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The neuroscience of cognitive enhancement:

Enhanced attention, working memory and visual information processing speed using 3D-MOT

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Résumé

Des interventions ciblant l'amélioration cognitive sont de plus en plus à l'intérêt dans nombreux domaines, y compris la neuropsychologie. Bien qu'il existe de nombreuses méthodes pour maximiser le potentiel cognitif de quelqu'un, ils sont rarement appuyé par la recherche scientifique. D'abord, ce mémoire examine brièvement l'état des interventions d'amélioration cognitives. Il décrit premièrement les faiblesses observées dans ces pratiques et par conséquent il établit un modèle standard contre lequel on pourrait et devrait évaluer les diverses techniques ciblant l'amélioration cognitive. Une étude de recherche est ensuite présenté qui considère un nouvel outil de l'amélioration cognitive, une tâche d'entrainement perceptivo-cognitive : *3-dimensional multiple object tracking* (3D-MOT). Il examine les preuves actuelles pour le 3D-MOT auprès du modèle standard proposé. Les résultats de ce projet démontrent de l'augmentation dans les capacités d'attention, de mémoire de travail visuel et de vitesse de traitement d'information. Cette étude représente la première étape dans la démarche vers l'établissement du 3D-MOT comme un outil d'amélioration cognitive.

Mots clés : Amélioration cognitive, 3D-MOT, entrainement perceptivo-cognitive, entrainements cérébrales

Abstract

Cognitive enhancement is a domain of burgeoning interest in many domains including neuropsychology. While there are different methods that exist in order to achieve cognitive enhancement, there are few that are supported by research. The current work examines the state of cognitive enhancement interventions. It first outlines the weaknesses observed in these practices and then proposes a standard template for assessing cognitive enhancement tools. A research study is then presented that examines a novel cognitive enhancement tool, 3-dimensional multiple object tracking (3D-MOT), and weighs the current evidence for 3D-MOT against the proposed standard template. The results of the current work demonstrate that 3D-MOT is effective in enhancing attention, working memory and visual information processing speed, and represent a first step toward establishing 3D-MOT as a cognitive enhancement tool.

Key Words: Cognitive Enhancement, 3D-MOT, perceptual-cognitive training, brain training

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2-dimensional	2D
3-dimensional	3D
Analysis of Variance	ANOVA
Attention Deficit/Hyperactivity Disorder	AD/HD
Brodmann Area	BA
Cave Automatic Virtual Environment	C.A.V.E.
Chief Executive Officer	CEO
Comité d'éthique de la recherché en santé	CERES
Control group	CON
d2 test of attention	d2
Delis-Kaplan Executive Function Systems Test	D-KEFS
Electroencephalography	EEG
Functional Magnetic Resonance Imaging	fMRI
Geometric	GEO
Hertz	Hz
Integrated Visual and Auditory Continuous Performance Test	IVA+Plus®
Magnetic Resonance Imaging	MRI
Multiple Object Tracking	MOT
National Sciences and Engineering Research Council of Canada	NSERC
Training Group	NT
Quantitative Electroencephalography	qEEG
Rapid Eye Movement	REM
United States of America	U.S.
United States Dollars	USD
Weschler Adult Intelligence Scale Third Edition	WAIS-III
Weschler Adult Intelligence Scale Fourth Edition	WAIS-IV

To anyone who has, and everyone who will,

set out on an epic adventure within their own mind.

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Introduction

The greatest minds of our time are just that: minds. Religious figures, philosophers, writers, neuroscientists, and almost anyone lying in bed unable to sleep at night have contemplated the elusive and yet undeniable existence of consciousness. The mind is all we really know of existence; some of best known works involve the mind and its importance in the experience of life, including Rene Descartes's "cogito ergo sum" or translated: *"I think, therefore I am"*.[1] Thoughts then, according to him, are the essence of existence. It is a sentiment echoed by centuries of philosophical exploration[2], and even nowadays in modern neuroscience.[3] And yet, by today's more rigorous scientific standards, Descartes is but one among many who fail to adequately define what *think* actually means. Thoughts have origin in the mind, but what are they?

The notion of thought seems so ingrained in our experience of existence that understanding or defining it is at once almost redundant, and yet a hugely daunting task. Suffice it to say that even for the greatest minds of our time, to think about thinking seems to open up a Pandora's box. While some argue that a comprehensive definition of the mind will forever elude us[4], some would argue that the mind is nothing but a dynamic flow of perception and memory.[5] To say *nothing but* those things is a little gratuitous. It is a magnificent thing to be able to experience sensory information and remember experiences as if we were actually living them in the present.

This holy grail of philosophical thought is now being sought out by modern neuroscience. Researchers are attempting to define the mind, develop a comprehensive theory of consciousness, find where in the brain the mind and thoughts are rooted, and discover the mind's neuroelectric and neurochemical signature. It is too daunting a task for a master's memoir to achieve this, but this paper will nonetheless discuss another pursuit of burgeoning interest: maximizing the potential of the mind, or said another way: *enhancing cognition*.

Modern neuroscience has finally shed the antiquated, *static brain* dogma of the past. We now readily acknowledge that the brain is *plastic,* and can and does reorganize itself on a daily basis based on experience.[6] This change in paradigm has led to many explorations into the arena of enhancing and maximizing the efficiency of the brain and thus unlocking the potential of the mind. In turn, these explorations have led to the development of a number of *brain training* programs, exercises geared toward improving a person's cognitive abilities. As exciting as this pursuit is, the majority lack sufficient research to support their use[7], but that has not impacted their profitability in the marketplace; in 2012 revenues in this market surpassed the 1 billion U.S. dollar mark and forecasts predict that in 2020 this figure will grow to 6.2 billion USD.[8]

While there is a massive influx of money primarily from the private sector, adequate research to back up the purported claims of these training programs is grossly lacking[7,9,10]. The following work has two aims: first, to prescribe a standard by which cognitive enhancers can be assessed, and second, to examine one of these brain training programs in particular, 3-dimensional multiple object tracking (3D-MOT), against the proposed standard.

Following an extended introduction and methods sections, an upcoming research article to be published in Clinical EEG and Neuroscience is presented. Some of the information contained in the article may be slightly redundant to this memoir; the memoir contains a more thorough examination of the efforts of the author. All attempts were made to repeat as little information as possible, while still allowing for an adequate and logical flow. Following the presentation of the article, an extended discussion examines the work completed, its potential influence on the current state of affairs in the domain of cognitive enhancement, and avenues for further research and exploration.

Cognitive Enhancers

Before discussing 3D-MOT as a cognitive enhancer, it is important to examine the types of cognitive enhancers that currently exist. Many different types of cognitive enhancers have been proposed and a brief overview is provided below.

First, pencil and paper tasks (e.g., crossword puzzles, Sudoku) are one of the simplest types of cognitive enhancers in that they require few resources in order to train.[7] Some studies have found that crosswords may slow the cognitive decline observed in those who later develop dementia[11], but other studies have found no effect.[12] Sudoku puzzles are another example of this, with research having established a link between performance on Sudoku puzzles with working memory[13] and others finding positive results of training related to cognitive decline[14]. Still, arguments exist as to whether this is due to actual cognitive enhancement, or if it is more related to cognitive maintenance – following the principal of *use it or lose it* – meaning that rather than actually enhancing cognition, those performing these tasks are simply maintaining their current abilities.[15] Evidence that these activities actually enhance a person's cognitive abilities rather than simply provide maintenance is still lacking.[13, 15]

Computer-based training programs (e.g., Lumosity[16], Cogmed QM[17], Captain's Log[18]) range from the digital equivalent of pencil-and-paper type tasks, to more complex tasks requiring attention, memory and problem-solving skills.[7] Studies in normative populations have reported positive results using these types of programs, noting enhancements in memory[19,20,21,22], attention[21], and working memory[23], while others demonstrated no evidence of cognitive enhancement[24], or significant degradation of gains over relatively short periods of time (one month)[22].

Video games have also made the foray into the cognitive enhancement domain, older games like Tetris®[25] and newer ones like Brain Age[26] are both examples of games touted to enhance cognition. Some studies report findings of increased speed[27],[28], working memory[29] and executive function[28,30,31]. Here as well conflicting reports exist, as other studies report no significant differences following training[32,33].

For both computer-based interventions and video games, a large number of criticisms are raised even for the studies that demonstrate improvement. These include small sample sizes, lack of randomization, inadequate control groups, conflicts of interest (e.g., financial incentives due to commercial interests), unclear and variable transfer effects[7], limited amount of practise time, inadequate cognitive batteries utilised to measure transfer[34] and the absence of longitudinal follow-up.[35]

Neurofeedback training involves the use of a brain-computer interface and relies on conditioning to normalize or enhance a person's brain activity.[36] Traditionally, this is done using an electroencephalogram (EEG) but can also be done using various brain imaging techniques such as functional magnetic resonance imaging (fMRI).[37] Numerous studies have demonstrated the beneficial effects for attention-deficit population (see Arns et al.[38] for a review), autistic spectrum disorders (see Coben et al.[39] for a review) as well as many others including learning disabilities[40], epilepsy[41], anxiety and depression[42], traumatic brain injuries[43]. With regard to healthy populations, research has demonstrated improvement in general cognitive and memory enhancement[44,45], sporting performance[46], musical[47] and acting performance.[48] Critics of neurofeedback cite methodological issues including difficulties in active control groups, difficulty maintaining the researcher's blindness as to subject condition[38] and a general failure to elicit unambiguous changes in baseline brain activity[37] and lack of long-term follow-up.[38]

Pharmacological interventions are the first-line treatment of choice for cognitive disorders.[49] Healthy populations may also stand to benefit from pharmacological and nutritional supplements, and this is a domain of burgeoning interest.[49] To that end, the Academy of Medical Sciences have published a report[49] on the research evaluating the use of pharmaceutical and nutritional supplements to enhance cognition. The report offers little to support the use of all evaluated substances in cognitively healthy populations (they acknowledge the benefit of use in clinical populations) and is a little dated (2008), however it stresses the need for more research and highlights the political and ethical issues surrounding the use of these substances.[49] Some reviews of more recent research demonstrate promising trends toward finding drugs capable of enhancing cognition[50], however all are unanimous in echoing the views of the Academy of Medical Sciences report: more research is needed.[50,51,52]

Another way of enhancing cognition is though exercise. A rather simple intervention, aerobic exercise has been shown to have a beneficial impact on cognitive functions (e.g. memory[53]), has been shown to counteract the mental decline associated with age[54] and facilitate recovery following a brain injury.[55] Exercise is also touted to have anti-depressant, anti-anxiety and other beneficial effects on mood.[56] With regard to exercise, there are few who question the benefits of exercise and physical health on cognition although researchers stress caution when interpreting the data.[53,55,56]

3-Dimensional Multiple Object Tracking: 3D-MOT

Multiple object tracking (MOT) was initially developed as a research tool in order to test a theory of visual indexing, and can be dated back to Plyshyn and Storm.[57] The theory, referred to as the FINST Indexing Theory, hypothesized that there was a cognitive mechanism responsible for indexing visual objects or features for subsequent cognitive processes.[57] The MOT tool was initially developed to examine theories of visual indexing: whether there was one single locus of attention that acts as a beam that shifts from location to location, or whether attention could be divided across multiple targets.[57] Generally speaking, an MOT paradigm involves the identification and tracking of a target stimulus, amidst identical distractors as they move about through a delimited space over a fixed period of time.[57] In the first part of the task, the objects (i.e., targets and distractors) appear for a pre-defined duration. Next, the target stimuli are identified; this can be done through movement, color change, flashing, or other salient variations to break the homogeneity of the target from the distractor stimuli. After homogeneity is restored, the objects move and tracking begins. After a period of time, the movement ceases; the participant must identify the target stimuli.

Using the MOT paradigm, researchers have discovered a number of properties of tracking and attention. For instance, targets can be tracked even if occlusion occurs[58] and in certain cases even when all objects disappear from view (e.g., during a blink).[59,60] Tracking also appears to be an on-line process, meaning that new information it is refreshed often and old information essentially deleted. This is exemplified by data demonstrating that when objects are correctly tracked their initial positions or identifying labels are poorly recalled when compared to typical tracking performance.[61] Tracking is also possible when targets change direction or location when occluded; although as the degree of change increases tracking accuracy decreases.[62] The inhibition of non-targets appears to be distinct from the allocation of attention to targets and inhibition seems numerically less-limited resource than attention however from a functional standpoint it is more limited.[63] As speed decreases MOT capacity increases[64], however research has also demonstrated that speed may not be a limiting factor in MOT performance.[65] Experience playing a videogame also increases MOT performance.[66] Tracking can be carried out independently in each cortical hemisphere[67] and object tracking can occur into the visual periphery.[68]

Subsequent manipulations of the initial MOT paradigm where then implemented by researchers, including varying the number, shape, colour and size of targets and distractors can vary[64], as can their speed[65], location[67], direction[62] and duration of movement.[69] Researchers has established that for the vast majority of MOT paradigms four or five targets are the most that the average person can track[57], however other research has discovered contexts in which tracking more targets is possible.[64] Further examinations of MOT in research settings led to the discovery that over time, individuals improve in task performance for both repeated trajectories[70] as well as novel ones.[71] In aging populations, improvements in 3D-MOT have demonstrated transfer to perception of biological motion.[72] Athlete populations are also said to benefit from training, as sports involve complex scene dynamics and heavily tax perceptual abilities, including biological motion perception.[73] In a limited sense, with regard to aging populations and athletes the idea that MOT could serve as a cognitive enhancer was thus born. Since MOT is a task that is founded on a number of cognitive functions including attention, working memory and visual information processing[57,58], research examining the possible transfer to these domains is the next logical step.

Another type of cognitive enhancement intervention, video games, has demonstrated a direct link to MOT ability. Research has shown that those who regularly play video games are able to track approximately two more items in an MOT task than non-gamers[74], those trained on certain types of video games (involving abilities similar to MOT) demonstrated improved abilities in an MOT task[75], and expert gamers demonstrate faster information processing speed abilities in an MOT paradigm than non-gamers.[76] Interestingly, these studies used MOT to demonstrate transfer following video-game training but did not address the possibility that MOT itself could be a cognitive enhancer, although one research team noted that the MOT task resembled one of the training paradigms which led to cognitive enhancement[75], and another study noted that with repeated MOT testing abilities in the task also improved, however this did not appear to be the factor underlying the cognitive enhancement in that study.[76]

What is it then, about 3D-MOT that makes it a candidate as a cognitive enhancer? The characteristics of the MOT program examined herein are distinct and warrant examination. There are four specific and defining characteristics that distinguish the current paradigm from the other cognitive enhancers, and even other forms of MOT.

The 3D-MOT paradigm under investigation differs in four ways from the above-mentioned cognitive enhancers, which will be discussed below. These characteristics of 3D-MOT contribute to two important factors that cognitive enhancers must address: *learning*[77] and *ecological validity*.[78] Learning is essential to any cognitive enhancer; it is essentially the effect underlying improvement that one hopes to achieve using a given intervention.[77] Ecological validity is what gives a cognitive training tool the ability to relate to and have an impact on everyday life.[78]

First, in order to put the following explanation in context, consider that one 3D-MOT trial consists of five phases: presentation, identification, movement, response and feedback. First, the targets and distractors are presented in the 3D environment. Next, the targets are identified. Once homogeneity is restored, the targets begin to move about along a linear path in 3D-space. Following movement, trainees must attempt to identify the targets. Finally, feedback is given as the targets are revealed. In the research article found below, Table 3 describes these phases while Figure 1 offers a visual representation of these phases. All full examination of the 3D-MOT paradigm can be found in the Method section below.

The first element is that the task is first and foremost a *multiple object tracking* (MOT) task. In this version of the task, there are four targets and four distractors. With regard to ecological validity, having multiple objects to track is important because there are often multiple points of focus in everyday situations.[79] Multiple object tracking is also dynamic in nature, and the utilisation of a dynamic environment versus a static environment also contributes to ecological validity.[80]

Second, the task utilizes a *large visual field*. While the majority of a person's visual acuity is relatively quite small – a circle called the *fovea* – pertinent information often occurs beyond this tiny range. Both the fovea and the larger field of visual attention can vary widely based on the task[81], what is important with regard to 3D-MOT is that it utilizes a much larger visual field than other cognitive enhancers (e.g., pencil-and-paper type tasks computer-based interventions, video games, and neurofeedback). Since we must often attend to information beyond the fovea[79], utilizing a large visual field ensures ecological validity in the task.

Third, this version of the task is in a *stereoscopic 3-dimensional environment*, hence *3D*-MOT. As in the case of MOT and large field of view, the use of 3D stereoscopy ensures ecological validity. A 3D environment is not subject to the same spatial limitations as a 2D one, for example it allows one to distinguish between collision and occlusion.[73] As a result, previous research has shown superior tracking in a 3D environment versus a 2D environment.[82] Since the locus of attention in the real world occurs over all three dimensional plains, in order to maximize the ecological validity and efficacy of the task it is essential that the training occur in all dimensions.

Fourth, the speed of movement is modulated based on performance following an *adaptive staircase*. In this paradigm, this is referred to as *speed thresholds*. If a given trial is correctly answered (all of the targets are correctly identified), the speed of the subsequent trial slightly increases. If a given trial is incorrectly answered, the speed of the subsequent trial slightly decreases. As will be discussed further below, this ensures that the trainee is always active at a level which is equal to, or slightly greater than, their current ability. Due to the design, the success rate for a series of trials is consequently around 50-60%; but the task is never too hard or too easy, it is in a range (or *zone*) virtually always at the highest achievable level or slightly above it. This proverbial sweet spot is often referred to in learning paradigms as the *zone of optimal development*, and it is said to lead to the greatest amount of learning.[83] The reason for this is because research has shown that more learning occurs when the level of difficulty is near and above to the learner's current level of ability rather than far.

This design inherently draws on multiple cognitive functions, which are discussed at length in the sections below, as well as in the research article. First and foremost, the task places demands on attentional processes.[57] In order to succeed at the task, one must be able to maintain attention on targets, while inhibiting the perception of the distractors. Second, the task draws on memory processes; the correct targets must be remembered in short-term visual memory.[84] A transformation of the items stored is also required as the targets move through space, and so visual working memory is also involved.[84] Since this occurs at a speed at or slightly above the current ability level of the trainee, information processing speed is heavily implicated.[85]

Dr. Jocelyn Faubert of the University of Montreal developed the version of the task under investigation; further methodological specifics for the task can be found in Faubert and Sidebottom[73] who examine its application in an athletic context.

The research article within this memoir examines the application of 3D-MOT to a healthy population in order to examine its potential as a cognitive enhancer, including assessment using neuropsychological tests and a functional brain scan. This is the first in-depth study of this kind involving 3D-MOT. The primary research goal was to determine whether or not 3D-MOT is an appropriate cognitive enhancement tool for a normative population. The ultimate goal is to determine the appropriateness of applying 3D-MOT to various healthy and clinical populations at large, and this effort represents a first step toward that goal.

A secondary goal is an attempt to set a precedent for research into cognitive enhancement. Current research into cognitive enhancement tools is sorely lacking: studies lack of consistency in measurements, methodologies and standards.[7] This study thus seeks to establish a standard by which all cognitive enhancers can and should be evaluated. Although this is a secondary goal, because the development of the study follows these guidelines, it is presented first.

Designing a standard for cognitive enhancement

In order to address the creation of a flawless methodology, one must examine the weaknesses of studies that have been performed. The research article below outlines these issues as follows: "Generally speaking, the complaints against these interventions are: transfer effects are not consistently observed, the effects observed do not persist in time, the methods are invasive and include risk of significant side-effects, a significant monetary and time investment is required, and there are the ethical issues associated with the use of these interventions." [86]

The article then proposes a theoretical framework for a "standard" cognitive enhancers: "With these limitations in mind, the standard in cognitive enhancement would thus be an intervention that shows (1) robust effects with transfer, (2) no side effects or risk of toxicity, (3) minimal time and monetary investment, (4) lasting effects, (5) no ethical issues and (6) can be used in combination with others. This intervention should (7) apply to virtually any population." [86]

It is impossible to achieve the standard defined above with one simple research project, however this memoir will nonetheless examine the research presented herein against this standard in order to identify avenues for future research. Future studies can then address the issues not sufficiently addressed here, and other independent groups should confirm research findings.

1. Robust transfer effects

First and foremost, in order for a cognitive enhancer to be valuable, the gains derived from the task must generalize to different contexts. This is called a *transfer* *effect*.[9] If training at a task only improved one's ability in a very specific and closed context (e.g., performance on the test itself), then the value of the intervention is quite limited. This is called *near transfer*.[7] An example of this is when a person is repeatedly trained on a task very similar to the test that is being used to assess the ability supposedly being trained; when this occurs the person may score better on the test but it is only in the closed context of the task and test, it does not apply to other contexts.[7] By contrast, *far transfer* means the transfer effect is broad and applies across various contexts.[7] For example, training attention in a specific context would also lead to positive changes in attention across a wide variety of contexts.[7] To that end, the more far transfer occurs, the more valuable the intervention.[9]

There are a number of ways to examine far transfer effects. The first is using standardized tests, such as neuropsychological evaluations. These tests have been designed and validated to measure global cognitive functions; if a test shows a strong score the ability in question is said to be strong across virtually all contexts.[87] For example, continuous performance test are often used to measure attention; if a person scores below a normal level, it is understood that their attentional abilities across all similar contexts (e.g., school) is subpar.[88] A second manner of acquiring information on far transfer is to gather information from the person's daily life. This can include, but is not limited to administering questionnaires[87], and analyzing work[89], or academic performance.[90] Questionnaires are interesting because they can be administered to the trainee, but also to friends, family and those in a supervisory role. The weakness of questionnaires is that they are subjective, and are prone to bias.[87] Analyzing data from work or academic performance is also valuable from a research standpoint as it can be used as a measure far transfer to real-world scenarios; however it is extremely difficult to account for all the possible confounding variables.[89,90]

Finally, functional and structural neuroimaging may also be used to measure the degree of the observed effects and of transfer. An already large and still-growing body of research demonstrates the link between brain function and task performance, especially in the case of attention.[91] In the case of attention, there are various networks said to be at play, and utilizing non-invasive imaging techniques it is possible to assess the neural correlates of attention and changes in attention.[38,91] These measurements cannot be due to compliance effects; it is difficult to near impossible to falsify brain function.[91]

It is one thing to observe an effect, and another to evaluate the size of the observed effect. Aiming for a *robust* effects means that the gains observed are relatively large and consistent rather than small and inconsistent. This means that a large percentage of individuals should experience relatively large benefits, versus a small percentage of individuals experiencing relatively limited benefit. A cognitive enhancement tool should aim for robust effects, represented by a large magnitude. The magnitude of effects effects can be statistically measured using effect size.[92]

2. No Risk of Toxicity or Side Effects

An ideal cognitive enhancement intervention should not present any health risk. Risks of toxicity or overdose are significant factors and, because of their nature, plague almost exclusively nutritional and pharmacological interventions.[93]

In terms of side effects, while many side effects are tolerable (e.g., slight fatigue, mild transient headache), they nonetheless cast a cloud over the intervention, which may lead individuals to avoid the intervention, or not complete the full intervention protocol. As soon as side effects are possible, a cost-benefit analysis becomes a very pertinent part of the valuation of a cognitive enhancer. In other words, an individual would be faced with a question of: is the benefit derived from this intervention worth the cost? A standard cognitive enhancer should thus have a cost of zero or near zero in this regard. In the case that side effects are present, they should ideally be weak rather and strong, transient and not persistent, and should occur in a small number of individuals instead of universally.

The assessment of a cognitive enhancement tool should include a thorough analysis of the side effects, and risks associated with the intervention. This should be extended to clinical as well as normative populations. In the case that side effects or other health risks are observed, a cost-benefit analysis should be performed.

3. Minimal time and monetary investment

The notion of a cost-benefit analysis is once again appropriate when examining the investment required enhancing one's cognitive abilities. An ideal intervention should take little time to perform, and performance gains should be seen as early as possible after the intervention is initiated. A tool that requires a person to dedicate a significant amount of time is of limited applicability, as long-term adherence becomes an issue. When evaluating and comparing multiple types of cognitive intervention, a cost-benefit analysis involving the amount of temporal and financial investment required also becomes appropriate. The lower the cost and the more accessible the intervention is, the better.[94]

4. Lasting effects

The longevity of observed effects is an issue not often addressed by studies examining cognitive enhancement.[7] Many of the interventions currently used either do not measure longevity or demonstrate no lasting effects.[12,22,24,32,33,35,38] Planned follow-up studies should examine the extent to which effects endure over time. In the case that degradation or extinction does occur, studies should examine and report on how much maintenance is required.

5. No ethical issues

The ethical issues surrounding cognitive enhancement are mostly cultural and societal in nature.[95] These cultural and social ethic issues are related to pharmacological interventions and concern three primary domains: medical safety, coercion and fairness (for a comprehensive review, see Schelle and colleagues[96]).

In terms of medical safety, this is classically viewed as a cost-benefit analysis, or as Schelle and colleagues discuss, a focus on the "potential trade-offs between benefits and risks".[96] This is a very complex issue because this calculation must be done on a case-by-base basis, and it is possible that not all risks are known.[96]

Coercion is related to autonomy and freedom, and is another very complex issue. Coercion can be direct, (e.g., an employer or government order), or indirect (e.g., in a competitive environment, if all of one's competitors are *using* there is a pressure on the individual to use as well).[96] That said, there are those who argue that the use of a cognitive enhancer allowing a person to have heightened cognitive abilities would in turn give them a heightened capacity for autonomy.[97]

In terms of fairness, Schelle and colleagues discuss equality of opportunity, honesty and authenticity.[96] Equality of opportunity is a two-fold and fairly self-explanatory concept; first: a cognitive enhancer should be available to all and not only to a select few, and second: a cognitive enhancer could create significant societal inequality.[96] Honesty, in turn, is the referred to as competitive fairness[98] and cheating.[99] Much of this argument is based on the goal behind use; if the reason for using a cognitive enhancer is to acquire more knowledge it is seen as legitimate, however if the purpose is to perform better at a competition (e.g., university admission exam) this is seen as cheating.[99] Finally, authenticity considers the effort one puts into a task and the value or meaningfulness of this effort.[96] There appears to be a society-judged difference between the willingness to use a cognitive enhancer for functions related to performance and outcome (e.g., memory, attention) when compared to emotional and social functions (e.g., mood, social comfort).[100]

When designing and assessing a cognitive enhancement intervention, these ethical factors should be included. As society advances and we continue to develop our technological and biological abilities with regard to cognitive enhancement, it must be accompanied by research into moral and ethical enhancement.[94]

6. Can be used in combination with others

While the pinnacle of cognitive enhancement would be to find a single technique that universally and globally enhances all cognitive functions, it is unlikely that it exists. Cognitive functions are vast and the types of interventions currently in practice have a specific and narrow scope.[7] At least with regard to the current state of affairs, there is no one universal intervention; the specific nature of these interventions essentially predicates that fact. Above, we refer to the idea that a cognitive enhancer must *isolate* a specific or limited set of cognitive functions in order to then *overload* that or those functions (to ask slightly more of them than they are currently capable of), which is what brings about change.[83] Multiple cognitive enhancement tools would thus need to be used to cover the spectrum of cognitive functions. An ideal cognitive enhancer, then, should not be mutually exclusive, as a given intervention that can only be used in isolation of others is of limited value. Thus, an ideal cognitive enhancer should be able to be used in combination with other types of intervention in order to maximize effects.

Medication and nutritional supplements are those most susceptible to mutual exclusivity because interactions can often occur on the physiological or neurological level.[101] Not to be neglected are the fatigue effects of other types of interventions, since a persons cognitive load is a limited resource (e.g., working memory) repeatedly taxing a resource would not lend itself to increased learning.[102] If a given intervention is demanding in the temporal and frequency domains, then the effects of cumulative fatigue may also lead to limits in combining types of interventions.[103,104]

7. Can be applied to any population

The more widely applicable a given cognitive enhancer is, the more valuable it is because more people are able to benefit from it. A cognitive enhancer designed to enhance attention, for example, should be applicable to a variety of populations. First, populations who exhibit deficits in attention (e.g., attention deficit/hyperactivity disorder, autistic spectrum disorders, learning disabilities) should all be able to see clinically significant benefits with a given intervention. Additionally, individuals who do not display any deficit in attentional capacities should observe some enhancement of their cognitive abilities. It is unlikely for every individual to develop supra-normal attention; however relatively speaking gains in these capacities should still be notable and have real-world benefits. If there are strict limiting factors to a given intervention, it limits the applicability of this intervention. In order to ensure a wide-applicability of an intervention, it should ideally rely on low-level abilities and not require complex skills (e.g., reading, problem-solving).[7]

Methodological logic dictates that research begins in informed, consenting, healthy, normative populations. Once the effects (e.g., side-effects, benefits or lack thereof) are substantiated and more about limitations, and other potential causes for concern are known, exploration into the clinical domain should begin. It is important to note, however, that normative populations may not demonstrate a significant benefit from a cognitive enhancer while a clinical population could and the opposite is also true. To that end insignificant results regarding the benefit to a healthy population should not spell disaster for all potential applications. In order to assess potential applications, the age of participants, gender, degree of abilities and deficits, and other population-specific demographic measures should all be included in a comprehensive analysis.

Study Design & Hypotheses

With all of these factors of the standard in mind, design began for a preliminary study into 3D-MOT as cognitive enhancer. The general objective of this limited study was to examine which and to what extent different cognitive functions play a role and benefit from training in healthy individuals and in an immediate context.

While an attempt was made to adhere as much as possible to the standard, in the context of a Master's thesis with limited time and funding available, it was not possible to pursue and resolve every issue that would have allowed for the standard to be attained in this research project. In fact, inherent to the standard is that it is virtually impossible to achieve the standard in a sole project, since it implies for example: exploration into effects and side effects in a normative population before the application to a clinical population, testing in isolation from and then conjunctively with other cognitive enhancers, follow-up testing over an extended period of time and replication. The specific issues addressed below are those that were possible to address in a limited study.

1. Robust transfer effects

The current study set about examining the hypothesis that 3D-MOT is a cognitive enhancer. The task appears to draw on multiple cognitive abilities – namely attention, memory and information processing speed – and we hypothesize that training at the task should enhance these abilities.

Learning

As discussed above, in tradition MOT paradigms learning is observed for both repeated[70] and variable trajectories.[71] The first hypothesis relates to the learning within the task itself, as this is a precursor to transfer. If there were no learning within the task, then it would be highly unlikely that a transfer effect would be observed. In order to show improvement in cognitive abilities, there should be an improvement at the task itself.

Hypothesis 1: Learning

Individuals trained on 3D-MOT will see an increase in their speed thresholds. That is, they will be capable of accurately tracking the targets at higher speeds than controls.

Attention

Attention appears to be at the core of the 3D-MOT task.[57] When discussing attention, it is important to distinguish the different types of attention. While various models of attention exist, for the purpose of the research at hand we are primarily concerned with three types of attention: selective attention, sustained attention, and inhibition of attention.

Selective attention is defined as the ability to *focus* or direct one's conscious perception on a given *stimuli* (i.e., a piece or pieces of information).[105] With regard to the 3D-MOT task, this translates to allocating attention to (focusing on), or *selectively attending* to, the target spheres.

Once a target is selected by attention, then an individual can maintain selective attention over a given period of time, which is termed *sustained attention*.[105] Early studies into vigilance and sustained attention demonstrated that on a simple, non-stimulating task performance drops off as a function of the length of time a person has been doing the task, and that after a period of approximately 30 minutes a significant decline in performance can be observed.[106] Typically sustained attention tasks require that attention be maintained over a period of approximately 20 minutes.[105] In the 3D-MOT task, it is not initially obvious why sustained attention would be at work. Attention must only be consistently sustained during the tracking, which occurs during the movement phase lasting only 8 seconds. In spite of this, there are two reasons why sustained attention is at work. First, attention must be maintained over the full 8 seconds without the slightest lapse. During a trial there are a great number of interactions between targets and distractors. If the attentional focus drops off during the target tracking and a target is lost, then the target is quickly intermixed with other targets and distractors. If a target is lost, it is impossible to reacquire a lost target. Second, because of the large number of trials completed, the actual time required to complete a training session is approximately 30 minutes. As a result, attention was regularly taxed over a prolonged period.

Inhibition is connected to selective attention. While selective attention is the "positive" application of attention to a stimulus, inhibition is the "negative" application. This means that inhibition is the ability to block focus or directed conscious perception toward a given stimuli or stimulus.[105] With regard to the 3D-MOT task, it is essential to inhibit the distractor spheres so that they are not confounded with the target stimulus as previous research in traditional MOT suggests.[61,63]

There are two other components of the 3D-MOT task worthy of discussion in relation to attention. First, the task demands that individuals spread their attention across four target stimuli. In the literature, this is often referred to as *divided attention* or *multifocal attention*.[107] In this case, trainees must divide their attention on four focal points: each one of the targets.

The second component of the 3D-MOT task concerns the *dynamic* element to the task. As a general rule, each target is not allocated the same amount of attention. We will refer to the amount of attention given to each item as *attentional load*.[108] For example, a target that is alone in a corner of the cube requires less attention that a target in an opposite corner but surrounded by two or three distractors. A heavier attentional load is associated to this latter target in order to maintain focus on it and inhibit the distractors. Targets and distractors are in constant movement and interaction, thus constantly changing the attentional load associated with each target. If a trainee is unable shift the load to follow the flow of targets amidst the distractors, their performance in the MOT task will suffer. The ability to shift the attentional load fluidly will be referred to as *dynamic attention*, and it also lies at the core of 3D-MOT.[64] This ability is additionally taxed as movement speed increases since there are more interactions between targets and distractors as a result. It has a strong value in terms of everyday situations, as an individual's locus of attention is rarely static.[79]

Measuring attention

Computerized continuous performance tasks are commonly used to measure attentional capacities in both healthy and clinical populations.109 For the research study in question, the test selected was the Integrated Visual and Auditory Continuous Performance Test (IVA+Plus®).[110] The reason for this selection was because the IVA+Plus® tests attention across both visual and auditory modalities, and measuring attention in a modality other than the one being trained is another means by which one can assess transfer. Reliability studies have demonstrated that repeated testing, even over a short period of time (1 to 4 weeks) does not significantly affect the reliability of the results.[111] Other studies have found similar results, indicating that the IVA+Plus® achieved a sensitivity of 94% and a specificity of 91% in accurately identifying attentional capacities.[112] Although the 3D-MOT occurs solely in the visual domain, certain models of attention posit shared resources for these modalities[113], and researchers have shown that common neural substrates exists between aspects of visual and auditory attention.[114] The IVA+Plus® also subdivides attention into different measures, including two global categories of response control and attention, and further into subscales defined as: prudence, consistency, stamina, vigilance, focus and speed, allowing for additional decomposition of the various elements of attention. An additional strength of the IVA+Plus® is that it also allows for comparisons of both raw values and normalized scores based on age. A limitation of this test, like many other continuous performance tests, is that it can be prone to ceiling effects in high-performing populations.[88]

In order to attempt to overcome this limitation, another type of attention test, the d2 test of attention was added to the battery.[115] The d2 attention test is a pencil-and-paper type test that is much less subject to ceiling effects; however it is purely a visual assessment. Like the IVA+Plus®, the d2 also yields both raw and normalized scores.[115] While the IVA+Plus® has subscales that allow for the examination of the different subtypes of attention, the d2 gives a global attentional measure and number or error of omission (inattention) and commission (impulsivity).[115]

Finally, the color-word interference subtest of the Delis-Kaplan Executive Function System test (D-KEFS) includes a measure of inhibition and a measure of divided attention. It is largely because the D-KEFS provides these specific measures of attention that it was included in this study.[116] These tests are all described at length in the *Method* section.

Hypothesis 2: attention

<u>Individuals who train on 3D-MOT will show enhanced attentional abilities following training.</u>

As discussed above, since attention is the cognitive ability that lies at the forefront of the 3D-MOT task, it is expected that individuals trained on 3D-MOT will demonstrate significant improvements in attention. Since many of the neural substrates of attention share their resources across modalities and these resources are in play specifically in the case of 3D-MOT[113], both visual and auditory attention are expected to benefit from training in spite of the fact that the training paradigm occurs solely in the visual domain. Visual gains are nonetheless expected to be relatively larger.

Short-term memory

Short-term memory is defined as the ability to retain information over a short period of time.[105] Short-term memory is a requisite to even the lowest level of performance in 3D-MOT. Specifically, if a person cannot recall which items were targets and which were distractors, the task becomes extremely difficult. That said, because all participants in the current study were confirmed to have an intact capacity for short-term memory, and since short-term memory is not subject to *overload* in this paradigm 3D-MOT, short-term memory is not likely to show any improvement. This paradigm could be modified to include short-term memory, for instance by extending the amount of time in the pause interval (between the identification and movement phases) short-term memory would be taxed. However, this was not done here.

There is another type of memory involved in 3D-MOT. Since the targets move about in space there is a transformation of the information stored in short-term memory, and thus this task requires *working memory*.[117]

Working memory

Working memory is the ability to manipulate information stored in short-term memory.[105] It is considered a higher-order cognitive ability, in that it draws upon a lower-order ability, in this case: short-term memory.[118] As mentioned above, the hypothesis is that while short-term memory is required to retain the targets, working memory is more significantly implicated because of the dynamic nature of the retention involved. Prior research has shown that when working memory is simultaneously taxed using secondary tasks, individuals perform poorly on MOT tasks, thus confirming working memory's role in MOT.[119]

In this regard, it appears as though the working memory component is intertwined with the dynamic attention component. Researchers have observed interaction between visual attention and visual working memory in an MOT paradigm[120] and as such it is important to isolate the ability of each as much as possible. As research suggests, the two could possibly share a neural substrate.[121]

Measuring short-term and working memory

In order to examine the effects of 3D-MOT training on short-term and working memory, selected subtests of the Weschler Adult Intelligence Scale 3rd edition (WAIS-III) were used.[122] The WAIS-III was selected because of the large body of research that has been developed on its tests; it is reportedly "the most widely used measure of adult intelligence".[123] Notably, the number sequence task and letter number sequence task were used to measure short-term and working memory respectively, in the auditory domain. The spatial span task was used to measure working memory in the visual domain. These tasks are fully explained in the *Method* section.

Hypothesis 3: memory

Working memory will improve following training, while short term memory will remain relatively unchanged.

As discussed above, because the task demands a manipulation of the information stored in memory, this heavily implicates working memory. With regard to short-term memory, since a relatively small amount of visual information (i.e., four items) must be retained, and since participants have intact short-term memory, gains are not expected.

Information processing speed

Information processing speed is defined as the speed at which one is able to incorporate information into the stream of consciousness.[105] Information processing speed is thus inherent to the 3D-MOT task[57]; since the task utilizes an adaptive staircase; the speed at which the trainee can incorporate information is consistently pushed slightly beyond the current level of ability and is thus subject to overload, keeping the task in the zone of proximal development in order to lead to a significant amount of learning.[83]

Measuring information processing speed

There are many tests used to measure information processing speed, and some of the tests mentioned above also have speed components involved. Various subtests of the WAIS involve information-processing speed and were selected for that purpose. They include Symbol Search, Code, and Block Design.[122] The IVA+Plus® test also includes a speed subscale[111], and the global score of the d2 test of attention is greatly influenced by information processing speed.[115] The first two components of the D-KEFS color-word interference test, color naming and word reading, are essentially measures of information processing speed.[116] Each of these tests is described in the *Method* section.

Hypothesis 4: information processing speed

<u>The speed at which trainees will be able to process information will be greater following 3D-MOT training.</u>

Overloading the level of information processing speed is another built-in component to 3D-MOT. Using an adaptive staircase to modulate speed thresholds ensures that individuals are consistently forced to attempt trials slightly beyond their current level of ability and as discussed above this should lead to strong gains in information processing speed.

Structural and functional brain imaging

Instead of simply measuring changes in capacities and behaviour, researchers are now going to the source: the brain.[124] Brain imaging is another manner in which one can assess transfer. Many studies have established correlations between cognitive functions and structural and functional brain imaging.[124] Changes in the brain are colloquially referred to as *neuroplasticity*. All learning is a result of neuroplasticity; it is necessarily the result of changes in the brain.[6] Complex learning, for example mastering a new language, brings about significant change in the brain, however even learning a single word in a new language is predicated on a neuroplastic change.[125] The important factor then, is the degree of change. Current non-invasive neuroimaging techniques are not sensitive enough to detect the miniscule changes associated with learning a single new word, for example, but can identify significant – especially clinically significant – changes in brain structure and function.[6]

Since 3D-MOT purportedly enhances attention, working memory, and information processing speed, there should be quantifiable differences in brain function following training in the areas corresponding to these functions. Within the framework of MOT paradigms, previous research has linked attention to the posterior parietal areas (including the intraparietal sulcus and the superior parietal lobule)[126], visual memory to the posterior parietal and superior occipital cortex[127] and information processing speed the intraparietal sulcus as well as frontal cortical areas.[128]

Measuring structural and functional changes in the brain

The current research project used a functional brain measure referred to as *quantitative electroencephalography* or *qEEG*. QEEG is a relatively older measure of brain function and lacks the spatial sensitivity of newer methods (e.g., functional magnetic resonance imaging).[37] That said, electroencephalography (EEG) has high temporal precision, and adding a quantitative element (i.e., multiple electrodes at different measurement sites) has been shown to enhance the spatial resolution.[129] As such, qEEG can be used as a measure of cortical activity and this analysis can yield important results about attention.[91] Newer techniques such as sLORETA[130] and eLORETA[131] have provided theoretical solutions to the inverse problem of EEG (i.e., the inability to measure subcortical brain activity) and qEEG data will be subject to this type of analysis at a later date. Due to the relatively low cost in comparison to fMRI, ease of use, and formidable body of research, qEEG was the tool selected for the current research study. A resting state 32-channel qEEG was performed at the time of initial and final testing for both the active and control group. The training group also underwent a 2-channel EEG (to be analyzed for a later project) from choice sites during training in order to analyse attentional processes during 3D-MOT. More details regarding the qEEG and 2-channel EEG recordings can be found in the *Method* section below.

The EEG can be interpreted in a number of ways (e.g., quantitatively, evoked potentials, slow cortical potentials).[37] When considering qEEG, readings are often filtered and transformed using a fast Fourier transform into different *frequency bands* for analysis (e.g., delta, theta, alpha, beta, gamma).[37] Each of the frequency bands is said to define a different *cognitive state*.[37] Each frequency band and the corresponding cognitive state will be reviewed shortly, however it is important to note two things when discussing frequency bands and their definition.

First, there is no absolute cut-off when referring to frequency band definitions. Traditionally, Delta brainwaves are referred to as the frequencies that fall between 0.5Hz to 4Hz, while Theta brainwaves are from 4 to 8Hz. Having no absolute cut-off means that, for example at 4Hz, delta brainwaves do not simply stop being delta and at 4.1Hz become theta. The age of the individual, the origin of the oscillation, the morphology, the amplitude and the concurrent oscillations are all factors in determining one type of wave from another and studies typically set frequency band cut-offs based on the person or population under investigation.[37] The most important factor in defining a frequency band remains the type of cognitive activity it represents. The frequency bands and their standard definitions for adult populations as set below are generally observed in most people at most times and are utilized for this study, but exceptions are possible.[132]

The *amplitude* of a frequency band corresponds to the amount of that activity present at a given electrode site.[37] The second factor to retain with regard to EEG frequency band analysis is that there in each individual, a given *amplitude* of each type of brainwave that at each site at any given time is normal.[132] This means that even if delta activity is dominant (i.e., has the largest amplitude), there will simultaneously be beta present as well, although at a smaller amplitude. That said, there is no ideal amount of each to have per se; when a clinical analysis is conducted, a person's neuroelectric activity is compared to a *normative database*. This normative database is a group of normal, symptom free individuals whose brainwave activity has been collected and compiled into an averaged register. While there is no perfect brain with ideal levels of each type of activity, anything far enough outside of a certain range, typically defined as two standard deviations from the norm, is typically considered anomalous.[133] Following that notion, both significant *excesses* and *absences* of any type of brainwave can indicate dysfunction. The *absolute power* (i.e., amplitude of activity in microvolts) and the *relative power* (i.e., the percentage amount of each frequency as compared to all other frequencies) are both considered since their interactions with one another are important.[132]

The first frequency band to be discussed is *Delta*. Delta brainwaves (0.5-4Hz) are the slowest brainwaves observable using conventional EEG instrumentation. Seemingly originating in layer V of the cerebral cortex, they are seen primarily during REM sleep, but can also be seen in learning disabled children or people who have experienced significant physical brain trauma.[132] Eye blinks and movements can produce EEG activity mimicking delta waves.[132]

Theta brainwaves (4-8Hz) appear to originate primarily from the thalamus and limbic system.[132] In adults, a dominance of theta waves may indicate being drowsy or inattentive, and also normally occurs during the transition from waking to sleep (*hypnagogia*).[132] Other rises in theta may occur from visualization (especially at 7Hz), memory retrieval, or cognitive processing of information (especially 6 to 8Hz).[132]

Alpha brainwaves (8-13Hz) are sinusoidal waves that dominate an adult's EEG with eyes closed. Low alpha (8-10Hz) is typically associated with dissociative states, and cortical rest or *idling*.[132] High alpha (11-13Hz) is concomitant with a state of external *open awareness*, linked with fast and accurate responses.[132] The source of alpha rhythms is debated, although most believe they originate from the thalamus and surrounding thalamic structures.[132]

Beta brainwaves (13Hz and above) are produced in the brain stem and in the cortex.[132] Local beta typically indicates functioning in the underlying cortical area revealed by the EEG.[132] Beta is often broken down into different sub-bands by frequency, the speeds of which roughly correspond to the level of arousal of the cortex. This can range from idling (for instance, the sensory-motor rhythm, 12-15Hz, observed over the sensory motor-strip), to hyper-vigilance and anxious states (24-36Hz).[132]

Gamma brainwaves (various definitions above 30Hz) are relatively new to EEG analysis. However, more recent research evidence has shed light on the importance of these fast brainwaves. Recent reports on the gamma rhythm reveal that gamma indeed has impacts on a great diversity of cognitive processes including attention, short-term memory, motor control, and visual integration.[134] Further, the gamma band has been associated with neuroplasticity and learning.[135]

Hypothesis 5: changes in qEEG

Individuals trained on 3D-MOT will show differences in resting state qEEG activity corresponding to the changes in cognitive abilities following training.

This hypothesis is twofold: first, it states that changes should be observed, but it also necessarily demands that the changes seen are directly related to the cognitive changes observed; the changes in brain function should not be random or haphazard. Each expected change is outlined below.

Two aspects regarding qEEG analysis and interpretation were discussed above. A third factor worth mentioning is with regard to clinical populations: different disorders present different types of anomalies in the brain as measured by qEEG. Although there is no absolute rule regarding disorders and their presentation as observed from qEEG, there are patterns or *phenotypes* that emerge. One of the patterns of interest to the current study regards attention deficit/hyperactivity disorder (AD/HD). In AD/HD, the predominant qEEG phenotype shows excesses of theta brainwaves and relative deficits in beta brainwaves.[38] The majority of interventions targeting AD/HD symptoms, for example psychostimulant medications or neurofeedback, have the effect of *normalizing* this pattern, thus increasing beta brainwaves and decreasing theta brainwaves.[132, 136]

The first change that was expected is with regard to slower brainwaves: delta, theta and alpha. As mentioned, slower brainwaves are associated with less cognitive activity than relatively faster brainwaves. These slower brainwaves are often associated with inattention and, lack of focus[136], slower response times, and dissociative states.[132] 3D-MOT training purportedly enhances attention and focus, these brainwaves should be less present following training.

The second expected change is intimately tied with this first; increased beta brainwaves. Beta, contrary to the slower brainwaves, is fast and is associated with cognitive activity and cortical activation.[132] For the same reason that slower brainwaves should be less present, faster brainwaves should be relatively more predominant.

A third anticipated change involves the higher frequency brainwaves: gamma. The gamma band has been associated with neuroplastic changes as well as rhythmic binding and cortical synchronicity.[135] Thus, any areas involved in the changes in cognitive functions undergoing neuroplastic change should display more gamma band activity. These regions are the frontal lobes, which are responsible for attentional control and executive functions like working memory, and the occipital lobes, which are responsible for visual processing.[137]

The location of these changes is expected to be the same regions that have been demonstrated by previous research to be involved in MOT; the posterior parietal areas[126,127,128], the superior occipital cortex[127], and the frontal cortex.[128]

2. No Side Effects or Risk of Toxicity

Previous research has not documented any side effects or risks of toxicity; however researchers did not address these questions directly.[72,73,138,139]

Measuring side-effects and toxicity

In order to address side effects, questionnaires are used at the beginning of each session, and participants are encouraged to report any side effects during or after training. Any reports were to be brought to the attention of the lead researcher immediately. Due to the absence of side-effects form previous research, no long-term follow-up examining this aspect is planned.

Hypothesis 6: Side effects

No significant short-term side effects or risk of toxicity are expected. Future studies must examine this issue in greater depth, especially with regard to long-term follow-up and vulnerable, at-risk populations (e.g., older individuals and clinical populations).

3. Minimal time and monetary investment

Participation in the training portion of the study required approximately 45 minutes, twice a week. Sessions could be shortened to 30 minutes by removing the EEG montage, however real-time EEG data was also collected for later analysis and the installation of this equipment lengthened sessions by approximately 15 minutes. The time required for a training session is thus considered to be 30 minutes.

No monetary investment was required, however CogniSens Athletics Inc., the company who produces the commercial version of the 3D-MOT paradigm utilised in this study does charge for the purchase and use of the software.[140] The financial cost is not assessed in the present study. Further research should take this into consideration.

Measuring temporal and financial investment

Because sessions have a predetermined length, the calculation of how much time is necessary to invest is relatively simple. As mentioned, no financial impact assessment was included in this study and needs to be addressed in the future.

Hypothesis 7: temporal investment

<u>Ten 30-minute sessions, twice a week for a period of five weeks is sufficient to demonstrate significant effects of training.</u>

More training may show more substantial improvement. Less training may still lead to significant improvement. However, for the purpose of this study, the number of training sessions will remain constant and thus no hypothesis regarding either of these statements is possible. Once again future research will be needed to examine these possibilities. Future studies should also factor in the financial variables surrounding the use of 3D-MOT.

4. Lasting effects

Participants were tested once in the week prior to training and final testing occurred in the week following the final training session. While this offers very little data regarding longevity, it was necessary to first demonstrate that a short-term change occurred before answering the question of how long the effects endure. Future research should follow-up participants at regular intervals following training.

<u>No hypothesis can be made regarding long-term effects.</u>

5. No ethical issues

In terms of ethical issues, the project was assessed by the Comité d’éthique de la recherché en santé (CERES) of the Université de Montreal, and no problems were noted. Further assessing the ethical implications of a cognitive enhancer would require examining the general public opinion using polls, focus groups and interviews.[96]

As preliminary research into the domain, this was not of great importance to the goals of the present study. As mentioned in the section above, and from a strictly scientific standpoint, it must first be shown that 3D-MOT works before any ethical issues regarding public opinion are addressed. Philosophical, political and religious doctrines may disagree with this retrospective approach, however from a scientific standpoint it is of little interest to first answer the question of whether or not any of these issues will arise for something that is not of value to begin with.

Hypothesis 8: ethical implications

No ethical issues are expected.

All of that said, because this type of intervention has been previously used in numerous other research studies without any indication to the contrary[72,73, 138,139], and since the project was approved by an ethics committee, Future studies should not neglect the factors beyond ethics board approval, as Persson and Savulescu[94] note, "if research into cognitive enhancement continues, as it is likely to, it must be accompanied by research into moral enhancement.

6. Can be used in combination with others

Once again, this is a preliminary exploration into the question of whether 3D-MOT is a cognitive enhancer; it is premature to attempt to address the efficacy of combining it with other interventions. Following the currently established research, no contraindications were expected. Future research should assess possible contraindications that would consequently limit involving other types of cognitive enhancement tools in a larger training scheme, and then symbiotic combinations should be tested.

7. Can be applied to any population

The first step for any cognitive enhancement tool should be to examine the effects on a healthy population. Once the benefit of training is established, relevant clinical populations can then be targeted. Of course, most research does not follow this logical sequence, and this for a number of reasons. The first is that there is little clinical benefit from enhancing cognition in an otherwise “healthy” person, so efforts often delve into clinical populations directly. Second, non-public funding often drives research and decides the population that will undergo the intervention; for example if funding comes from a foundation that deals with an attention deficit population, the research will most likely be targeted to that population to expedite the overall process.

3D-MOT, in this sense, is no exception. Previous research has shown the benefits for older individuals in biological motion perception from 3D-MOT training.[72] Athletic populations took a vested interest following these findings, since many athletic contexts involve highly dynamic and complex visual scenes.[73] Research has shown that professional have greater-than-average abilities at the task, more so that even amateur athletes whom also show better results than a university student population.[141]

The current research study was designed to show the foundational changes that result in these findings, but also to then be able to better target suitable clinical populations for further investigation. Built on the idea that that 3D-MOT training enhances attention, working memory and visual information processing speed, the hypothesis that follows is that populations that are deficient in these functions could benefit from training. These include those with attention deficit/hyperactivity disorder, learning disabilities, autistic spectrum disorders, executive dysfunctions, as well as a preventative tool to help maintain cognitive functions and combat the changes that occur with normal aging.

Future research will have to address this issue and training in these populations.

Method

Prior to beginning the research project, all aspects of the study were approved by the ethics board (Comité d'éthique de la recherché en santé; CERES) of the Université de Montréal.

Subject recruitment

Participants for the study were university-aged students from the city of Montreal area. A total of 20 participants were included in the project. Ten subjects were recruited for the training portion of this project, while ten were recruited to participate in the control group. The number of subjects was low as this project was designed as a preliminary study of the effects of 3D-MOT on cognitive functions. No discrimination was made regarding gender, however the age-range was restricted to 18-30 years in order to control for differential capacities through the lifespan.[138] Exclusion criteria included any self-reported marked deficits in vision that could not be appropriately corrected with eyewear. In these instances participants were asked to wear their corrective eyewear. Further, any individual who had knowingly been diagnosed with a clinical disorder (for example attention deficit/hyperactivity disorder, epilepsy, or depression) whether or not they were medicated were offered training, but were excluded from final analysis. None of the participants declared any such condition.

Consent, Compensation and Benefits to Participation

Interested candidates were asked to communicate with the lead researcher either by phone or e-mail, at which time they were sent a consent form for review. During the initial testing session, participants first signed the consent form, and were then administered an initial questionnaire to ensure eligibility, and were given a series of guidelines for participation.

As a compensation for participation, subjects were paid $10 per hour they were present for the study. Initial testing was roughly two hours while training took 45 minutes per session for a total of 7.5 hours, and final testing was also two hours. Those in the training group thus received a total of $115 for 11.5 hours of total participation while control subjects received $40 for four hours of participation.

Participants in the training group were generally aware of the hypothesis regarding 3D-MOT training (i.e., they knew it was a training program designed to enhance cognitive capacities) and were told that their participation was to establish 3D-MOT as a cognitive enhancer, however the individual cognitive functions at play were not specifically discussed. Participants in the control group were told that their participation was important to measure the improvements seen from simply repeating the measures over a short period of time. The control group was a non-active control, and was included to account for test-retest effects.

In terms of expected adverse effects, participants were made aware of the possibilities: sore eyes, headache, fatigue, and mild-nausea induced by the 3D. They were encouraged to report any of these or other symptoms to any member of the research team, and team members routinely asked participants how they were feeling. At any point participants were free to discontinue their involvement simply by notifying a member of the research team.

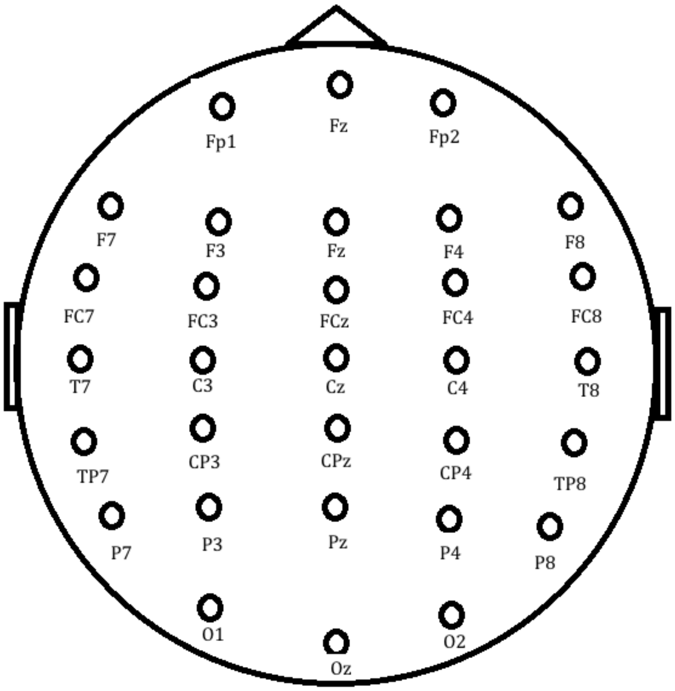
Initial assessment

The first meeting between a participant and researcher was an initial testing session. In this session, two types of assessment tools were used in order to evaluate the effects of 3D-MOT. First, standardized neuropsychological tests were used to measure attention, short-term and working memory, and information processing speed. Second, a functional measure of brain activity – quantitative electroencephalography – was used to assess resting state brain function. Finally, a baseline 3D-MOT session was also performed.

Resting state qEEG

The first step of the assessment was to measure resting-state neuroelectric brain function. This was done first in order to ensure that no cognitive fatigue resulting from performing neuropsychological tests or 3D-MOT training was observed. QEEG data was acquired using a 32-channel system (Model 202, Mitsar Medical.[142]) This qEEG system allows for the simultaneous recording of EEG activity from 32-different channels; 31 active electrodes placed on the head with one reference pair (A1/A2; linked ears) and one ground (AFz). Active electrodes were placed according to an augmented 10-20 system[143], shown in figure 1-1.

Figure 1-1: Augmented 10-20 System



All methods used and described below are standard procedure for qEEG measurement. For detailed information, the authors suggest the reviewing the standards proposed by Nuwer and colleages.[144]

An Electro Cap[145] was placed on subject's heads for the recording of qEEG. To ensure proper impedance, subject's ears and forehead were first prepared with a skin-cleaning agent, NuPrep.[146] Following this, Electro-Gel (Electro-Cap International, Inc.[145]) was injected using a blunted syringe into the electrodes (designed with holes for this purpose) in the cap. To ensure proper impedance (i.e., below 5kOhms), the blunted syringe was also used to gently rub the scalp, parting any hair and softly removing any dead skin and grease that might interfere with proper measurement.

Subjects were seated and given a fixation point straight ahead and slightly below eye-level in order to minimize ocular artifacts. To obtain the baseline EEG activity for each subject, five minutes of continuous EEG data were recorded with eyes open, and another five minutes with eyes closed. From this data, one minute of artifact-free EEG was manually selected and retained for analysis. The recordings were coded by a co-author so that the analyzer was blind with regard to the participant and condition (pre- or post-training) of the scan. The recording was then analyzed using Neuroguide (version 2.7, Applied Neuroscience, Inc.), a qEEG software platform with a normative database and statistical data analysis tools.[147]

Baseline neuropsychological evaluation

The tests selected for this research project were based on the a priori hypotheses regarding the functions involved, elaborated above. The tests are grouped below according to the function of interest they measure.

Attention

Integrated Visual and Auditory Continuous Performance Task

The Integrated Visual and Auditory Continuous Performance Task (IVA+Plus®) is a computerized test of the different types of attention across visual and auditory modalities.[110] The test lasts approximately 20 minutes, and involves a motor response (via clicking a mouse button) when presented with visual and audio stimuli (the number ‘1’), and inhibiting the motor response when presented with an alternate stimulus (the number ‘2’). Although typically used to aid in the diagnosis of attention deficit disorders (with or without hyperactivity), its use in research concerning factors of attention is well documented.[111] The test yields data on both visual and auditory attention. The subscales given are associated with different functions, and these are described in the research article. The validity of the IVA+Plus® in measuring attention is comparable to other commonly-used measures of attention, with a sensitivity or 92% and specificity of 90%, and test-retest reliability over a 4 week period for the Full Scale Response Control reporting correlations ranging from .37 to .41 and for the Full Scale Attention Quotient ranging from .66 to .75.[112]

The d2 Test of Attention

The d2 test of attention is used to measure attention and information processing speed. In this task, subjects are shown three examples: a lower case ‘d’ with two dashes above, a lower case ‘d’ with two dashes below, and a lower case ‘d’ with one dash above and one dash below; each possible combination of a ‘d’ with two dashes. They are then shown a series of sequences in which the targets – the three examples mentioned above – are randomly placed amidst distractors. Distractors are lower-case letters ‘d’ and ‘p’ with one to two dashes placed above and below the letter, for a maximum of four dashes for any given distractor. Subjects are asked to cross out targets and ignore distractors over a series of 14 sequences, each containing 47 items. There is a 20-second time limit for each sequence.[115] In terms of validity and reliability, the d2 measures used for this project fall within the norms for neuropsychological tests (see Bates & Lemay[148] for a breakdown of all scores).

For the purposes of this study, the score used was the *Total minus Errors* score. This score is a measure of global attention calculated based on the total number of items coded (all items counted up until the final identified item), minus the number of errors of omission and commission.[115]

Short-term and Working Memory

Digit Span (WAIS-III)

The Digit Span task is used to measure short-term memory and working memory in the auditory domain. The administration of this task is straightforward: subjects are read a series of numbers and are asked to repeat them in the same order (initial trials) and in reverse order (later trials). Each trial contains a new number sequence, and after every second trial, sequences increase in length; i.e.: trials 1 & 2 are two digits long, 3 & 4 are three digits long, etc. Points are awarded based on the successful completion of each trial.[149]

Letter-Number Sequencing (WAIS-III)

The Letter Number Sequencing Task is used to measure auditory working memory. A sequence of letters and numbers are read to the subjects and they are asked to retain, rearrange and subsequently read aloud the string of items in a specific sequence; numbers first and in ascending order, followed by the letters in alphabetical order. As with the digit span task, sequences get longer as trials progress, with an addition of one character (a letter or a number) at each third trial. Points are awarded based on the successful completion of each trial.[149]

Spatial Span (WAIS-III)

The Spatial Span is an adaptation of a test of visuo-spatial working memory, initially developed by Corsi.[150] It is very much like the digit span task, except that sequences are shown in the visual modality, using a board on which is mounted a series of 10 cubes.

Subjects are shown a sequence of blocks, demonstrated by the examiner. The test consists of two parts: *forward* and *reverse*. In the first, they must repeat the sequence in the same order in which it was demonstrated to them. In the second half subjects must repeat the patter in reverse order. A trial is correct when the subject is able to correctly repeat the pattern in its entirety. After every second trial, an additional cube is added; i.e.: trials 1 & 2 are two cubes long, 3 & 4 are three cubes long, etc. Each half of testing ends when subjects fail both trials within one level. Subjects are scored on the number of items (visual span) they can answer correctly.[150]

Information Processing Speed

Block Design

The Block Design task is primarily used to measure spatial perception, visual abstract processing and problem solving. Subjects are awarded more points when trials are completed quickly, and in this case it is especially the speed at which this task is completed that was under scrutiny. In this task, the subject is given a series of blocks – for the first trials 4, the latter trials 9 – and is asked to recreate a model displayed in the WAIS-III stimulus booklet. These blocks are identical and have two entirely red sides, two white sides, and two half-white, half-red sides (dissected on the diagonal). A subject must correctly select the side of each block and arrange them accordingly to properly recreate the model. For each trial there is a maximum time limit, and points are awarded based on successful completion and the time taken for each trial.[149]

Symbol Search

The Symbol Search is used to measure visual information processing speed. Each trial is comprised of a sequence of symbols: two targets and a series of five distractors.

The goal of the exercise is to determine whether either of the two target symbols is present within the sequence of distractors. The subject must answer by checking a box that says *Yes* or *No*. Each trial must be completed in sequence, within a time limit (120 seconds). Points are awarded for each correct trial, minus each incorrect trial.[149]

Coding

The Coding task is another measure of visual information processing speed. Subjects are shown a diagram in which each digit from 1-9 has been paired with a symbol. On the same page is a grid, with each digit presented in a random sequence. Below each digit is an empty box in which the subject must fill in the appropriately paired symbol, one after another, in sequence, within a given time limit (120 seconds). Points are awarded based on the number of correct symbols coded during the time limit.[149]

The full-scale reliability of the WAIS-III is high (.96) and the various individual subtests range from .7 to slightly above .9 while validity studies report that correlations are regularly above .8 when compared with other indices.[151]

Delis-Kaplan Executive Function System (D-KEFS) Color-Word Interference Test

The Delis-Kaplan Executive Function System (D-KEFS) Color-Word Interference Test is used to measure selective visual attention, inhibition, cognitive flexibility, and information processing speed. This test is a variant of the Stroop task, in which subjects must inhibit a more automatic response (reading) and instead respond to the dissonant colour in which the word is written. The D-KEFS is a standardized test in which subjects are scored on their ability to complete this task quickly, and based on the number of errors (corrected or uncorrected) that they commit. Contrast measures, the comparisons between scoring on each sub-task can also be used for analysis.[116] The speed at which each subtest was completed was retained for analysis in this project.

There are four sub-tasks within the test: (1) Color Naming, (2) Word Reading, (3) Inhibition, and (4) Inhibition/Switching. For all subtests, three colours are used: blue, green and red. In Color Naming, subjects are simply asked to name the colours of a series of coloured squares. In Word Reading, subjects must simply read the word (the three colours) written in black ink. In the Inhibition task, subjects must say the colour of the ink the word (the three colours) are written in, and not read the word that is written. For example, the word 'green' may be written in red ink, in which case the participant must say 'red'. In the Inhibition/Switching task, participants must say the colour of the ink, as in the Inhibition task, unless the stimulus presented is in a box – in which case they must read the word written.[116] With regard to the D-KEFS, the reliability and validity measures on subtests are also well within the norms for neuropsychological tests[152,153,154] and the individual scores can be found in the technical manual.[155]

For the purpose of the research at hand, Color Naming and Word Reading were used as measures of information processing speed, Inhibition was used as a measure of Inhibition, and Inhibition/Switching was used as a measure of divided attention.

3D-MOT session

The 3D-MOT sessions were performed in the C.A.V.E. (Cave Automatic Virtual Environment).[156] The C.A.V.E is an 10 foot by 10 foot by 10 foot enclosure onto which is projected the 3D-MOT task. The MOT environment consists of a large cube measuring approximately 1.5 meters in length, width, and height. The trainee is then seated at a distance of 1.5 meters from the screen and is given a fixation point located in the center fo the cube. Consequently, the 3D-MOT task utilises a visual field of approximately 45 degrees. The use of a cube as the environment allows for the amount of horizontal and vertical movement to remain unbiased. The 3-D aspect of the MOT task is achieved using stereoscopic projection and active shutter lenses synchronized to 120Hz.

Each trial of 3D-MOT consists of the five phases outlined below. Each series of 3D-MOT consists of 20 trials and yields a threshold score. Each session consisted of three series of 20 trials, yielding three threshold scores that were then averaged to give the *session score*. Subjects in the training group as well as the control group performed a 3D-MOT session during initial and final testing.

There are five phases to each trial:

1. *Presentation*: all eight spheres appear, coloured homogeneously in yellow. This phase lasts two seconds.

2. *Indexation*: the four target spheres turn red, with a surrounding white halo. This lasts two seconds. The four target spheres return to their original colour and restore homogeneity. This lasts one second.

3. *Movement*: all eight targets move along a linear path in the virtual 3-D cube. If a sphere comes in contact with another sphere or a wall of the cube, it bounces off and resumes its trajectory. This phase lasts eight seconds. During tracking the trainees eyes must remain focused on a neutral fixation point; in this case a red dot located in the middle of the virtual cube; the tracking element occurs primarily in the periphery.

4. *Stoppage and identification*: all eight spheres cease movement and are labeled with numbers (1 to 8). Subjects verbally state their responses. The answers are input by a trainer using a keyboard, and the selected targets are identified with a halo. The verbal response ensures that subjects are not encumbered and so they do not need

to move their focus from off the screen. The subjects also have a video-game controller that allows them to rotate the cube and make the foreground spheres transparent in order to reveal any spheres that might be hidden behind another sphere in the 3-D virtual space. This phase ends when the subject validates their response by pressing a button on the controller.

5. *Feedback*: the target spheres are revealed, and feedback (number of target spheres correctly identified) is given. This phase lasts two seconds.

If a subject correctly identifies all four target spheres, the speed of movement increases for the subsequent trial. If all four target spheres are not identified, the speed of movement decreases for the subsequent trial. The changes in speed were variable and follow an adaptive staircase. The design of the adaptive staircase was such that larger variations (up to 100%) occurred in initial trials (to more quickly reach the appropriate speed) and smaller variations (as low as 10%) in later trials (to maintain the zone of optimal development). For each trial, the speed and number of correct targets identified is recorded. At the end of 20 trials, a threshold speed score is displayed for subjects and recorded in a database.

Training

This section details the intervention applied to the training group only. The control group was a non-active control and were only seen for initial and final testing.

Each training session consisted of three series of 20 trials as described above. The amount of time spent training in each session was approximately 30 minutes, however there was an extra 15 minutes allotted for the installation of EEG equipment. Sessions were performed twice a week between 9am and 5pm on non-consecutive days. Ten total sessions were completed over a period of five weeks.

At the outset of each training session, participants were asked to complete a short questionnaire about how they were feeling, the amount of sleep they had, and any psychoactive substances they may have recently ingested (for example coffee or alcohol). This data was not included in final analysis and served only to gather anecdotal data about any observed side effects and to control for confounding variables such as the ingestion of significant amounts of caffeine, alcohol or other substances that may have affected results.

Real-time EEG measurement

EEG data was recorded and retained for future analysis. EEG data was recorded during 3D-MOT training from sites Pz and Fz according to the 10-20 international classification system.[157] The active electrodes were referenced to linked ears and grounded at Cz.

Thought Technology Limited[158] manufactured the equipment used to acquire the 2-channel EEG data. Application of electrodes followed the standard procedure and was done by first lightly abrading the skin using a gel designed for that purpose, NuPrep, then sticking the electrode to the ear or scalp using Ten20 conductive paste. Subsequent analysis will evaluate the activity of these brain areas during 3D-MOT training.

Electrode location Pz is over the medial parietal cortex. This site is said to measure activity corresponding to Brodmann areas 7 (the somatosensory association cortex/precuneus), 23 and 31 (posterior cingulate cortex).[159] These areas are associated with a convergence between vision and proprioception, visuo-motor coordination, working memory, visuospatial processing, and directing attention in space.[132] This site was chosen for these functional reasons, and also because of its central location. The MOT task involves complex visual processing requiring multiple cortical areas in both hemispheres of the brain, and this cortical connectivity and inter-hemispheric communication becomes vital.[160]

Electrode location Fz is over the medial frontal cortex. This site measures activity corresponding to Brodmann areas 8 (the frontal eye fields), 9 (a subdivision of the dorsolateral prefrontal cortex) and 24, 32 and 33 (the anterior cingulate cortex). These brain regions are functionally associated with the control of eye movements and the planning of complex movements (BA8); the management of uncertainty, planning, organization and regulation of motor systems, integration of sensory information and working memory (BA9); motor learning, imagination, decision making, attention (especially target detection and action observation), working memory and rational thought processes (BA24, 32, 33).[132,159] These cortical areas act in a "top-down" manner to influence the sensory processing stream that occurs parietally/occipitally, toward Pz.[132]

Final assessment

The final assessment was identical to the initial assessment and occurred approximately six weeks after initial testing for both training and control groups.

Statistical analysis

The statistical analysis used for this research follows similar studies in cognitive enhancement.[9,161] This includes a repeated measure ANOVA in order to establish main effects and interactions, as well as pre- and post-training t-tests of behavioural (transfer) measures in order to establish significance with respect to the a priori hypotheses. These results are presented in the research article below. Essentially, the t-tests demonstrate that a significant change has occurred. In the extended discussion section, the magnitude of the change will be examined using measures of effect size.

Research article

Clinical EEG and Neuroscience accepted this manuscript for publication on November 17th, 2014 and has since been published online under the following citation:

Parsons, B., Magill, T., Boucher, A., Zhang, M., Zogbo, K., Bérubé, S., Scheffer, O., Beauregard, M., & Faubert, J. (2014). Enhancing Cognitive Function Using Perceptual-Cognitive Training. *Clinical EEG and neuroscience*, 1550059414563746.

Title

Enhancing cognitive function using perceptual-cognitive training

Authors and contributions

Parsons, B., Magill, T., Boucher, A., Zhang, M., Zogbo, K., Bérubé, S., Scheffer, O., Beauregard, M. and Faubert, J.

Brendan Parsons conceived and designed the study, was responsible for the all evaluations, contributed to the training of participants, collected and analysed all of the data and drafted the manuscript. Tara Magill, Alexandra Boucher, Monica Zhang, Katrine Zogbo and Olivier Scheffer all contributed to the training of participants. Sarah Bérubé also trained subjects and participated in the scoring of some of the neuropsychological tests. Mario Beauregard and Jocelyn Faubert contributed to the design of the project and the interpretation of the data. All authors revised the manuscript and gave their final approval.

Abstract

3D-MOT is a perceptual-cognitive training system based on multiple object tracking (MOT) in a 3-dimensional (3D) virtual environment. This is the first study to examine the effects of 3D-MOT training on attention, working memory, and visual information processing speed as well as using functional brain imaging on a normative population. Twenty university-aged students were recruited and divided into a training (NT) and non-active control (CON) group. Cognitive functions were assessed using neuropsychological tests, and correlates of brain functions were assessed using quantitative electroencephalography (qEEG). Results indicate that 10 sessions of 3D-MOT training can enhance attention, visual information processing speed and working memory, and also leads to quantifiable changes in resting-state neuroelectric brain function.

Keywords: MOT, Cognitive enhancement, Brain training, Attention, qEEG

Introduction

Cognitive enhancement is a domain of burgeoning interest, spanning the remediation of clinical disorders (eg, attention deficit/hyperactivity disorder), to enhancing the performance of healthy individuals, professional athletes, and CEOs, to combatting the deleterious effects of time on the growing aging populace. In 2012, despite a significant lack of credible evidence to support their use, the market revenues of computer-based training programs alone were more than 1 billion dollars.[1]

Many different kinds of interventions have been proposed, including rudimentary pencil-and-paper type tasks (eg, sudoku puzzles, crosswords), more advanced computer/video-game type programs (eg, Lumosity), brain-computer interfaces (eg, neurofeedback), nutritional supplements (eg, omega-3 fatty acids, caffeine), and even pharmacological drugs such as stimulants and cognitive enhancers/nootropics (eg, Ritalin, Nuvigil). Less invasive methods for enhancing cognition include adopting appropriate lifestyle habits related to nutrition, exercise, and sleep.

Arguments in favor or against each type of intervention are vast; suffice it to say significant issues plague each of these types of interventions. For a review, the authors suggest reading Dresler et al,[2] Jak et al,[3] the special report prepared by the Academy of Medical Sciences,[4] and Gruzelier.[5] Generally speaking, the complaints against these interventions are the following: Transfer effects are not consistently observed, the effects observed do not persist in time, the methods are invasive and include risk of significant side-effects, a significant monetary and time investment is required, and there are the ethical issues associated with the use of these interventions. While a thorough analysis of each individual cognitive enhancement tool is beyond the scope of this article, shown in Table 1 is a general assessment of each specific intervention type. As can be seen, little research has been conducted to support the widespread use of the majority of these methods, and much more is needed before definitive conclusions can be reached.

With these limitations in mind, the gold standard in cognitive enhancement would thus be an intervention that shows (*a*) robust effects with transfer, (*b*) no side effects or risk of toxicity, (*c*) minimal time and monetary investment, (*d*) lasting effects, (*e*) no ethical issues, and (*f*) can be used in combination with others. In addition, this intervention should (*g*) apply to virtually any population. The current study aims at providing preliminary evidence for such gold-standard achievement using an intervention of perceptual-cognitive training: 3D-MOT.

Table 1: General assessment of various methods of cognitive interventions

	Pencil & paper	Computer games	Brain-computer interface	Nutritional supplements	Stimulants & nootropics
(1) Robust Effects with Transfer	Inconsistent[3]	Inconsistent[2,3]	Yes[5]	Yes[2]	Inconsistent[2,4]
(2) Side Effects/Toxicity	None reported	Insignificant[3]	Insignificant[5]	Signifcant[2,4]	Significant[2,4]
(3) Investment	Continuous[3]	20+ hours[3]	10+ hours[5]; 30-40 hours[6]	Continuous[2,4]	Continous[2,4]
(4) Lasting Effects	Not reported	Unknown[3]	Yes[5,6]	No[2]; Tolerance[2]	No[2,4]
(5) Ethical Issues	None reported	None reported	None reported	None reported	Yes[2,4]
(6) Mutually Exclusive	No reported contra-indications	No reported contra-indications	No reported contra-indications	Some contra-indications[4]	Some contra-indications[4]
(7) Potential Populations	Healthy aging[3]	Various	Various[5,6]	Various[4]	Various[2,4]

3D-MOT

Three-dimensional multiple object tracking (3D-MOT) is a perceptual-cognitive training program adapted by Dr Jocelyn Faubert of the University of Montreal.[7] Initially devised by Pylyshyn and Storm[8] as a research tool, the multiple object tracking (MOT) task has since been adapted as a training tool called NeuroTracker.[7] So far, this tool has been used in aging populations to improve biological motion perception[10,11] and linking athletic performance levels and learning capacity on this task.[7,9]

As a cognitive enhancer, 3D-MOT has 4 defining characteristics essential to achieving the gold standard. First, the training uses (*a*) MOT, (*b*) a large visual field, and (*c*) binocular 3D. All these contribute to the ecological validity of the training. Daily, we must attend to multiple pertinent sources of information while inhibiting nonrelevant information (MOT) across our entire 3D perceptive field (large visual field and binocular 3D). By using speed thresholds, the training is adaptive and consistently maintains the difficulty level within the zone of proximal development.

The task also follows 2 principles fundamental to training cognitive abilities (for a comprehensive review, see Faubert and Sidebottom[7]). First, it is rudimentary and does not require a complex strategy but instead requires low-level cognitive systems. Second, it consistently asks the trainee to perform at and above their current level of functioning. The principles behind 3D-MOT training are thus to *isolate* and *overload*.

Isolation in this sense means that a number of functions solicited for the task should be limited and consistent. A training task should not draw on a random and inconsistent combination of cognitive functions to complete. If isolation does not occur, training effects are reduced.

Overloading a function means soliciting it beyond its current ability. To properly train any function, overloading must occur so that adaptation (in the brain:

neuroplasticity) can take place. It is important to note that in any learning paradigm, overloading should be maintained within a range to ensure it falls within the zone of proximal development.[12] Speed thresholds ensure an appropriate level of *overload*.

Cognitive Functions

The cognitive functions engaged in 3D-MOT are theorized to be (*a*) attention, (*b*) working memory, and (*c*) visual information processing speed. The reason will become apparent in the description of the task in the methods section, and will be further explained in the discussion. The working definitions of each function are described in Table 2.

Table 2: The cognitive functions involved in 3D-MOT

Cognitive Function		**Definition**
Attention	*Sustained*	The ability to maintain selective attention over time
	Selective	The ability to attend to/focus on/cognitively process a given thing
	Divided	The ability to selectively attend to multiple loci at once (multifocal)
	Inhibition	The ability to not attend/focus on/cognitively process a given thing
Short-term Memory		The ability to retain information over a short time span (20-30 seconds)
Working Memory		The ability to retain and transform information over a short time span
Information Processing Speed		The time needed to consciously integrate perceptual stimuli

Source: adapted from Banich & Compton[13]

We hypothesize that the cognitive functions described above will demonstrate significant improvement following 10 sessions of 3D-MOT training. Quantitative changes in brain function should also be observed fitting the established patterns of these cognitive functions; namely we expect increased beta relative to slower brainwave frequencies, and increased gamma over the occipital cortex.

Methods

Twenty university-aged students were recruited from the greater Montreal area and assigned randomly to either the 3D-MOT training (NT; n = 10) group or control (CON; n = 10) group. Both groups had an equivalent number of years of postsecondary education (NT = 4.40 ± 1.35), CON = 4.40 ± 1.17) and were similar in age (NT = 23.54 ± 2.56 years, CON = 23.02 ± 2.78 years). No individuals taking psychoactive medication, nor with a known diagnosis of a cognitive disorder were included in the study. The project was approved by the Université de Montréal ethics committee (CERES; Comité d'éthique de la recherche en santé). No high-level athletes were included in the sample because of their enhanced learning ability in this task.[9]

Evaluation

All subjects underwent identical initial and final testing. The testing sessions lasted between 2 and 2.5 hours. Testing consisted of a quantitative electroencephalogram (qEEG), a battery of neuropsychological tests, and a 3D-MOT session. Neuropsychological measures included the Integrated Visual and Auditory Continuous Performance Test (IVA+Plus CPT; www.braintrain.com), selected subtests from the Wechsler Adult Intelligence Scale (WAIS-III),[14] including symbol search, code, block design, number sequence, letter-number sequence and spatial span, the d2 attention test,[15,16] and the Delis-Kaplan Executive Functions System Color-Word Interference Test (D-KEFS).[17] The 3D-MOT portion of the evaluation was identical to the training sessions described below.

The IVA+Plus is a computerized continuous performance task designed to measure attention. In this task, subjects are asked to identify target stimuli—the number "1" presented visually and auditorily—by clicking the left button on a mouse. Amid these target stimuli, are distracting stimuli—the number "2" presented both visually and auditorily—and subjects are asked not to respond to these stimuli. The task lasts approximately 20 minutes.

The WAIS-III symbol search is visual information processing speed test. A pencil-and-paper task, subjects are shown 2 target symbols followed by a string of 5 symbols. They are asked to answer either "Yes" or "No." A "Yes" answer means they have identified that 1 of the 2 target symbols is present in the string of 5 symbols.

The WAIS-III code task is also a pencil-and-paper task designed to measure visual information processing speed. In the code task, each digit from 1 to 9 has an associated symbol at the top of the page. Below this, the numbers 1 to 9 are displayed in random order in a grid with an empty space underneath. Subjects are asked to fill in the symbol paired with each digit in the space below each, provided for that purpose.

The WAIS-III block design is a visuospatial abilities task in which subjects are asked to recreate images displayed to them with the use of blocks. Each block has 2 fully red sides, 2 fully white sides and 2 half-white, half-red sides. For each item, the subject is shown the image and must recreate it as quickly as possible. The first 5 items require the use of 4 blocks; the final 5 items require the use of 9 blocks.

In the WAIS-III number sequence, a test to measure auditory short-term memory and working memory, subjects are read aloud a string of digits and are then asked to repeat them back. This is first done with subjects repeating the items in the same order in which they are given, and then they are asked to repeat the task using new items while giving the string back in reverse order. Items are grouped into levels of difficulty, with each level adding a digit to the length of the item.

The WAIS-III letter-number sequence is an auditory working memory task similar to the number sequence, with the addition of letters to the strings given for each item. Additionally, the subjects are asked to reorganize the digits and letters given as follows: letters first, in alphabetical order, followed by numbers, in ascending order.

The WAIS-III spatial span is a visual short-term memory and working memory task. It uses a rectangular board on which are 10 identical cubes. The cubes are numbered so that only the tester may identify them by number, while the subject must only rely on their location. The subject must repeat a sequence demonstrated by the tester by tapping on the correct blocks in the proper order. As in the number sequence task, items are grouped by 2 into levels, with each subsequent level adding one block to the string.

The d2 attention test is a pencil-and-paper type test, in which subjects are looking to cross out target stimuli amongst distractors. Targets are the lowercase letter “d” with 2 vertical dashes on top, 2 vertical dashes on bottom, or 1 vertical dash on top and another on bottom. Distractors consist of lowercase “d”s and “p”s with 1 to 4 vertical dashes above or below the letter, with a maximum of 2 dashes on either side.

The D-KEFS color-word interference test is a visual inhibition test composed of 4 different subtests. Each subtest is timed and the number of uncorrected and corrected errors is noted. The subtests consist of identifying 1 of 3 colors: red, blue, and green. For each subtest, the stimuli are presented listwise, and subjects proceed down the page from left to right, top to bottom. There are 2 lines of 5 items that serve as examples, followed by 5 lines of 10 items, which consist of the timed test. The first subtest is color naming: subjects must simply identify the colored squares. The next is word reading: subjects must read the colors printed in black ink. The next is inhibition: subjects must identify each item based on the ink color and not read the word that is written. The final subtest is inhibition/switching: subjects must identify each item based on the ink color and not read the word that is written, unless the item is in a box and in that case they must read the word that is written.

It should be noted that some of the tests used are typically not readministered in quick succession because of the possibility of test–retest effects, notably learning or practice. Considering the time frame of the current study, the tests most prone to test–retest effects include the WAIS-III and all included subtests,[14] and the D-KEFS Color-Word Interference Test.[17] The utilization of a control group should adequately control for these effects.

The qEEG data were acquired using a Mitsar 202 system (www.mitsar-medical.com) at 500 Hz using an augmented 10-20 system; however, only the data from the standard 10-20 electrode placement system[18] were retained for this analysis. The data were recorded using WinEEG (www.mitsar-medical.com) and were analyzed using the NeuroGuide qEEG normative database.[19]

Training

For the NT group, each training session was identical. For each trial, the speed and correct number of targets identified was recorded. Each session lasted between 45 minutes and 1 hour. Sessions were performed between 9 AM and 5 PM twice per week over a period of 5 weeks. The CON group was a nonactive control.

A training session consists of 3 series of 20 trials in which the trainee tracks 4 spherical targets among 4 identical distractors that move linearly through a virtual 3D cube. The cube was projected onto a square projector screen measuring 8 × 8 feet; each side of the cube measured 1.5 m while targets measure 10 cm diameter. The speed for each trial is measured in meters per second and initial start speed of each series is 0.3. All other methodological specifics can be found in Faubert and Sidebottom.[7]

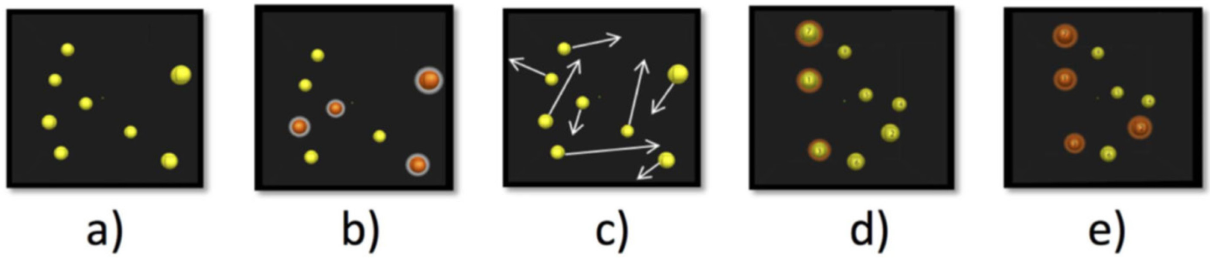
During the first phase of each trial, all 8 spheres appear in yellow and are stationary. Next, the 4 target spheres that the trainee must track appear in red for 2 seconds, before switching back to yellow. The spheres begin movement and tracking then occurs over a period of 8 seconds. All 8 spheres move along a linear path through the cube; should any sphere encounter an obstacle it bounces off that obstacle and continues along its new path. At the end of this phase, each sphere is identified with a number and the trainee is asked to verbally state their responses. Table 3 outlines each phase of a 3D-MOT trial and a visual representation can be seen in Figure 1.

Table 3: 3D-MOT Trial

Phase	**Description**	**Duration**
Presentation (a)	Eight spheres appear, coloured homogeneously in yellow.	2 seconds
Indexation (b)	Four target spheres turn red with a surrounding white halo.	2 seconds
Pause	Targets turn back to yellow, restoring homogeneity.	2 seconds
Movement (c)	All spheres move along a linear path in the 3D cube. If a sphere contacts another sphere or a wall of a cube it bounces off and continues along its new trajectory.	8 seconds
Identification (d)	All eight spheres cease movement and are labeled with numbers (1 to 8). Subjects verbally state their responses.	User determined
Feedback (e)	The target spheres are revealed, and feedback (number of target spheres correctly identified) is given.	2 seconds

See Figure 1 for a visual representation of each phase.

Figure 2-1: The Phases of a 3D-MOT Trial



If all 4 targets are correctly identified the speed of the subsequent trial increases. If an incorrect response is given, the speed of the subsequent trial decreases. The speed changes are based on an adaptive staircase: Initial speeds vary more widely than later trials to ensure that the optimal zone for training is quickly attained. Ideally, in order to maintain a zone of proximal development, the majority of trials should be at and slightly above the trainee's current level of ability. An adaptive staircase[9,10] ensures this while adjusting for endurance and fatigue. At the end of a series of 20 trials, a final speed threshold score is given. A subject's session score comprises the average threshold score of the 3 series of 20 trials. Four targets are used as research has shown that most people can generally track four elements in such a context.[20]

Data Analysis

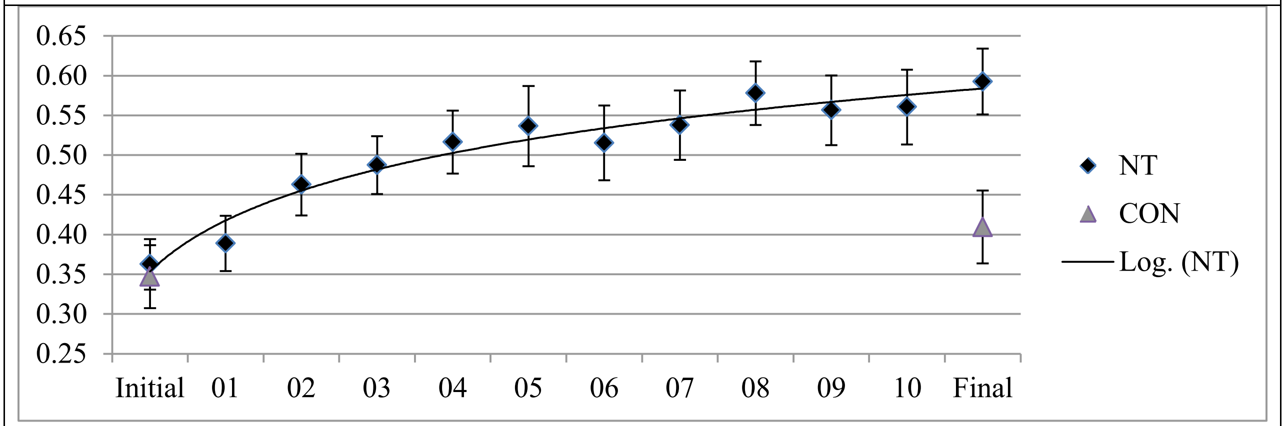
All the neuropsychological tests were scored and EEGs analyzed by the first author. One minute of artifact-free data from the pre- and post-qEEGs were selected by the author respecting a blind design using the NeuroGuide Normative Database (version 2.7.9, 2013). Test-retest and split-half reliability measures were kept higher than .90.

Results

3D-MOT

As expected, 3D-MOT session scores showed significant improvement ($P < .01$) from initial to final testing for the NT group. Interestingly, the CON group also showed a strong improvement ($P = .016$) from their initial to final testing session. The 2 groups differed significantly in their final session score ($P < .01$). Session scores for both groups along with log trend line for NT group are shown in Figure 2.

Figure 2-2: 3D-MOT session scores for NT & CON groups; GEO Mean with Standard Error



The final session score for the CON group is statistically similar to the 1st training session of the NT group. Initial session scores were 0.36 for the NT group and 0.35 for the CON group. Standard errors were 0.03 and 0.04 respectively. The NT group's first session was 0.40 with a standard error of 0.03, while the CON group's final session was 0.41 with a standard error of 0.05.

Cognitive Functions

A Levene test yielded no significant differences in homogeneity between groups ($P > .01$; only WAIS letter-number sequence was significant at $P < .05$) between groups prior to training. An analysis of variance of initial results demonstrated that there was no significant difference between groups on neuropsychological tests prior to testing. A repeated-measures analysis of variance was also performed with training condition (training or control) as the between-subject factor. A main effect of training was found ($F = 36.232$; $P < .01$), as was an interaction for training × group ($F = 13.201$; $P < .01$). As a consequence of the a priori hypotheses regarding cognitive functions, planned follow-up t tests were used to compare neuropsychological measures pre- and posttraining. Because of the exploratory nature of the research at hand and the accordingly lenient nature of the statistical tests used, a more stringent alpha of $P < .01$ was required to achieve significance. The mean pre- and posttraining, the degree of change, and results of the planned t tests can be seen in Table 4.

Table 4: Neuropsychological test results: pre-post within group t-tests

	NT Group (n=10)				*CON Group (n=10)*			
Measure	**Pre**	**Post**	**Change**	**Sig.**	**Pre**	**Post**	**Change**	**Sig.**
IVA+Plus® Auditory	93.40	101.58	8.18*	.007	97.30	98.98	1.68	
IVA+Plus® Visual	97.57	104.60	7.03^{+}	.071	97.80	97.92	1.12	
WAIS-Symbol Search	43.40	48.40	5.00*	.004	45.50	49.40	2.90	
WAIS-Code	91.40	101.10	9.70*	.000	88.00	95.50	7.50^{+}	.015
WAIS-Block Design	51.20	59.20	8.00*	.000	56.10	58.60	2.50^{+}	.024
WAIS-Number Sequence	20.00	19.90	-0.10		19.60	19.70	0.10	
WAIS-Letter-Number S.	13.90	15.70	1.80*	.008	12.20	13.30	1.10	
WAIS-Spatial Span	19.40	22.20	2.80^{+}	.021	19.00	20.60	1.60	
d2 Test of Attention	437.70	498.10	60.40*	.000	465.10	509.30	44.20^{+}	.017
D-KEFS Color Naming	27.30	23.60	-3.70*	.006	24.90	24.40	-0.50	
D-KEFS Word Reading	20.00	18.10	-1.90		19.10	19.30	0.20	
D-KEFS Inhibition	43.80	38.40	-5.40*	.004	44.10	40.20	-3.90^{+}	.020
D-KEFS Inhibition/Switching	49.50	42.80	-6.70*	.004	50.80	45.60	-5.20*	.009

* significant at p<.01; $^{+}$ trend toward significance p<.1

The NT group demonstrated significantly higher scores with regard to the IVA+Plus Auditory, WAIS Symbol Search, WAIS Code, WAIS Block Design, WAIS Letter-Number Sequence, d2 Test of Attention, and D-KEFS Color Naming, Inhibition and Inhibition/Switching subtests ($P < .01$). The NT group also displayed a couple of trends toward significance, including IVA+Plus Visual and WAIS Spatial Span ($P < .1$). With regard to the individual IVA+Plus subscales, there were significant improvements in Visual Consistency ($P < .01$), and Auditory Speed ($P < .01$). Auditory Stamina ($P < .05$), Auditory Focus ($P < .05$), and Visual Speed ($P = .068$) also showed a trend toward significance.

Table 5: Improvements in cognitive functions as measured by neuropsychological tests following 3D-MOT training

Cognitive Function		**Measure**
Attention	*Selective*	IVA+Plus® (Consistency & Focus[+]), WAIS (Symbol Search), d2
	Sustained	IVA+Plus® (Stamina[+], Consistency, Focus & Sustained Quotient), d2
	Divided	d2 test of attention, D-KEFS (Inhibition/Switching)
	Inhibition	D-KEFS (Inhibition & Inhibition/Switching*)
Short-term Memory		N/A
Working Memory		WAIS (Spatial Span[+] & Letter-Number Sequencing)
Information Processing Speed		IVA+Plus® (Speed[+]) WAIS (Symbol Search, Code, Block Design), d2, D-KEFS (Colour Naming & Word Reading)

* Note that the CON group also demonstrated significant improvement in D-KEFS Inhibition/Switching

[+] Indicates a trend toward significance

With regard to the CON group, only the D-KEFS Inhibition/Switching subtest attained significance, while WAIS Code, WAIS Block Design, d2 Test of Attention and D-KEFS Inhibition subtest demonstrated trends ($P < .1$).

Initial IVA+Plus testing demonstrated higher scores in the visual domain (97.57) contributing to a ceiling effect that is observed to a lesser extent in the auditory domain (93.40). This is likely the reason why visual attention comparisons do not attain significance but do trend toward significance; visual attention scores remained higher in posttraining measures (104.60 vs 101.58 for auditory).

Table 5 shows which tests demonstrate significant improvement, where relevant, related to each of the cognitive functions being assessed. This is discussed at length in the Discussion section.

QEEG

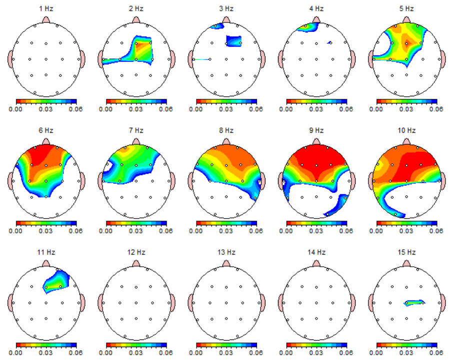
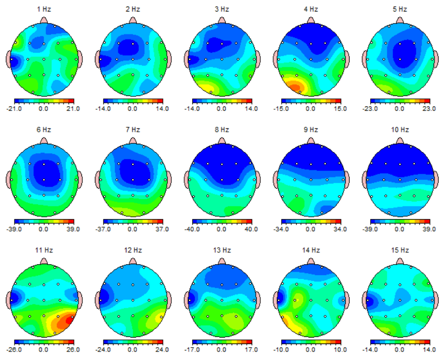
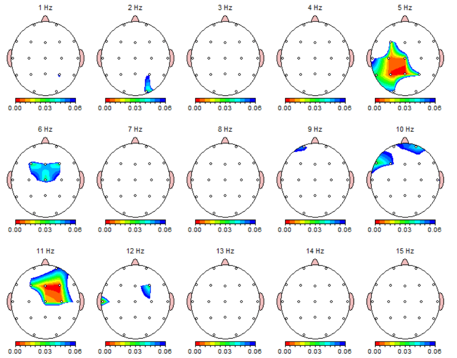
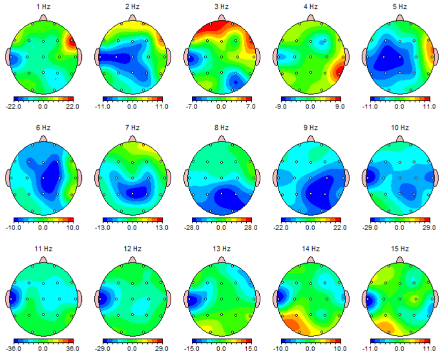
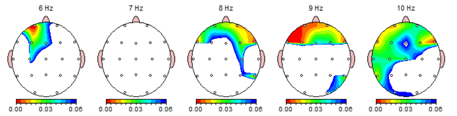
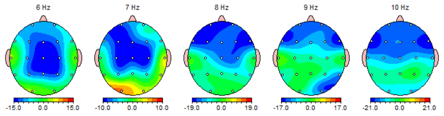
In considering the changes hypothesized with regard to cognitive functions, specific changes in qEEG were expected to occur. The figures below demonstrate significant differences in qEEG analysis following training for the NT group. The left figure shows the results of the planned paired 2-tailed *t* test while the figure on the right shows the direction of the change in percent differences in pre–post EEG power. The left figure shows the degree of significance of changes; white indicates no significant change, blue is a change at $P < .05$ and red $P < .001$. The color in the right image shows the direction of the change; blue indicates decrease and yellow-red indicates increase.

Since no consensus on the exact definition of frequency bands exists, the authors discuss specific individual frequencies. For the sake of conformity, the authors refer to the frequency bands as defined in the NeuroGuide database. These are delta (1-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (13-30 Hz), and gamma (30-50 Hz).

Decreased Delta, Theta & Alpha

As hypothesized, the NT group demonstrated significant absolute power decreases in the theta and alpha frequency bands. The delta band also showed some lesser but still significant reduction. Specifically, decreases were observed across 2 to 11 Hz with eyes closed and 2, 5 to 6, 10 to 11 Hz with eyes open. The changes were noted primarily in the frontal lobes (electrodes FP1, Fp2, F7, F3, Fz, F4, F8, C3, Cz, and C4) while the changes in theta could also be observed over the parietal cortex, most dominantly in the left hemisphere (P3, Pz). These changes can be observed in Figure 3. The CON group did not demonstrate this trend.

Figure 2-3: Pre-Post changes in Delta, Theta and Alpha Amplitude

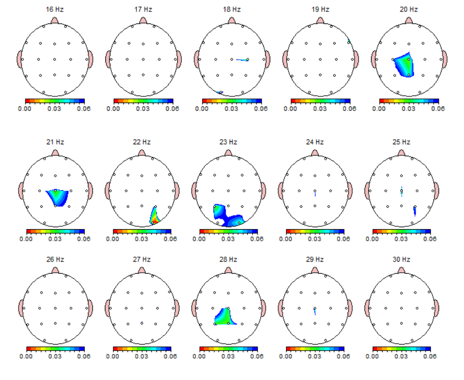
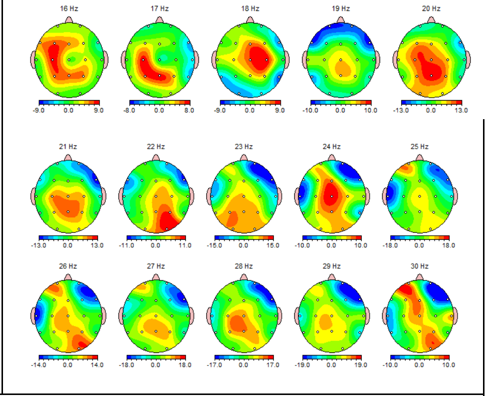
Absolute Power	Eyes Closed		
	Eyes Open		
Relative Power	Eyes Closed		

Note: bandwidth segments cut to show significant changes only. Full qEEG maps are available in supplemental figures.

Increased Beta

Following the hypothesis of decreased slow-wave power, it was expected that the faster beta frequencies would show a more dominant presence. As expected, the NT group demonstrated significant relative power increases in various frequencies within the beta bandwidth, specifically 14, 16 to 18, 22 to 40 Hz with eyes closed and 20 to 23, 28, 34, 37 to 39 Hz with eyes open. These changes were observed across frontal regions (Fp1, Fp2, F7, F3, Fz, F4, F8, C3, Cz, and C4), and are shown in Figure 4. As these changes were limited to the relative power spectrum (there were no significant changes in corresponding frequencies in absolute power) these increases must be interpreted with caution as they may be the result of decreases in other frequencies. Once again, the CON group did not demonstrate this change.

Figure 2-4: Pre-Post changes in Beta Amplitude

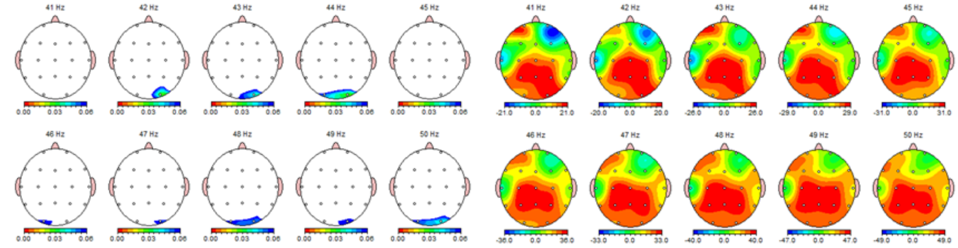
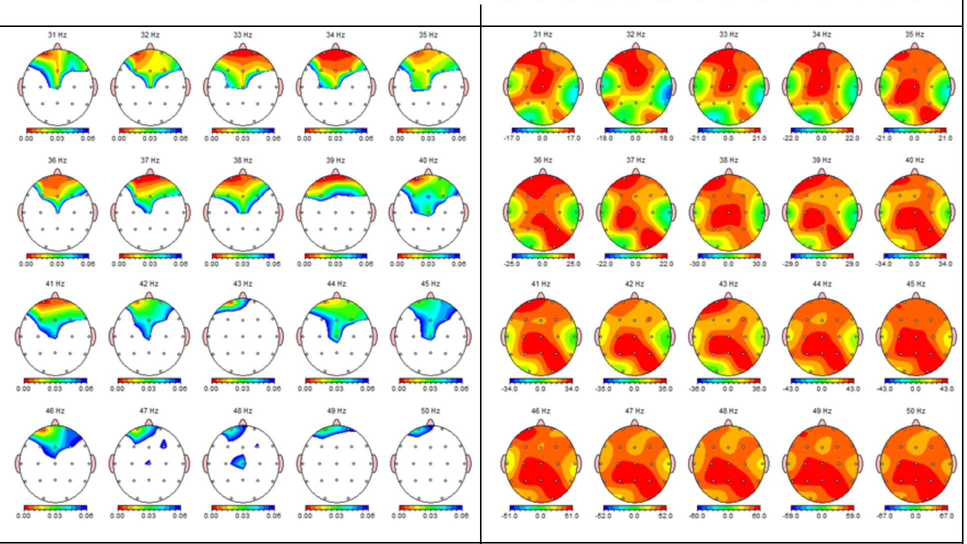
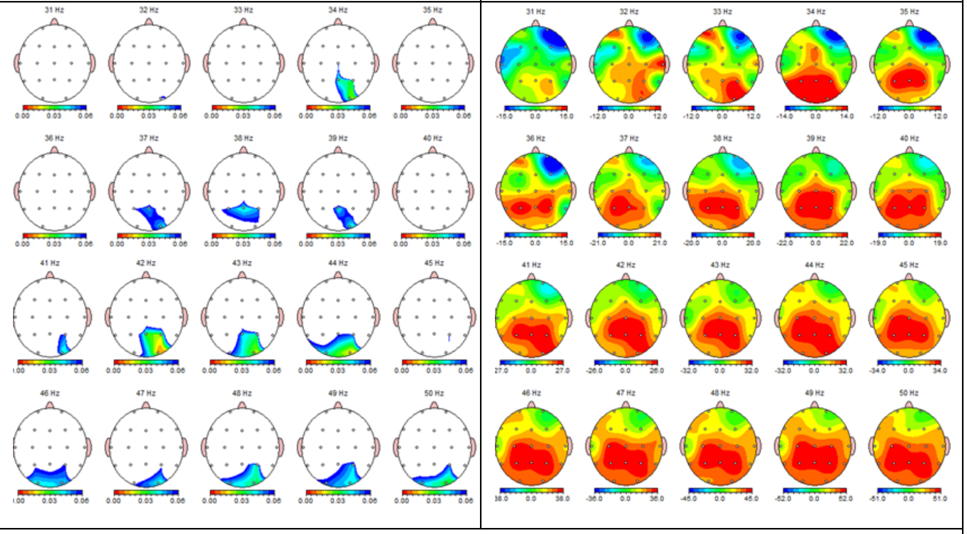
Relative Power	Eyes Open		

Note: bandwidth segments cut to show significant changes only. Full qEEG maps are available in supplemental figures.

Increased Gamma

The final hypothesis put forth was that the NT group would demonstrate significant increases in Gamma band frequencies, especially at occipital sites. This was the case with eyes open; as shown in Figure 5, the 40-50Hz bandwidth saw significant gains in occipital and parietal sites (O1, O2, Pz, and P4). Interestingly, and also shown in Figure 4, an unexpected trend occurred with eyes closed: the same bandwidth saw significant increases across frontal sites (Fp1, Fp2, F3, Fz, F4, and Cz). The CON group actually showed the opposite effect decreased gamma power at O1 and O2 with eyes open, and no significant difference with eyes closed.

Figure 2-5: NT group Pre-Post changes in Gamma Amplitude

Absolute Power	Eyes Open	
Relative Power	Eyes Closed	
	Eyes Open	

Note: bandwidth segments cut to show significant changes only. Full qEEG maps are available in supplemental figures.

Other significant changes

No other significant changes fitting any attentional theory were observed. Full qEEG maps for each testing condition are available in supplemental figures (available at http://eeg.sagepub.com/content/by/supplemental-data).

Discussion

3D-MOT

As expected, the NT group improved over time at the task and even the final session scores continued to show improvement. While the current study does not assess longevity, results suggest that the benefits observed may persist in time. This is demonstrated in the improvement in 3D-MOT scores of the initial and final testing sessions for CON group. The CON group significantly improved over 7 weeks and their session scores resemble the first 2 sessions of the NT group. It appears that the CON group is able to consolidate and maintain an effect from the first testing session despite a 7-week delay between sessions.

Cognitive Functions

Attention

The 3D-MOT task most heavily solicits attentional resources, and results indicate that sustained, selective and divided attention as well as inhibition can be enhanced with 10 sessions of training. Attention is essentially the gateway of perception into consciousness, it is what “decides” what we see, hear, feel, taste, and smell. Attention modulates our ability to learn and communicate with others, and is a fundamental component of the human mind and consciousness.[21,22]

Since 3D-MOT is purely visual, it begs the question: Why are gains observed in the auditory domain? As described by Wickens,[23] attentional capacities across different modalities are limited by a common resource pool. For example, when performing a complex visual procedure (eg, a complex driving scenario), auditory tasks (eg, maintaining a conversation) become more difficult.[24] It stands to reason that when the substrates of this shared pool are improved all implied modalities would show gains.

Sustained Attention

Traditionally, sustained attention tasks require that attention be maintained over a relatively long period of time. The 3D-MOT task taxes this as a session is approximately 30 minutes. More, sustained attention tasks must also be sensitive to slight variations on the scale of fractions of a second. The movement phase of a 3D-MOT lasts only 8 seconds per trial; however, the trainee must consistently maintain attention on all 4 targets. If a target is lost, it cannot be reobtained; Even the slightest lapses in attention result in the failure of the trial.

Selective Attention

A trainee must also selectively focus on targets and not on distractors. As the speed of trials increases there are more interactions between targets and distractors. The distribution of attentional resources must remain fluid; a target close to a distractor demands more attention than a target in relative isolation.

Inhibition

Inhibition, in contrast to selective attention, is the ability to not focus on nonpertinent information. They are complementary processes although are considered different constructs.[25] In 3D-MOT, inhibition is regularly called upon: Targets and distractors interact often during the movement phase and one must inhibit focus from distractors.

Divided Attention

In MOT, divided (multifocal) attention plays an important role.[26] The 3D-MOT trains an ability to dynamically shift attention along multiple loci, a fundamental principle of divided attention.[27]

Short Term & Working Memory

Short-term memory is the ability to temporarily retain a limited amount of information in consciousness.[28] Working memory is the ability to manipulate information stored in a temporary bank to suit the task at hand.[29] Previous research has shown a strong link between short-term memory and working memory, the former often posited as being a limiting factor of the latter.[28] Working memory is a higher order task, often being considered a necessary precursor to executive function.[30] Attention is strongly implied in working memory, as is seen in the deficits in working memory in attention deficit populations.[31]

In 3D-MOT, targets must be retained in temporary memory stores (short-term memory) while the targets' movement is internally processed (working memory). The task may affect working memory by improving attention or may directly improve working memory. Once again it appears that shared resources are at play as auditory working memory shows gains similar to those seen in the visual modality; the research of Saults and Cowan[32] supports a shared resource pool.

Visual Information Processing Speed

Perceptual stimulus first enters through sensory organs before being transferred to primary processing areas and then through higher order processing or "association" areas. The speed at which this "bottom-up" transfer occurs is referred to as information processing speed, and can impact decision making and reaction time.[33]

The speed thresholds directly evoke visual information processing speed capacities. Previous work[9] has demonstrated that as individuals progress through training their speed threshold scores increase.

Quantitative EEG

Theta/Beta & Attention

In examining attention using qEEG, studies observe high amplitudes of slow wave activity (2-11 Hz) and relative deficits in faster beta activity (12-20 Hz) in those with attention deficits.[6,34] Psychostimulant pharmacological and neurofeedback interventions for attention deficits have a normalizing effect on the EEG in that they decrease excessive slow waves and increase deficient beta and note resulting improvements in attention.[6,34,35] These findings are concurrent with those observed in this study: improvements in attention in the NT group corresponded with decreases in 2 to 11 Hz slow-wave activity and relative increases in beta.

Gamma, Binding & Neuroplasticity

The gamma band is relatively new to the family of EEG analysis.[36] The gamma band is traditionally seen as the “binding rhythm” in the brain responsible for the coordination and mobilization of cognitive resources for the task at hand.[37] It is said to reflect underlying large-scale cortical cooperation and phase synchrony triggered by thalamic pacemakers, playing a large role in attention and memory, and a critical role in synaptic plasticity.[37]

The changes observed here in the gamma band are focused on the occipital cortex, the region of the brain responsible for visual processing.[38] The parallel improvements in visual attention, visual working memory, and visual information processing speed are thus reflected in these gamma band increases.

Limitations of the Study and Suggestions Further Research

This study employed a relatively small sample size; however, considering the promising results of the current study, the authors suggest replication with a higher number of subjects. Different neuropsychological tests and brain imaging techniques as well as questionnaires regarding observed changes in day-to-day life could be used to verify transfer as well as control for test–retest effects. A greater number of sessions, longer training periods, and longer test–retest intervals could yield information on the ideal frequency and duration of training as well as shed light on longevity. The use of an active control group could ensure that observed changes were indeed due to 3D-MOT and not due to nonspecific factors. These changes would ensure stronger statistical significance, and further understanding of the cognitive functions and neural substrates at play in 3D-MOT.

Conclusion

This preliminary study demonstrated that 3D-MOT improves cognitive functions in a healthy population and corresponding changes in brain function were observed. The current study is a first step toward establishing 3D-MOT as a gold-standard cognitive enhancer. Training 5 weeks with 3D-MOT demonstrated robust effects on attention, working memory, and visual information processing speed as measured by neuropsychological tests while corresponding changes measured by qEEG were also observed. Together, these findings suggest that transfer to daily life should be observed; however, further research could include real-world variables for verification. No side effects were noted other than anecdotal reports of mild fatigue immediately following training, and dissipating within 20 to 30 minutes following a session. In terms of time investment, 1 hour per week is sufficient; however, more research is needed to determine the optimal frequency and duration of training. It is currently unknown whether or not the effects of training persist over extended periods of time. No negative ethical issues were observed with regard to 3D-MOT training. Combining 3D-MOT with another type of cognitive intervention could yield superior results; further research is needed. No contraindications for 3D-MOT were observed. Finally, in terms of appropriate populations, this study further solidifies findings of transfer in healthy populations. Clinical populations exhibiting deficiencies in cognitive functions associated with those shown to improve following training would be good candidates for further research. 3D-MOT training could be beneficial for populations suffering from deficits in attention, working memory, and/or visual information processing speed, for example those with attention deficit disorder[39,40] or autistic spectrum disorder.[41] Table 6 resumes the findings of this study to that end.

Table 6: 3D-MOT as a gold-standard cognitive enhancer

Standard	Status	Details
(1) Robust Effects with Transfer	Yes	Attention, working memory, visual information processing speed; corresponding changes in brain function
(2) Side Effects/Toxicity	Insignificant	Occasional mild fatigue immediately following training, dissipating within 20-30 minutes
(3) Investment	5 hours	Optimal training frequency and duration is unknown; 1 hour per week is sufficient.
(4) Lasting Effects	Unknown	
(5) Ethical Issues	None	
(6) Mutually Exclusive	Unknown	Further research to examine training in combination; no contraindications were observed.
(7) Potential Populations	Known: Unknown:	Healthy, healthy aging, athletes. Clinical domains.

Author Contributions

BP was responsible for the design of the project, trained, and supervised the research assistants administering training, performed all pre- and posttesting, and performed all analysis. Authors JF and MB provided supervision and contributed to the design of the research project. TM, AB, MZ, KZ, SB, and OS, performed training sessions. B. Parsons was responsible for redaction and all authors approved the final version of the article.

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Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: BP is a scientific advisor of CogniSens Athletics Inc., which produces the commercial version of the NeuroTracker used in this study. JF is Director of the Visual Psychophysics and Perception Laboratory at the University of Montreal and he is the Chief Science Officer of CogniSens Athletics Inc, which produces the commercial version of the NeuroTracker used in this study. In this capacity, he holds shares in the company.

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Discussion

This section is presented in addition to the discussion in the research article above.

3D-MOT: the strength is in the design

What makes the 3D-MOT a tool appropriate to use for cognitive enhancement?

As discussed in the methods section, there are four characteristics of this paradigm that explain why it works. They are multiple object tracking, large visual fields, stereoscopic 3D, and speed thresholds. The task is designed to be ecologically valid (multiple object tracking, large visual fields and stereoscopic 3D) while also keeping the trainee in the zone of optimal development (adaptive staircase speed thresholds).

Fundamentally speaking, there is no strategy to 3D-MOT training. The training relies on basal cognitive functions, thus *isolating* them from any possible strategy. This isolation implies that other cognitive functions cannot be relied upon (or used to cheat) in the task. Once a cognitive function is properly isolated, it can be *overloaded*.

Overloading is a fairly simple concept: it means demanding more of a cognitive function than it is normally capable of performing. If this is done haphazardly, the demands are likely to be too far beyond the current level of ability that no adaptation can occur. When this is done within the zone of optimal development, adaptation and learning occur. The thinking is that over time, the learning is consolidated, the underlying functions improve, and this in turn leads to generalized enhanced cognitive functioning.

Up against the standard

The current research is a first step toward establishing 3D-MOT as a cognitive enhancer. The following sections discuss the current state of 3D-MOT to that end. As quickly becomes apparent, while the work is a first step toward that goal, it is impossible to achieve the standard with one small-scale research project like the one discussed herein. The limitations of the study are discussed where appropriate, as are suggestions for future research.

1. Robust transfer effects

First and foremost, the very first hypothesis is confirmed: the training group were able to increase their abilities within the 3D-MOT task. Further, with regard to hypotheses 2, 3 and 4, the current research study demonstrated significant gains in attention, working memory and visual information processing speed. As an addition to table 4 above, the results including average change, t-test p value, and effect size (r) are below in table 7. Note that p values corresponding effect sizes are only listed where p<.1.

As discussed in the article, a main effect of training was found $F(13,6) = 36.232$, $p = .000$, eta squared = .987; as was an interaction for training × group $F(13,6) = 13.201$; $p = .002$, eta squared = .966.

Table 7: Neuropsychological test results: extended table											
	NT Group (n=10)						*CON Group (n=10)*				
Measure	**Change**	**Lower CI 95%**	**Upper CI 95%**	**Sig.**	**ES**		**Change**	**Lower CI 95%**	**Upper CI 95%**	**Sig.**	**ES**
IVA+Plus® Auditory	8.18*	2.81	13.55	.007	.30		1.68				
IVA+Plus® Visual	7.03$^+$	-.75	14.82	.071	.24		1.12				
WAIS-Symbol Search	5.00*	2.04	7.96	.004	.36		2.90				
WAIS-Code	9.70*	6.80	12.60	.000	.35		7.50$^+$	1.87	13.14	.015	.23
WAIS-Block Design	8.00*	5.06	10.94	.000	.44		2.50$^+$	.414	4.59	.024	.19
WAIS-Number Sequence	-0.10						0.10				
WAIS-Letter-Number S.	1.80*	.59	3.01	.008	.24		1.10				
WAIS-Spatial Span	2.80$^+$	.54	5.06	.021	.43		1.60				
d2 Test of Attention	60.40*	40.27	80.54	.000	.38		44.20$^+$	10.06	78.34	.017	.24
D-KEFS Color Naming	-3.70*	-6.01	-1.39	.006	.43		-0.50				
D-KEFS Word Reading	-1.90						0.20				
D-KEFS Inhibition	-5.40*	-8.59	-2.22	.004	.28		-3.90$^+$	-7.02	-.78	.020	.26
D-KEFS Inhibition/Switch.	-6.70*	-10.58	-2.83	.004	.40		-5.20*	-8.78	-1.62	.009	.37
* significant at p<.01; $^+$ trend toward significance p<.1											

Regarding attention, there were a few interesting things to note. First, although the task is purely visual, gains were seen in the auditory domain as well. It appears as though the mechanisms underlying the gains in attention are subject to a pool of shared-resources.[113] As a matter of fact, the stronger gains in terms of modality were in the auditory domain (*r* = .30); however this is likely due to ceiling effects observed in visual results. As briefly discussed in the article, the visual t-test yielded only a *P* value of .071, which indicates a trend toward significance, however a small effect was nonetheless noted (*r* = .24). The d2 test of attention, not prone to ceiling effects did demonstrate a substantial and significant improvement for the training group with a medium effect noted (*r* = .38). While that does support the theory that visual attention is fundamentally at play, performance in the d2 is also reliant on information processing speed. More data is needed. Further research targeting normative populations should attempt to use another type of continuous performance test less prone to ceiling effects.

Working memory also appears to benefit from 3D-MOT training, and once again these gains are cross modal. Gains were notably larger in the visual domain (r = .43) than in the auditory modality (r = .24). There is, however, a weakness is in the tools utilised to measure working memory. It is difficult to appropriately isolate working memory from other cognitive functions since it is a higher order function that relies on lower order systems. It is possible that the gains seen in working memory are actually due to gains seen in other cognitive functions, for example attention.[121] Future research should utilize stricter statistical tests and attempt to further isolate working memory from other cognitive functions to better evaluate this change. That said, from a clinical standpoint, the source of the change isn't relevant for the well being of the person. Working memory skills are enhanced, and if a person is able to benefit from those enhancements in their daily life, the underlying source of the change is not inherently important to them.

Information processing speed was only measured in the visual domain, other than the one auditory speed subscale in the IVA+Plus® which did not demonstrate significance. The effect on information processing speed ranged from small to large (r = .28-.44). Information processing speed is an important component in the ever-evolving technological world. In today's information age, stimuli are delivered at an unprecedented speed, and faster capabilities in treating this information become important. There are equally many clinical populations that suffer from information processing speed deficits, and these impacts have real-world consequences that can impair cognitive functioning.[162]

Globally speaking, further research should examine the transfer effects using different validated measures not subject to the same ceiling effects observed here. By using real-world variables including academic or work performance, as well as subjective questionnaires assessing perceived change, valuable insight into the benefits of 3D-MOT training could be gathered. Using a greater number of subjects could also yield superior statistical analysis, including a correlational analysis to examine if there are any fundamental cognitive functions for 3D-MOT. At the moment, it is unknown what factors are responsible for initial differences in 3D-MOT performance.

Now that it has been established that 3D-MOT training enhances attention, working memory and information processing speed, these results need to be replicated in clinical populations. The first clinical populations worth examining are those who demonstrate deficits in these capacities, for example attention deficit/hyperactivity disorder, autistic spectrum disorder, and in cases of learning disabilities. More, other cognitive functions should be included as they may also demonstrate benefit from 3D-MOT training. Some higher-order functions, for instance reading, are likely candidates.[162]

Hypothesis 5 posited that there would be observable changes in qEEG that would reflect these enhancements. The research article above substantiates this claim, and thus this hypothesis is upheld. Future analysis will use the data obtained, but not yet analysed. This work will first examine the 2-channel EEG data acquired during training. This insight into what brain activity occurs during a 3D-MOT session will be valuable in order to better understand the changes seen following training. Next, the full 32-channels of EEG data will also be useful to analyse using other qEEG methods, for example standardized and exact Low Resolution Electromagnetic Tomography (sLORETA and eLORETA). These methods utilise algorithms to solve the *inverse problem* in EEG and thus extrapolate the origins of electrical activity in the brain.[130,131]

Further research could utilize different neuroimaging techniques in order to add to these findings. Magnetic resonance imaging (MRI) could provide data about structural changes, while functional magnetic resonance imaging (fMRI) during the task in real-time could yield more spatially precise information about which neural substrates are at play in 3D-MOT.

2. No Side Effects or Risk of Toxicity

As hypothesized, no notable adverse effects of 3D-MOT training were noted; hypothesis 6 is tenuously upheld. A few participants mentioned fatigue following the initial training sessions, but this subsided over the course of training. One subject complained of a mild headache in two instances, and in both instances the headache disappeared within an hour following the session.

In the future, researchers should examine these aspects more thoroughly. It is possible that different populations respond to training differently, and thus side effects may occur that are not observed in healthy populations.

3. Minimal time and monetary investment

Once again an initial hypothesis (hypothesis 7) proved true: 10 sessions of 3D-MOT training was sufficient to enhance cognitive functions and have a measurable effect on brain function. Further research should examine whether less training is needed in order to document changes, and if training over a longer period leads to further enhancement.

4. Lasting effects

Unfortunately, the current study offers very little information with regard to the longevity of the effects observed. No follow up testing was performed, and thus no hypothesis regarding long-term effects was presented. That said there is an interesting trend that suggests that gains may persist in time, at least with regard to the task itself.

In considering the initial and final assessment, the control group demonstrate significant improvement in the 3D-MOT task. Their final session, although it occurred six weeks after their initial testing session, is statistically equivalent to the very first training session of the training group, which occurred only days later. This suggests that the same learning and consolidation that occurred for the training group over the period of a few days was also maintained over six weeks in the case of the control group. This suggests that even with minimal exposure, learning occurs and can perhaps persist over long periods of time.

While this matter is far from established, it is an encouraging finding that warrants further examination. Studies that perform follow-up investigations at intervals spanning months and years are needed.

5. No ethical issues

While this current study did not at all attempt to address this issue, anecdotal data can be assessed in a general sense. First, the ease with which participants were recruited goes to the idea that there are not likely any ethical issues of great concern. Second, the inexistent dropout rate demonstrates that no new issues came up during the course of training. While it can be argued that individuals who might have issues would not have volunteered for participation, candidates had no knowledge of the task in question before receiving the consent form shortly before their initial session. This suggests that there were indeed no ethical issues at play, and hypothesis 8 is cautiously confirmed.

6. Can be used in combination

The current study examined 3D-MOT alone and thus cannot directly speak to the possibility of using it in conjunction with other interventions. That said, no contraindications were observed. The only possible note to that end is with regard to fatigue; because 3D-MOT demands a significant effort, there were some reports of fatigue following training. Other types of intervention that are prone to or would suffer from the effects of fatigue may not be appropriate when applied in quick succession with 3D-MOT.

7. Can be applied to any population

Much more research is needed before claims can be made regarding the applicability of 3D-MOT to clinical populations. Previous research has shown the benefit for aging populations, and this study suggests that there are a great number of other candidate populations. Healthy populations benefit from gains in cognitive functions following 3D-MOT training, and the degree of benefit appears to be small to medium. The day-to-day significance of these gains has yet to be established and, as discussed above, future studies could make use of real-world variables to that end.

Conclusion

The market for cognitive enhancement tools is growing, and although they are the driving force behind a now billion-dollar market, these tools are rarely the subjects of intense scrutiny. The paradigm under which these tools are assessed is inconsistent at best, and it is thus very difficult for even someone well versed in the matter to adequately judge each and every intervention.

After examining much of the research into these interventions and the rebuttals of critics, it was possible to establish a standard for cognitive enhancement tools. These tools should be strong in their main and transfer effects, have little or no risk of side effects or toxicity, involve little time and monetary investment, not raise ethical issues, be feasible to combine with other interventions, and should finally have a wide range of application.

To that end, 3D-MOT demonstrated significant effects with consequent transfer to measures of attention, working memory and information processing speed. Functional changes in the brain were also observed. There were no significant side effects associated with training. A relatively small investment was needed, only 5 hours over 5 weeks. No ethical issues were noted, and no contraindications that might show that 3D-MOT and other types of interventions are mutually exclusive. Finally, the current study yields data on healthy individuals, and suggests future populations for study including those with attention deficit/hyperactivity disorder, learning disabilities, autistic spectrum disorders, executive dysfunctions and in aging.

While much work is still needed, this project was a first step toward establishing 3D-MOT as a cognitive enhancement intervention. The research into 3D-MOT is promising and warrants further work. More, the establishment of the standard criteria set a barometer against which all cognitive enhancement tools can be measured.

Budget & Declaration of Conflicting Interests

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