those in the control condition. ^{*}One-way t-test $p=0.01$; Bars=Mean, SE; d =Cohen's d .

Control vs. All GMT: Interaction models. We additionally aimed to determine whether GMT differentially impacted metacognition dependent on pre-training levels of metacognitive abilities. We used the Frontal Systems of Behavior Evaluation (FrSBE) Executive Scale as an indicator of perceived executive dysfunction. Note that all participants were objectively impaired on executive functions via testing so elevations on the FrSBE may be interpreted as accurate metacognition, while minimal reporting may be interpreted as poor metacognition; 43.8% of the HIV/SUD sample reported elevations on the FrSBE Executive Scale. However, the FrSBE Executive Scale (continuous T-score) did not significantly interact with study condition (control vs. All GMT) in predicting any aspects of metacognition ($p > 0.05$).

Other Moderating Factors

Lastly, we explored the possible roles of other demographic/background (i.e., age, education, sex, race, sleep, exercise), psychiatric and substance use (lifetime alcohol, methamphetamine, or cocaine use disorders, Beck Depression Inventory-II (BDI-II), or lifetime major depressive disorder), HIV disease (i.e., nadir CD4, plasma HIV viral load), or functional (i.e., employment, IADL symptoms, cognitive symptoms (PAOFI)) factors in moderating the effect of GMT (control vs. All GMT) via a series of multivariable interaction models. We only conducted models for those outcome variables on the Everyday MT and metacognition that the GMT demonstrated a small-to-medium effect across intervention conditions (i.e., Everyday MT task switches, simultaneous task engagement, tasks attempted, and total points, and metacognitive task appraisals).

Everyday Multitasking Test. None of the models examining demographic background factors demonstrated a significant moderating effect with GMT on Everyday MT performances ($p>0.05$).

In terms of psychiatric functioning, the BDI-II demonstrated a significant interaction with study condition (control vs. All GMT) in predicting number of tasks attempted ($b=-0.02$, $p=0.02$) and total points earned ($b=-0.26$, $p=0.02$) on the Everyday MT. Specifically, among HIV/SUD individuals with high levels of current depression ($BDI-II \geq 17$), those in the All GMT condition attempted more tasks ($t=2.1$, $p=0.047$, Cohen's $d=0.93$) and tended to complete more points ($t=2.1$, $p=0.051$, Cohen's $d=0.82$) on the Everyday MT compared to controls. Performances between the All GMT and control conditions did not differ among participants with low current depressive symptomology ($p>0.05$; $BDI-II < 17$). Additionally, diagnoses of lifetime methamphetamine use disorders showed a significant interaction with study condition for Everyday MT total points earned ($b=2.3$, $p<0.05$); among HIV/SUD individuals who met criteria for a lifetime methamphetamine use disorder, those who completed the GMT earned more points on the Everyday MT than those who completed the control condition ($t=2.5$, $p=0.01$, Cohen's $d=0.75$). Additionally, Everyday MT performances did not differ between All GMT and control conditions among individuals without lifetime histories of methamphetamine use disorders ($p>0.05$). Notably, BDI-II and lifetime methamphetamine disorders were not associated with dual tasking abilities ($p>0.15$; i.e., these moderating effects are independent of the moderating effect of dual tasking capacity reported above). There were no other significant interaction models for psychiatric or substance use factors in predicting Everyday MT.

HIV disease and daily functioning factors were not significant moderators in the relationship between study condition and Everyday MT ($p>0.05$).

Metacognitive Task Appraisals. No demographic or background factors, psychiatric or substance use, HIV disease, or daily functioning factors significantly moderated the effect of GMT on metacognitive task appraisals.

Study and Training Feedback

In all study conditions, participants reported comparably ($p>0.05$) high levels of acceptability regarding the trainings and overall study participation. Using a Likert-scale (1=*Not at all* to 5=*Very much*), levels of study satisfaction ($M=4.5$, $SD=0.83$), engagement in the study trainings (i.e., origami, GMT, or Meta+GMT; $M=4.7$, $SD=0.66$), and perceived helpfulness of the trainings ($M=4.4$, $SD=1.0$) averaged at or above 4.4 for each of the scales (Figure 10). It is important to note that even participants in the control condition received an “active” psychoeducational component, which likely contributed to their ratings of training helpfulness and study satisfaction. Similarly, those individuals who received the GMT (as part of the Metacognitive Training or not), on average reported that they perceived the GMT as “helpful to very helpful” ($M=4.4$, $SD=0.84$) when completing the Everyday MT, and “agreed to strongly agreed” that the GMT could be helpful in their daily lives ($M=4.6$, $SD=0.73$). Of note, HIV/SUD individuals who completed GMT training (as part of the Metacognitive Training or not) reported that they actively used the GMT, on average, for only about half of the Everyday MT ($M=3.3$, $SD=1.2$). Finally, among participants who additionally completed the Metacognitive Training, they noted that receiving feedback regarding their executive dysfunction was “helpful to very helpful” (4.3, $SD=1.2$), and that they “agreed to strongly agreed” that they would be able to use the feedback information in their daily lives ($M=4.6$, $SD=0.68$).

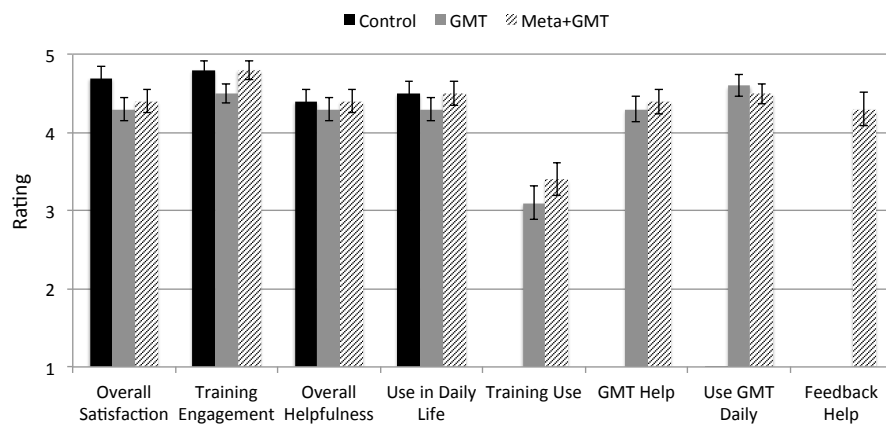


Figure 10. Feedback regarding trainings and participation by study arm.

DISCUSSION

This study aimed to evaluate the efficacy of a brief Metacognitive Training plus Goal Management Training strategy module as a possible neurorehabilitation tool for HIV/SUD individuals with executive dysfunction. HIV/SUD individuals were randomized into one of three study conditions: 1) active control; 2) brief executive strategy (Goal Management Training, GMT); or 3) Metacognitive Training in addition to the GMT executive strategy (Meta+GMT). This is one of the first studies to explore possible neurorehabilitation tools among HIV+ substance users, and the first study to specifically determine the effectiveness of either GMT or GMT with Metacognitive Training in this neurocognitively-vulnerable population.

Training Benefits

Everyday Multitasking Test. One of the primary outcomes of interest following completion of one of the study conditions was performance on a laboratory-based daily functioning task, the Everyday Multitasking Test (Everyday MT). We hypothesized a stair-step effect, with HIV/SUD individuals who completed the control condition performing the worst, followed by those who completed the GMT, and those in the Meta+GMT condition performing the best. The omnibus models demonstrated null, but small-to-medium benefits of the latter two active study arms (compared to the control condition), with the positive effects of training largely comparable between the GMT and Meta+GMT conditions. Namely, the benefits on Everyday MT performances appeared to be primarily driven by completion of the GMT, while receiving the Metacognitive Training component (i.e., feedback regarding participants' executive dysfunction) did not significantly contribute to performances beyond GMT. These findings lead us to collapse the two active study arms, and we subsequently demonstrated significant, medium-to-

large positive effects of GMT (as part of the Metacognitive Training or not) on Everyday MT performances.

Specifically, HIV/SUD individuals who completed training on the executive GMT strategy (regardless if it was a part of the Metacognitive Training or not) demonstrated better performances particularly on the executive aspects of the Everyday MT, including more simultaneous task engagements and increased frequency of switching between tasks, than individuals in the control condition. Relatedly, completion of the GMT executive strategy training was also associated with a greater number of Everyday MT tasks attempted and a tendency to complete more of the overall task compared to those in the control condition. This pattern of results was particularly salient and demonstrated large effects ($d's=0.83-1.04$) among HIV/SUD individuals who had lower dual-tasking abilities prior to training. In other words, those HIV/SUD individuals who were potentially at the greatest risk of having multitasking difficulties (pre-training low dual-tasking performance) benefitted significantly and the most from GMT implementation on Everyday MT performances.

Although the mechanisms by which GMT resulted in better Everyday MT performances cannot necessarily be teased apart from our study design, there are several conceivable pathways. A possible framework that may be used to consider the efficacy of the Goal Management Training (GMT) is via Shallice and Burgess' (1991) conceptualization of multitasking deficits. According to these authors, multitasking deficits following damage to the prefrontal systems represent an inability to reactivate a previously generated intention (sub-goal) after a brief delay, especially when the sub-goal is not signaled by the environment (e.g., remembering to turn down the pasta so that it does not boil over *versus* turning down the pasta when it boils over). GMT may disrupt this maladaptive process in two ways; first, during the active training session,

HIV/SUD participants were instructed to verbally self-generate (i.e., describe in own words) and elaborate the overall goal and sub-goals of the Everyday MT, which may have resulted in deeper encoding processes allowing for easier “reactivation” (retrieval) during task performance itself. Another possibility is that participants had access to the GMT flowchart (Stop, Define, List, Learn, Do, Check) throughout task performance, and although the flowchart did not include any task-specific content, it may have served as a simple external reminder cueing engagement in task- and self-reflective processes during the performance. Together, these processes may have lead to a higher likelihood of reactivating the Everyday MT steps and sub-goals resulting in greater task switching and overall task engagement. Ultimately, GMT may be effective by promoting the ability to maintain and more flexibly engage with higher-order goals; these latter abilities aid in orienting behavior to the internal plans that are needed for everyday multitasking, rather than simply responding to environment cues (Roca et al., 2011).

Another parallel process may be that, by nature, individuals with executive dysfunction are less likely to engage in the reflective, flexible scheduling processes that allow individuals to select appropriate strategies when completing tasks, and ultimately have less executive resources to draw from during task performances (Meyer & Kieras, 1997). Therefore, provision of the GMT for these HIV/SUD individuals with executive dysfunction may have reduced the executive cognitive load associated with selection of a strategic approach from the outset. The reduction of strategic cognitive burden afforded by the GMT may have then freed those executive resources to be applied to Everyday MT performances themselves, resulting in greater success on the executive aspects of the test (i.e., task switches, simultaneous task attempts). This hypothesis may be supported by our finding that HIV/SUD individuals with especially limited executive resources (i.e., those with low dual tasking abilities) benefitted the most from the GMT.

Supporting this conceptualization, among healthy adults, reduction of load on cognitive control processes is associated with increased activation of task- or process-specific neural circuitry (Kelly & Garavan, 2005; Petersen, van Mier, Fiez, & Raichle, 1998). Subsequently, if the GMT was able to decrease the need for recruitment of cognitive control circuits, a more refined, task-specific network of activation may have resulted in the higher number of tasks attempted and overall greater number of steps completed for the Everyday MT. Alternatively, or perhaps in parallel, Salvucci and Bogunovich (2010) found that healthy individuals were significantly less likely to switch tasks when engaged in a higher overall cognitive workload task, than when performing a lower cognitive workload one. Therefore, perhaps the GMT facilitated increased task switching, in particular, by reducing the global cognitive burden associated with performing the Everyday MT. Whether via reduction of executive-related burden to increase overall task-specific engagement, or reduction of overall cognitive burden to release executive resources (or perhaps both), the GMT may have served to simply free resources that would otherwise be needed to be employed for task completion, resulting in greater task flexibility (e.g., task switching) and ultimately, better performances (e.g., more tasks completed). Likely, the GMT helps support several neurocognitive systems; regarding our conceptualizations here, perhaps the GMT indeed reduces the overall cognitive burden of a given task, which may then facilitate the ability to engage in the activation/re-activation processes outlined by Shallice and Burgess (1991) above. While simultaneously, the GMT promotes this activation/re-activation of sub-goals to promote successful multitasking performance.

Interestingly, Goal Management Training (GMT) did not demonstrate any effect on the number of errors committed on the Everyday Multitasking Test (Everyday MT). The brief (20-minute) nature of the GMT may have unduly weighted its effects toward

the effortful planning of future task performance during the training didactic period (prior to task completion), rather than allowing for deeper consolidation of the technique itself to be actively applied during task performance. In other words, GMT may have enhanced the structured approach to the Everyday MT (i.e., identifying goals/steps) allowing for greater retrieval and completion of sub-goals, but was not necessarily applied as an error-monitoring strategy during the task performance itself. Indeed, feedback from HIV/SUD individuals who completed the GMT (as part of the Metacognitive Training or not) noted that they used the strategy on average for only about half of the Everyday MT. Future studies examining graded application of GMT (e.g., 20-minute versus 30-minute training) and more direct instruction of how to apply the GMT during task performance are warranted in order to determine its optimal potency and efficacy for error-regulation of daily functioning outcomes.

Metacognition. The second primary aim of the project was to determine the efficacy of the Metacognitive Training + Goal Management Training strategy (Meta+GMT) for metacognitive abilities. Graded improvement across the three study conditions was again hypothesized with HIV/SUD individuals in the control condition demonstrating the poorest, those in the GMT only condition mid-level, and those in the Meta+GMT condition demonstrating the best metacognitive abilities. Global Metacognition was comprised of Metacognitive Knowledge and Online Awareness. Although there were no group differences on Global Metacognitive abilities or Metacognitive Knowledge, there was a significant upward trend across the study groups demonstrating benefits in Online Awareness ($\text{Control} \leq \text{GMT} \leq \text{Meta+GMT}$). Closer examination of the components of Online Awareness revealed that those HIV/SUD individuals who completed the GMT only or the Meta+GMT conditions tended to demonstrate more elaborate Task Appraisals (i.e., verbal plan of task approach) than

those in the control condition. Given that completion of the GMT (with or without the Metacognitive component) appeared to be driving the differences in metacognition, we subsequently collapsed the latter two active study arms and found that, indeed, HIV/SUD individuals who received GMT in any context tended to exhibit better Online Awareness, as driven by significantly more elaborate Task Appraisals. Taken together, our hypothesis that HIV/SUD participants who received the metacognitive feedback would demonstrate the best metacognition was not confirmed, and instead the largest effect sizes were observed on Online Awareness abilities simply for those individuals who completed the GMT executive strategy (as part of the Metacognitive Training or not).

Online Awareness refers to the ability to detect and regulate performance during the stream of action, and according to Toglia and Kirk (2000), it incorporates the development of task appraisals, ongoing self-monitoring, and accuracy of self-evaluations. Online Awareness is tightly linked with Metacognitive Knowledge in that discrepancies between what one does and what one expects to do, based on prior knowledge and beliefs, is what may lead to performance adjustments; however, given that Online Awareness abilities tend to vary with a task or situational context and are relatively more fluid, it is not surprising that we observed training differences on this construct, rather than on Metacognitive Knowledge (Brown, 1987).

When considering the multifaceted skills that comprise Online Awareness and may be driving the observed effect, we found that task and situational appraisal demonstrated a significant, medium effect size benefit ($d=0.50$) from Goal Management Training (GMT). Specifically, HIV/SUD individuals who completed GMT training elaborated their conceptualization of and plan for the upcoming task in greater detail than those in the control condition. This ability to identify and delineate task demands

relative to one's own capacity is needed for optimal strategy selection and to define the task expectations that will need to be regulated downstream during performance (Bandura, 1997; Hacker, 1998). A major component of the GMT is its provision of an overlaying structure to an otherwise unstructured task by encouraging individuals to define the primary task goals, and then list and learn the steps needed to complete each goal. This process thus promotes the formation of a superordinate hierarchy of goals and steps or, in other words, a plan for the upcoming task. Considered in the context of Norman and Shallice's supervisory attentional model of executive functions (Norman & Shallice, 1980), planning is mediated by the supervisory attentional system (SAS) and may be activated when a high-level schema (i.e., goal selection) is triggered and then passes on the activation to lower-level schemas (i.e., individual action). Therefore, the SAS is the critical cognitive construct that orchestrates the willed and deliberate planning of subsequent actions (sub-schema activations). Importantly, the SAS, which is subserved by the prefrontal cortex (Shallice & Burgess, 1991), is the system that is disrupted among individuals with executive dysfunction, such as the HIV/SUD participants enrolled in this study. Therefore, the GMT may have helped to serve as an externally fabricated SAS in our participants with such disrupted attentional systems in activating and developing such planning processes. Interestingly, given that it did not demonstrate an effect on online self-monitoring abilities (i.e., error corrections), the GMT did not appear to function as an activation trigger, per say, for an otherwise latent SAS, but instead perhaps temporarily operated in place of it. In other words, the GMT resulted in more elaborate planning before task engagement, similar to the role of a functioning SAS, but did not demonstrate any residual monitoring effects during task performance itself. Therefore, it appears that the GMT may have served to replace the SAS during the active training period to set up success on the task, but was not necessarily generalized

to check accuracy of completed schemas during performance itself. This may further support the notion that the SAS system is indeed more globally disrupted among our HIV/SUD individuals with executive dysfunction, and not simply an inability to reach activation threshold. Therefore, in the future, techniques that may support the sustained activation of the SAS throughout task performance may yield greater improvements across the other Online Awareness domains.

All considered, task appraisal and planning abilities are distinct executive skills needed for successful and accurate metacognition (Toglia & Kirk, 2000). The GMT significantly allocated resources to improve these skills, which highlights their potential malleability for improvement. Although the GMT did not more globally impact other metacognitive domains (e.g., self-monitoring), the general principles of this technique are clearly impactful and may be a potentially fruitful starting point in the development of future neurorehabilitation interventions among HIV/SUD individuals with executive dysfunction (see *Informing Future Directions* section below).

Other Moderating Factors for Goal Management Training (GMT) Benefits

When developing novel intervention tools, it is critical to ascertain the characteristics of the individual for whom an approach may be especially viable and efficacious. Although there were no individual-level characteristics that moderated the effect of GMT on metacognitive task appraisals, both mood and methamphetamine use influenced how GMT benefitted multitasking abilities. Importantly, these latter two moderating characteristics appeared to impact the benefit of GMT independent of dual tasking abilities. Therefore, regarding mood, HIV/SUD individuals with more severe depressive symptoms, providing an aid via GMT may have enhanced perceived self-efficacy of multitasking abilities potentially resulting in greater task engagement and

ultimately, performance (Bandura, 1997). Similarly, we found that in HIV/SUD participants with lifetime histories of methamphetamine use disorders (n=47), those who received the GMT completed more multitasking points than those in the control condition. Although all study participants met criteria for some lifetime substance use disorder, methamphetamine may have particularly prominent and lasting deleterious effects on these frontostriatal circuits in the context of HIV infection, which are heavily drawn upon when multitasking (Chana et al., 2006; Ellis et al., 2003; Gavrilin, Mathes, & Podell, 2002; Jernigan et al., 2005; Taylor et al., 2007). Indeed, Iudicello and colleagues (2014) demonstrated enduring adverse neurocognitive and functional outcomes following remote methamphetamine dependence among older (but not younger) HIV+ individuals. Therefore, there appears to be significant additional injuries to these neurocognitive systems when multiple risk factors are in play (e.g., aging, HIV infection, methamphetamine use) - with the effects of even remote methamphetamine use being particularly persistent. As a result, HIV+ methamphetamine users may be disproportionately in need of and responsive to such executive neurorehabilitation techniques.

Our results indicate a specific pattern of individual characteristics (i.e., HIV+ methamphetamine users with more severe current depression symptomology) that may especially warrant eligibility for GMT implementation. Continued future work developing more individualized neurorehabilitation techniques are needed given that the efficacy of these tools can significantly differ with the constellation of background and comorbid factors of a presenting patient.

Metacognitive Training Null Effects: Informing Future Directions

Although we hypothesized that HIV/SUD individuals who received the Metacognitive Training *and* GMT strategy (Meta+GMT) would perform the best on a daily functioning task and demonstrate the most accurate metacognition based on prior literature (e.g., Goverover et al., 2007; Ownsworth et al., 2010), there were several novelties and deviations in our approach to the training that may have impacted its efficacy.

Brevity and Potency. First, the brevity of our Metacognitive Training is particularly of note and the largest departure from the more intensive 3- to 16-week self-awareness trainings described in previous studies (e.g., Goverover et al., 2007; Ownsworth et al., 2006), which may have ultimately adversely impacted its ability to be effectively applied and therefore, its power. By contrast, our single-session training included approximately 10 minutes dedicated to feedback and psychoeducation regarding individuals' executive dysfunction, followed by 10 minutes of training on the executive strategy (i.e., Goal Management Training). We selected such a brief training both due to the limited scope and resources of the project, but also to develop a potential neurorehabilitation tool that may be applicable in other time-limited settings (e.g., outpatient clinics). However, it is possible that our brief Metacognitive Training was simply not salient or potent enough to initiate and maintain behavior change (beyond the effects of the GMT) for our HIV/SUD participants. Perhaps with greater training practice, enhanced fluidity and proficiency with the GMT skillset may have been observed on performances. Relatedly, given that all participants had current executive dysfunction, the concept of "neurocognitive impairment" may have been too abstract for them to fully appreciate, make personally meaningful, and then apply to their behaviors (multitasking performance or metacognitive perceptions) in such a limited time frame. For example,

Metacognitive Knowledge, which is a construct integrating beliefs about both the self (e.g., strengths/weaknesses) and the given task (e.g., previous experience with task), showed no demonstrable changes following Metacognitive Training. Therefore, it is possible that individuals' self- and task-related beliefs were too deeply engrained to be altered by a brief metacognitive feedback, especially given that these individuals were, by nature, largely unaware of these impairments prior to study participation. Indeed, a body of literature suggests that individuals' self-concepts are largely fixed in early adulthood and show little or no changes across time (McCrae, 1982); thus, a particularly prominent and personally-relevant event or experience may be needed in order to shift one's self-concept in a meaningful way enough to observe behavioral change. We discuss several potentially more salient feedback methods that may both further complement utilization of the GMT strategy and result in greater global behavioral effects.

One possibly more potent feedback approach that has been fruitful in improving both self-awareness and performance of activities of daily living is video review of performance (Ownsworth et al., 2010). Provision of more concrete evidence of ability levels and, especially, practice in tracking "real-time" task errors via video feedback may be particularly beneficial for individuals with executive dysfunction who have difficulty appreciating and applying abstract verbal feedback. Video feedback may be utilized to improve both Metacognitive Knowledge via enhanced accuracy of self- and task-knowledge, and Online Awareness by explicitly promoting appraisal, monitoring and error-detection abilities. Video feedback may also play a direct role in improving task performance itself through visualized practice. Prior studies suggest that the mirror neuron network is activated even during passive observation of activities, resulting in strengthened task-specific neural connections similar to those observed with actual

practice of the task itself (Buccino, Solodkin, & Small, 2006; Rizzolatti & Craighero, 2004). Not surprisingly, this continued “mirror neuron practice” ultimately is associated with behavioral improvements in the task performance itself (Petersen et al., 1998). Therefore, video feedback may additionally be utilized to engage in task practice at the neural level in order to improve final performance.

Another potentially more powerful method of feedback would be to enrich the perceptual experience of the task itself. For example, regarding metacognition, successful Online Awareness is contingent on an individual's ability to continuously update his/her behavior based on his/her incoming sensory perception during task performance (Pearson, Rademaker, & Tong, 2011). Therefore, implementation of additional auditory and/or tactual (e.g., vibration) feedback as cues to engage in monitoring or to signal real-time errors would enhance the sensory experience of the task, providing multiple modalities (beyond vision) and increased opportunity for the individual to detect and encode possible discrepancies in his/her internal state versus external goal. Given the lack of sensitivity of GMT or Meta+GMT to improve the number of errors committed on the Everyday MT, this technique may be particularly complementary in reducing error-related behaviors. These real-time perceptual cues may also be utilized to directly modulate and improve other aspects of task performance (e.g., a tone to initiate task switching). However, although such environmental manipulations have shown efficacy in initiating behavioral change (Bettcher et al., 2011; Brennan, Giovannetti, Libon, Bettcher, & Duey, 2009), more data are needed to determine the generalizability of their effects. Given that the real world environment is complex, ever-changing, and novel depending on the setting, it may not be realistic to implement such task-specific manipulations either across tasks or settings.

Sufficiency of Goal Management Training. Given that we found no statistically significant benefit of adding the metacognitive feedback to GMT, it may have been the case that simply providing a concrete executive strategy was the needed “active ingredient” to improve task performances and aspects of metacognition. Indeed, prior studies examining metacognitive trainings included the selection and application of strategies as part of the global awareness training (Goverover et al., 2007; Ownsworth et al., 2010). Therefore, it is possible that improvements observed in those studies might, in fact, be attributable to the strategy training, and not necessarily the other aspects of the awareness interventions (e.g., feedback). Ours is the first study that has begun to tease apart the most active components in such metacognitive training approaches. Given the complex nature and multiple possible “active” ingredients involved in real life neurorehabilitation techniques, including nonspecific training factors (e.g., therapeutic relationship), future work is needed to disentangle which aspects of trainings are critical versus those that may not meaningfully contribute to functional outcomes. Improving the economy of treatment approach will help address the limited time demands in the clinic and reduce both patient and provider burden moving forward.

Emotional Distress. Additionally, prior literature suggests that individuals may exhibit increased emotional distress (i.e., depression and anxiety) when developing more realistic self-awareness (Lucas & Fleming, 2005), which was not addressed in the current training. Perhaps receiving the neurocognitive feedback as part of the Metacognitive Training initially increased levels of affective distress for some participants, which could have negatively impacted task performances and metacognitive appraisals, and therefore reduced any observed effect of the training. Yet, those HIV/SUD individuals who were in the Metacognitive Training did not perform *more* poorly than those in the GMT as a group, suggesting that this was at least not the case

at the group-level. Nonetheless, techniques to promote readiness and facilitate acceptance of deficits may be an important complement to metacognitive trainings, particularly among individuals with preexisting affective distress. Motivational Interviewing (MI) is one therapeutic technique that has been widely applied to promote health behaviors in psychological settings, and is more recently gaining attention for use among individuals with brain illness or injury in the neurorehabilitation context. In brief, MI aims to facilitate and engage intrinsic motivation within the client in order to change desired behaviors (e.g., promote functional independence). For example, Watkins and colleagues (Watkins et al., 2007) found that application of MI improved mood in the acute stroke setting, over treatment as usual. Although there are several reviews suggesting its potential efficacy (Manchester, 2001; Medley & Powell, 2010), MI has not been used specifically in the context of self-awareness trainings. However, MI may be a particularly suitable primer before a metacognitive training by setting a foundation for constructive feedback, building initial therapeutic alliance, and developing motivation to learn about oneself in order to improve outcomes. As an empirically-based, manualized and replicable approach, even a brief single MI session is a good candidate for use in conjunction with metacognitive trainings to promote gains in self-awareness and self-efficacy, and ultimately, daily functioning outcomes.

Underpowered Statistical Analyses. Lastly, with only 30 participants per study arm, it is also feasible that our Metacognitive Training was simply underpowered and that a greater sample size is needed to detect differences between the GMT and Meta+GMT exercises on our outcomes. For instance, the hypothesized increasing stair-step effect across study conditions (Control < GMT < Meta+GMT) was indeed observed for Online Awareness and Everyday Multitasking task switches (see Figure 6), yet the pairwise analyses examining differences at each “step” effect did not reach statistical

significance. Therefore, although these preliminary data may point to a potential signal across study conditions, larger, more well-powered studies may be needed to better determine a possible effect. Of note, the large majority of the empirically examined metacognitive trainings to date have been conducted in single-subject or very small sample sizes ($n's \leq 10$; Fleming, Lucas, & Lightbody, 2006; Goverover et al., 2007; Ownsworth et al., 2006; Ownsworth et al., 2010). Therefore, despite its limitations in this regard, the current study represents one of the most well-powered study designs to date. However, small effect sizes are commonly observed in neurorehabilitation approaches due to the large degree of both intra- and inter-individual variability in response to treatment; as such, future studies are greatly needed that employ large sample sizes and/or within-subjects designs in order to increase power to detect even small, but meaningful changes in behavior.

Clinical Implications

The significant benefits we observed following Goal Management Training (GMT) have ecological implications for HIV/SUD individuals, as well. First, we found that HIV/SUD individuals who completed the GMT demonstrated more task switching, simultaneous task attempts, and increased task engagement on our performance-based multitasking test. Multitasking is a ubiquitous daily life activity; the large majority of real world tasks tap into and require the ability to organize and integrate multiple neurocognitive systems (e.g., driving; Burgess et al., 2000). Therefore, identification of techniques to improve such multitasking abilities, especially using a brief, non-resource-intensive tool, has potentially wide-reaching ramifications. Among HIV/SUD individuals, an increased ability to balance the demands of multiple ongoing tasks may be especially applicable for health-related behaviors that require ongoing monitoring, such as

antiretroviral medication adherence. For example, the GMT may help promote medication adherence as a set intention, while allowing for ongoing task engagement in other activities (e.g., task switching, simultaneous task attempts) until the designated dosing time. These benefits may also simply promote greater independence in task completion; given the prevalence of disability among HIV+ substance users (e.g., Blackstone, Iudicello, et al., 2013), techniques that can support capacities to engage in and more autonomously complete activities of daily living potentially have high public health relevance both economically (e.g., disability status) and at the psychosocial level (e.g., caregiver burden). Of note, our outcome multitasking measure was a laboratory-based task tapping into individuals' functional *capacities*, which may carry inherent limitations in terms of clinical generalizability (e.g., artificial environment, does not account for which activities individuals actually do in their daily lives). However, Scott and colleagues (2011) demonstrated significant, positive associations between performances on the laboratory-based Everyday Multitasking Test and multiple manifest real-world domains (independence on instrumental activities of daily living (IADLs) and employment status). Therefore, our preliminary results supporting the efficacy of GMT for the Everyday MT may indeed be more broadly applicable towards fostering success in real world IADLs.

Our second primary finding supports the efficacy of GMT in promoting metacognitive task appraisals, which may also have meaningful implications in enhancing day-to-day successes. Specifically, we found that HIV/SUD individuals who received GMT demonstrated more elaborate intentionality (detailed plan) than those in the control condition. Improvements in metacognitive task conceptualizations may help with task decision-making and strategy selection by encouraging both task- and self-reflective processes before engaging in the task, both of which are associated with

better performances (Fernandez-Duque et al., 2000). Additionally, in the context of the Theory of Planned Behavior, such planned intentions are posited as the most important determinant of future actions (Ajzen, 1991). Therefore, GMT may not only aid in defining the task steps and strategic approaches themselves, but also increase goal behaviors by developing intentionality. Indeed, previous studies support the link between more elaborate task planning and subsequent behavioral success (e.g., Allan, Sniehotta, & Johnston, 2013). In fact, among HIV+ individuals, Cattie et al. (2012) found that better cognitive planning capacities were associated with fewer declines in activities of daily living (e.g., medication management) and decreased risk for unemployment. Therefore, the observed GMT-related benefits in planning and intentionality may ultimately result in greater real world functioning successes among HIV+ substance users. In addition, techniques to enhance intentions may also be useful in reducing impulsive substance use or HIV risk behaviors. For example, GMT may be applied to promote premeditated thought and introspection regarding substance abstinence before entering a social situation, and ultimately, help HIV/SUD individuals adhere to substance-related goal behaviors (e.g., “I do not want to use tonight.”). Additionally, as a whole, enhanced metacognition is consistently associated with better everyday (e.g., increased community integration) and rehabilitation outcomes (e.g., increased treatment engagement and motivation; Fleming & Strong, 1999; Prigatano & Wong, 1999; Sherer et al., 1998; Trudel et al., 1998). Thus, improvements in even one aspect of metacognition may be a starting point in shifting accuracy of metacognitive processes as a whole, and ultimately, improvements in clinical outcomes.

Taken together, our results indicate initial promise of GMT as a potential neurorehabilitation tool, which has positive implications for the day-to-day functioning of HIV+ substance users. The brief (10-minute) nature of our training may also be

especially amenable to time-limited settings, such as outpatient clinics, which supports its clinical feasibility and utilization as well. Although our study was not able to examine the direct impact of the GMT on HIV/SUD individuals' manifest functioning outside of the laboratory, there are direct links between the outcomes measured here and real life abilities (e.g., IADL dependence, employment). Long-term, incremental improvement in such everyday abilities and promotion of community integration may help to alleviate both the individual and public health burden of HIV infection and substance use.

Training Feasibility and Acceptability

Importantly, HIV/SUD participants rated the training procedures as highly engaging and helpful. Even if a neurorehabilitation tool demonstrates high efficacy at improving outcomes, the training may never be used if it is not a pragmatically feasible and acceptable approach to the target patient population. Therefore, in conjunction with its significant beneficial behavioral effects, the high levels of positive feedback among individuals who completed the GMT support its potential feasibility for future use among HIV+ substance users. Of note, training acceptability did not differ by study condition (i.e., HIV/SUD individuals in the active control rated satisfaction as high as those in the GMT), which may suggest that there were some nonspecific effects of the examiner. In other words, the same examiner administered all of the trainings, which may have driven the similar ratings observed across study conditions. However, even though HIV/SUD in the control condition rated their training experiences equally positive to those in the active arms, only those in the active arms (received the GMT) demonstrated benefits in performances. Additionally, although HIV/SUD individuals who completed the GMT rated it as highly helpful and potentially useful in daily life, they reported only actually using it on average for “about half of the test.” Perhaps the GMT would have shown greater

outcome efficacy had participants applied it more consistently across task performances, which may be observed with greater strategy practice; future studies are needed to better delineate the barriers of GMT application during actual task completion in order to promote its most effective utilization. Overall, more work is warranted to further establish the acceptability of Goal Management Training across subtypes of clinical populations (e.g., methamphetamine versus alcohol users) and individual differences (e.g., severity of impairment, racial minorities), as well as the potential impact of examiner effects on the subjective patient training experience.

Limitations

There are several important methodological limitations to note in our study. First, given the small effect sizes observed, the current study design had limited statistical power with which it could detect such effects, potentially resulting in Type II error. Development of neurorehabilitation study designs with greater statistical power via larger sample sizes and/or a within-subjects method may reveal a stronger pattern of significant findings. Specifically, regarding the latter approach, our current between-subjects design employed balanced randomization to achieve comparability of background factors (e.g., demographics and severity of executive dysfunction) across groups and then examined the effects of training between groups. Instead, using a within-subjects design, participants would be assessed on the outcome measures both pre- and post-training, allowing for examination of relative gains and inherently accounting for intraindividual variability. Yet, although the current study only included 30 participants per study arm, ours is one of the largest neurorehabilitation studies in HIV infection or substance use, to date.

On the other hand, given our relatively small sample, we did conduct multiple analyses and emphasized interpretation of effect sizes, rather than p-values, which may have contributed to Type I error. Although we conducted false discovery rate p-values for follow-up pairwise analyses, we did not apply alpha value corrections for multiple comparisons in our primary analyses. Examination of non-significant effect sizes, however, may prove valuable in illustrating overall trends in the dataset and provides value for possible future directions to be learned from these preliminary data.

Additionally, although all participants evidenced current executive dysfunction, we did not screen for metacognitive deficits, per se, as inclusion criteria and we did not exclude participants who demonstrated impairment in other neurocognitive domains. The somewhat limited scope of this dissertation project precluded the screening of metacognitive impairment, given that this information was not consistently gathered at the prior study visit. Of note, we did find important specificity for the efficacy of the trainings (i.e., GMT was most beneficial for those with low dual-tasking). Therefore, it is possible that the Metacognitive Training did not demonstrate significant effects because not all participants had a meaningful metacognitive deficit. However, we found that 80% of participants endorsed “normal” levels of frontal systems behaviors on at least one of the three scales from the Frontal Systems Behavior Evaluation, and given that all participants evidenced executive dysfunction on testing, this suggests a potentially high proportion of metacognitive discrepancy in our sample. Additionally, our inclusion of participants with other types of neurocognitive impairment (e.g., episodic memory, processing speed in various patterns) may have increased the individual variability in response to our executive-specific trainings. For example, it is possible that a study participant had mild executive dysfunction, but more prominent memory impairment, the latter of which may have been more salient to the individual and potentially a more

clinically-relevant target for intervention. Although the current study was not able to screen for relative cognitive impairments as inclusion criteria due to the limited time frame for recruitment, future studies may benefit from targeting individuals' most severe or personally-relevant impairment in order to obtain the optimal gains. Of note, however, HIV+ substance users commonly demonstrate impairment across multiple cognitive domains, and executive dysfunction is consistently one of the most ecologically relevant ability areas (Casaletto, Weber, Iudicello, & Woods, in press). Therefore, our approach of allowing for inclusion of other domain impairment may have increased the generalizability of our findings, as well as have had the most clinically meaningful effect.

Of note, we were also only able to employ a single-blinded procedure in our training design. Although participants had no knowledge of which study condition they were completing, the examiner was not blinded to study condition during training or testing. The limited financial resources of this dissertation project did not allow for different examiners during the training versus assessment portions of the study. It is therefore possible that knowledge of participants' study condition biased the examiner's scoring on the outcome measures. However, the Everyday Multitasking Test has fairly concrete and standardized scoring procedures based on overt behaviors (e.g., "Measured one cup of pasta") that likely supported objective assessment. Additionally, for our other primary outcome, the majority of the metacognitive measures were self-report, which the examiner would not have directly impacted. Nonetheless, rigorous double-blinding procedures in future intervention work would preclude any possible examiner bias and provide a clearer picture of true training efficacy.

Lastly, the primary aim of our brief experimental training was to examine its efficacy on laboratory-based assessments, and did not include indicators of possible generalization or durability of effects. For instance, if we employed a follow-up

appointment several weeks to one month post-training, we could have assessed the outcome measures again, as well as completed measures tapping into participants' manifest daily functioning. These additional evaluations would help determine if the beneficial training effects were indeed robust across time and the extent to which they may have impacted HIV/SUD individuals' subsequent day-to-day activities. Durability and generalizability are critical concepts when developing neurorehabilitation tools; empirically supported techniques that have a more wide-reaching impact outside of the laboratory are greatly needed and an important future direction in the field (Weber, Blackstone, et al., 2013).

Summary and Other Future Directions

Our brief experimental design demonstrated modest benefits of Goal Management Training (GMT) for both everyday multitasking abilities and metacognitive task appraisals among HIV+ individuals with substance use. Regarding the former, the positive impact of GMT for multitasking was particularly salient among HIV/SUD individuals with poorer multitasking abilities prior to training, as well as those with more severe levels of current depressive symptomology and histories of methamphetamine use disorders. Although the Metacognitive Training did not significantly contribute to multitasking or metacognition beyond the benefits of GMT, further work is needed to better determine if this is indeed a needed or viable neurorehabilitation approach. Given that metacognition, itself, is consistently associated with rehabilitation outcomes (Prigatano & Wong, 1999) and that it demonstrates a mediating role between neurocognition and everyday functioning (Casaletto, Fazeli, Woods, & Moore, 2015), future studies are still warranted to explore other approaches that may help target these abilities (e.g., other executive strategies).

Moving forward, although it was developed in the context of everyday multitasking abilities here, the GMT may be utilized to support other goals, and should be examined for generalizability across functional domains (e.g., shopping, appointment and medication adherence). Additionally, the observed improvements in metacognitive planning are a start toward enhancing self-awareness accuracy in this population; however, given the lack of effect of GMT on the other domains of metacognition (e.g., self-knowledge, self-monitoring), more comprehensive tools may be needed. In particular, promotion of more narrative, extended self-reflective processing, rather than reliance on automatic, environmentally-driven pre-reflective processes, may be especially helpful in enhancing error detection abilities (Lou, 2015). Targeting these latter online error regulation abilities may be especially warranted, given that such abilities are a critical step in the complex decision-making process that must occur during successful task completion (e.g., slow down after detecting an error; (Laming, 1979). Additionally, recent data suggest that the neural networks involved in error detection abilities are associated with networks of overall task awareness and task confidence (Boldt & Yeung, 2015), which may therefore further promote metacognitive processes.

Of note, our study was a brief, experimental design that would need to be replicated in future intervention studies and, ultimately, clinical trials before delineating the important active ingredients and best practices for use in clinics. Again, our primary aim was to develop preliminary evidence for a tool that may provide direction for more extensive neurorehabilitation approaches in the future. Ours are some of the first findings supporting a compensatory neurorehabilitation tool in HIV infection or substance use and show promise as both proof-of-principle for cognitive rehabilitation in this

population (i.e., malleability of behavior) and specifically, Goal Management Training as an efficacious technique.

APPENDIX

Goal Management Training (GMT) is one of the most empirically supported and well-validated approaches for executive dysfunction (e.g., (Levine et al., 2000) which globally aims to improve patients' organization and goal-directed behaviors. GMT is conceptually based on Duncan's (1986) theory of behavioral disorganization, which posits that "goal neglect," or difficulty maintaining intentions, depends on higher-level control over basic cognitive abilities (i.e., executive functions). Such everyday disorganization difficulties are commonly observed following frontal lobe damage in which patients may omit relevant on-task behaviors (e.g., leaving one's lunch on the counter after preparing it instead of taking it to work – omitted taking lunch step) and experience intrusions of irrelevant behaviors (e.g., when preparing the lunch, get distracted by making a grocery list of household items for the week and lunch does not get made) during goal-oriented tasks (Duncan, 1986). Robertson and colleagues (1996) subsequently developed a manualized and interactive rehabilitation protocol to address these difficulties.

GMT employs the concept of goal lists to direct behavior as constructed in response to environmental or internal demands. The authors describe GMT as an iterative process in which a patient must continually monitor the current situation in order to determine if the current state of affairs matches the goal state, and if not, consultation of the goal-oriented actions must occur (I. H. Robertson, 1996). As such, GMT is divided into five stages representing these important aspects of goal-directed behavior (see Figure 11 and Table 2). Stage 1 is one of the most important steps in which participants are trained to orient to the current situation and direct attention toward the relevant goal. Stage 2 represents the period in which participants must select the overarching goal to be completed, and in Stage 3, participants subdivide the overarching goal into smaller

steps. Participants must then encode and consolidate the goal and steps, and finally, in Stage 5, participants are trained to monitor their behaviors (i.e., compare current actions with goal state). In this manner, GMT promotes continual mindfulness and awareness of current behaviors in order to reach a goal. GMT has been validated in several randomized controlled designs primarily in patients with frontal lobe damage. Improvements have been demonstrated on sustained attention (Levine et al., 2011; Schweizer et al., 2008), planning and problem solving (i.e., Tower Test; Jackson et al., 2012; Levine et al., 2011), and both laboratory-based and manifest everyday functioning tasks (Jackson et al., 2012; Levine et al., 2000; Levine et al., 2007; Schweizer et al., 2008). Importantly, the GMT has also been employed to successfully improve executive dysfunction among substance users (see Cognitive Rehabilitation in HIV/SUD section in Introduction; Alfonso et al., 2011). These studies illustrate the potential utility of GMT for individuals with executive dysfunction, both for remediation of neurocognitive functioning and especially IADL independence, following brain injury.

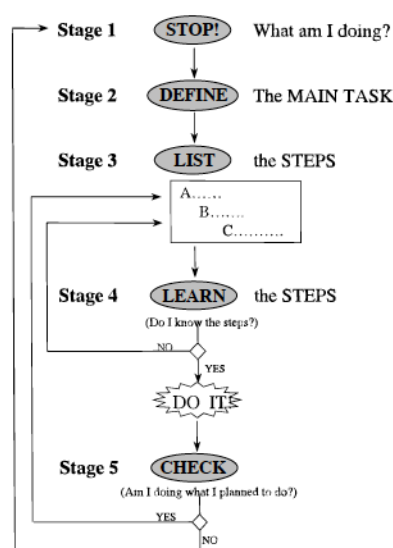


Figure 11. Flowchart illustrating the five stages of Goal Management Training as reproduced from Levine et al. (2000).

In the current study, we plan to apply a modified version of GMT as a strategy for executive dysfunction during online Multitasking Test performance. Specifically, GMT will be slightly abbreviated and taught in a one-session format as directly applied to the Multitasking Test performance (see Table 2). For example, although the main goal and subgoals of the Multitasking Test are predetermined for participants (i.e., rules of the task, steps to be completed), it will be important for them to encode and retain these steps, and particularly, to apply the monitoring strategies as outlined in GMT during task completion (i.e., orientation to task at hand and checking of tasks completed). By applying techniques to improve both metacognitive knowledge (i.e., education participants regarding their executive dysfunction) and online monitoring (i.e., application of GMT strategy during task performance), our training represents a holistic approach to metacognitive remediation that may be applied to everyday functioning abilities.

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