Tartu Ülikool
Psühholoogia instituut

Dmitri Filimonov

Exploring the functional system of mental imagery by rTMS targeted at different cortical areas

Magistritöö

Juhendaja: Talis Bachmann

Tartu
2013

Table of contents

Kokkuvõtte

Visuaalne kujundlikkuse funktsionaal süsteemi uurimus erineva ajupiirkondade rTMSi kasutades

Visuaalse vaimse kujundlikkuse loomus ja selle närvialus on keeruline ning ei ole lõplikult mõistetud. Vaimse kujundlikkuse närvialus tundub olema piisavalt hästi selgitatud (pakkub rohkem teadmisi selle filosoofiseks ja fenomenaalseks arusaamiseks), kuid osalised sarnasused visuaalse tajuga tegelikult teevad taju ja kujundlikkuse aju mehhanismide eristamist keeruliseks.

Erinevus visuaalse koore rolli mõistmises on oluline ja peab olema õigesti mõistetud. Kui visuaalne koor mängib sama rolli nagu taju – kujundlikkus võib olla muudetud selle üheks vormiks ja erineda ainult aste, kuid mitte liigi poolest. Kui visuaalne koor funktsioneerib erinevalt ja mängib teistsugust rolli, siis kujundlikkus võib olla nähtud kui rohkem iseseisev fenomeen, mis jagab mõningaid sarnasusi aste, vaid mitte liigi poolest. Korduv transkraniaal magnetstimulatsioon (rTMS) on sobiv viis uurida kausaalne roll valitud aju piirkonnad viauaalses vaimses kujundlikuses ja seepärast käesolevas uurimistöös tehti ettepanek, et rTMS võub modifitseerida kuhäirib kujundlikkust.

Experimentaalsed tulemused näitavad et statistiliselt olulisis käitumuslikke tulemusi pole nii korrektses ülesanne soorituses kui ka visuaalsuse hinnangus. Selline situatsioon võib olla ka valimi suuruse kui ka suhteliselt nõrga rTMS intensiivsuse tõttu. Kuna palju uurimused kasutavad 1Hz rTMS stimulatsioon ja nende tulemused on signifikantsed, selline uurimus ei leia mingi effekti cognitiivse ülesanne jõudluses seotud kujundlikkuse pilte manipulatsiooniga. Üks võimalik seletus on seotud liiga vähe rTMS impulssid.

300 impulssi iga piirkonna jaoks kasutamine on selles uurimuses põhjustatud selles et kui teha rohkem, üldine stimulatsiooni arv ja aeg ühel katsepäeval võib väsitama katseisikud, mida mõjutab tulemused. Suhteliselt nõrk intensiivsus, mis oli 65% fosfeeni lävest oli kasutatud seepärast et tugevam intensiivsus võib fosfäänid tekkima, mida interfereerib kujundlikkuse ülesannega.

Sellise katse peatulemus näitab et selline rTMS protokool ei mõjuta aju piisavalt viisil, mida tähendab vajadust uus katseprotokooli kasutada teiste stimulatsiooni reziimidega visuaalse vaimse kujundlikkuse fenomeeni uurimises.

Abstract

The nature of visual mental imagery and its neural basis is complicated and not conclusively understood. Neural basis of mental imagery seems to be quite well clarified in general (providing more knowledge for its philosophical and phenomenal understanding), but partial similarities with the visual perception actually make it complicated to differentiate brain mechanisms of perception and imagery.

The specification of the role of visual cortex is essential and its function in relation to imagery must be correctly understood. If the visual cortex plays the same role as in perception – imagery may be reduced to one of its forms and differ only in degree, not in kind. If the visual cortex functions differently and plays a different role, then imagery may be seen as a more independent phenomenon, which only shares some similarities in degree, but differs in kind. Transcranial magnetic stimulation (TMS) is a proper means to study the causal role of selected cortical areas in mental functions and we capitalize on this possibility in the present thesis.

The experimental results reported in this study showed no statistically significant effect of correct task performance and vividness ratings as dependent on rTMS conditions. In fact, this situation may be due to both small sample size and/or relatively weak rTMS intensity. Although many studies using 1-Hz rTMS stimulation have shown behavioral effects, this study failed to find significant effects on performance in the cognitive task based on covert manipulation with mental images. One possible reason for the absence of effects could be not too many rTMS pulses. The use of 300 stimuli for each condition in this study had a reason that overall time of one experimental day for each participant would be too long and make them tired, possibly jeopardizing the imagery task performance. The relatively small intensity of 65% of phosphene threshold was applied because with higher intensities, phosphenes would interfere with imagery-task performance.

The main result of the present study showing a negative experimental effect is that this rTMS design does not affect brain in a proper and/or strong enough manner, which means a necessity of new experimental design with different stimulation regimens to be chosen for further investigations of mental imagery aiming at exploring the relative roles of the selected cortical areas in mental imagery.

Introduction

The nature of visual mental imagery and its neural basis is complicated and not conclusively understood. To put it simply, visual mental imagery is an ability to experience something visually without using the eyes. Yet this concept has not been too often within the scope of scientific interest. General philosophical problems concerning the nature and scientific relevance of the problem of imagery are related to its very existence and its distinction from perception (for example, see Finke, 1989; Thomas, 1989; Wittgenstein, 1967; Kosslyn, 1980). These controversial issues can be presented as questions:

1. Does imagery exist as a phenomenon, or is it just seems like one?
2. Does imagery differ from perception in kind or just in degree?
3. Is visual mental imagery truly "visual" (and to what extent)?
4. Is mental imagery a grounding basis for semantics, or opposite to it?

In the research below I rely on the assumption that imagery is indeed a form of experience. If so, it has to be explained, like other scientific concepts (such as electrons, etc.). Referring to perception, imagery is a distinct phenomenon, yet *sharing* many common processes and outcomes with perception. However, at least phenomenologically these states are *not equivalent*. Not only the differences appear in vividness and transperancy, but when we experience mental imagery, we *know* it is different from visual perception. There is also a well known philosophical argument defending the phenomonological independance of imagery: its content is controlled and/or modulated by our will, compared to what we can do with perception (Wittgenstein, 1967; MacGinn, 2004).

Neural basis of mental imagery seems to be quite well clarified (providing more knowledge for its philosophical and phenomenal understanding), but partial similarities with the visual perception actually make it complicated to differentiate brain mechanisms of perception and imagery. Furthermore, there is evidence of functional, anatomical and phenomenal overlap between mental imagery and other cognitive functions as well: such as attention and working memory. The idea of this research is to shed some more light on the functional system subserving imagery.

It can be said that mental imagery and perception share internal similarities in their functioning. Ganis et al. (2004) summarized several of these findings:

1. The interference of visual imagery selectively with visual perception is greater than that with auditory perception (Craver-Lemley and Reeves, 1992).
2. Scanning greater distances across visualized objects requires more time (Denis and Kosslyn, 1999).
3. Eye movements made during imagery are similar to those made during perception (Laeng, Teodorescu, 2002; Ganis et al., 2004).
4. Both images and percepts encode spatial dimensions and spatial relations among objects (Pinker and Finke, 1980).
5. Closer visual inspection of an object from different points of view reveals its previously unrecognized properties. There is some evidence that manipulation of mental images can also reveal patterns in the image that were not apparent when the image was initially visualized (e.g., Brandimonte et al., 1992; Chambers and Reisberg, 1985).
6. Mental imagery and perception share intentionality (Harman, 1998), which may be assumed as one of the core properties.

History knows at least two main types of approaches to the imagery-perception problem: “analog” approach, which postulates similarities in visual mental imagery and visual perception in terms of their sensory “fabric” and “difference” approach, which emphasizes separate ways of functioning and anatomical-physiological distinctions of the two systems. Such dichotomy can be explained by the nature of imagery itself and its position, thus this approach is not surprising and not confronting. The first one of the above approaches is more widespread. For example, some researchers (Finke and Slayton, 1988; Intraub and Hoffman, 1992; Johnson and Raye, 1981) have demonstrated that subjects may confuse between actual visualization of a stimulus and mere imagination of having seen it.

Basically, all general ideas of “analog” approaches can be summarized in a cognitive model of visualization (Kosslyn, 1980) which puts forward a single visual buffer as being used in a ‘bottom-up’ manner to “display” visual percepts and a ‘top-down’ manner to “display” visual mental images. Mentioned approach also predicts neural and cortical structures of mental imagery functional system and propose visual buffer for its performance in the same retinotopically organized visual areas of the cortex that are essential for processing vision from external stimuli in case of visual perception (Kosslyn, 1994; Kosslyn et al., 1995; Tanaka et al., 1991). Along this line, several researchers hold the position that **primary visual cortex is actively involved in generation of visual mental images in the same functional manner as it works during perception and plays an essential role in mental imagery** (Douglas, Rockland, 1992; Miyashita, Chang, 1988; Kosslyn, Thompson, 2003; Kosslyn et al., 1996; Kosslyn et al., 1999; Sereno et al., 2001; Rockland et al., 1992).

Another but perhaps less popular approach – the ‘difference’ theory -- stands for functional separation between perception and imagery. In other words: it pays attention on differences, some of which may be critical for strict distinguishing of visualization and visual perception. The results mentioned earlier suggest that a functioning visual system may be necessary for visualization. However, the nature of activation of the visual system in this condition is not similar to perception (for example: Ganis, Shendan, 2008), as well as the role it plays.

Brain mechanisms of imagery are often studied with fMRI. The fact that a visual area is active at some point during a lengthy fMRI scanning period does not necessarily imply that neural activity during visual mental imagery is the same as the activity during visual perception. Some researchers suggest that visual mental imagery implicates visual processes at higher levels of integration than those performed by primary visual cortex (Bartolomeo, 2002), which also explains the data from reports of patients with occipital damage and perceptual deficits who nevertheless show preserved visual mental imagery (VMI). This point of view can be summarized with a following statement: **The visual cortex activation may alternatively be explained as a type of feedback from higher cognitive areas and/or as a form of maintenance for some of the mental imagery properties.**

The difference in understanding the role of visual cortex is essential and must be correctly understood. If the visual cortex plays the same role as in perception – imagery may be reduced to one of its forms and differ only in degree, not in kind. If the visual cortex functions differently and plays a different role, then imagery may be seen as a more independent phenomenon, which only shares some similarities in degree, but differs in kind.

Research question

The main idea of this research is to investigate complex relationship between frontal brain regions, which are meant to execute, support and coordinate behavior in a top-down manner (including deliberate manipulations of mental imagery), temporal areas, which are connected to long term memory (LTM) and thus provide stored information for imagery, and primary occipital cortex, which activates during mental image construction and perhaps makes it "visible", including activity necessary for representing features of the imagined objects. In the present thesis I take the position of the "difference" approach, which considers imagery as an individual phenomenon, with similarities to perception, but not equivalent to it.

The role of cortical frontal regions, occipital cortex and temporal-occipital junction can be investigated and checked with the help of transcranial magnetic stimulation (TMS) technique, which perturbs the normal perfomance of the cortical area where it is applied. Typically, perturbation by high-frequency repetitive TMS (rTMS) leads to facilitation of function and slow rate rTMS (e.g., 1-Hz) causes inhibition. Both imagery vividness and objective imagery task performance and its development can be measured in different conditions of targeting rTMS to different locations. In what follows I will describe the functional properties of cortical areas selected for experimental study and put forward what are the expected outcomes of rTMS stimulation of these selected areas.

Prefrontal cortex

Higher cognitive functions are all associated with consciousness and share a property of "being held in mind" for a period of time. Several neuroimaging studies indicate that it is associated with activity in a system involving both prefrontal cortex and posterior areas, determined by the nature and type of cognitive function (Frith, Dolan, 1996). Several studies propose that cognitive control and properties of working memory are connected with active maintenance of patterns of activity in the prefrontal cortex (Miller, Cohen, 2001), which seems to be extremely flexible and can be rapidly and reversibly increased or decreased by molecular signaling events (Arnsten et al, 2010).

Some researches showed that the amount of overlap in activation between imagery and perception varied across the brain, and was maximal in frontal cortex (Kosslyn, 2004), which can explain the earlier mentioned phenomenological similarities of imagery and perception in a way that subject performs similar (executive, exploratory) behavior with regard to the both phenomena. In this experiment it can be expected that frontal rTMS will disturb these properties so as overall mental imagery development.

Occipital cortex

As it was mentioned earlier, visual cortex is activated during mental imagery (Kosslyn et al., 1995) and some studies show that functional deactivation of visual cortex can alter the quality of such internally generated images (Kosslyn et al., 1999).

Yet the relationship between prefrontal and occipital cortex is not understood clearly. If we accept possible differences in occipital functioning during mental imagery and perception, then we nevertheless must give a theoretical explanation to the possible role of the occipital areas. Relying on previous knowledge and logic, it can be assumed that occipital cortex makes images "visible" and more "perception-like". In this case, higher occipital activity can lead to increasing vividness, but may at the same time also impair executive function (such as imagery task performance). One of the main assumptions is that when imagery becomes more perception-like (vivid and colored), the brain begins additionally process it in the way as it processes perception, which makes imagery less susceptible to the top-down control. In the present research I suggest that occipital rTMS will disturb imagery vividness, yet may preserve or even facilitate executive control over mental manipulations with imagery, which altogether must lead to decreased ratings of imagery vividness after rTMS (compared to sham) combined with unchanging or even improving task performance.

Temporal-parietal-occipital junction

Sevral studies of imagery showed that imagery requires information retrieved from long-term memory as well as participation of attention (Kosslyn, Thompson, and Ganis, 2006; Pearson, 2001; Pearson, Logie, and Green, 1996). It seems that temporal-parietal junction is also involved in processing in a manner of identification and evaluation of salient or unexpected sensory events (Corbetta et al., 2000; Arrington, Carr, Mayer, & Rao, 2000; Serences et al., 2005). Another interesting fact is that lesions of the temporal-parietal junction, mainly located in right hemisphere, may lead to deficits in the conscious perception of sensory stimuli (Friedrich, Egly, Rafal, & Beck, 1998). The junction has been proposed by some authors as interrupter of ongoing processes for the analysis of potentially relevant novel visual stimuli (Corbetta & Shulman, 2002). Several researches also propose that a putative fronto-parietal network may modulate visual processing via back projection influences (Ruff & Driver, 2006; Serences & Yantis, 2006; Miller & D'Esposito, 2005). In the context of mental imagery it may act as a modulator of attention and also may serve as a factor which can influence imagery task performance: it can alter accuracy, but preserve or facilitate vividness.

Because our knowledge in this domain is scarce, the present study can be regarded as an exploratory one aiming at getting firsthand knowledge on the relative roles of the aforementioned brain areas in mental imagery and its voluntary control. I will use 1-Hz rTMS for suppressing the functionality of the selected cortical areas. As a task where measurable cognitive performance essentially is based on manipulations within mental imagery I use the 'moving spot task' (Attneave and Curlee, 1983).

Theoretical premises and hypotheses

Consciousness and higher cortical integration levels, such as frontal lobes, play general role in mental imagery control and development, but occipital cortex plays the role of additional support system and makes imagery more vivid and detailed. More specifically:

1. More expressed frontal activity may facilitate executive functions and performance on mental imagery related tasks, but make it less perception-like (less vivid and colored).
2. Stronger occipital activity can lead to increasing vividness, but lowering executive function (such as imagery related task performance) by making imagery less controlled and more perception-like (vivid and colored) or leaving it unchanged.
3. Right parietal activation will affect vividness as it is likely to engage the system of attentional top-down control either leading to suppression of visual images or facilitation of them.

Thus, main experimental assumptions are:

1. Occipital rTMS will lead to better imagery task performance, but lower vividness.
2. Frontal rTMS will lead to poorer imagery task performance.
3. Parietal rTMS may increase or decrease vividness.

Method and experimental procedure

Participants

At first, there were 15 healthy, right-handed individuals (age: 19 – 27 years) recruited for participation. The selection criteria included the necessary standardized requirements for subjects health and personal history accepted in the TMS research worldwide (e.g., absence of epilepsy, surgical implants, no pregnance, no relatives in the risk groups, etc.) to provide safety for the participating subjects. Each participant signed the informed consent paper where experimental methods (such as TMS definitions) and participation criteria as well as possible treatment effects were described. It was also explained that if any participant would want to quit the experiment, (s)he could do it at once. Each participant was subjected to MRI scan and acquired a MRI image of his/her brain necessary for individualized neuronavigation of TMS. During experiment some subjects had to be excluded from the final sample. Several participants fell ill (for reasons different from the participation in the experiment) and had to quit; thus at the end there were 9 participants: 1 male and 8 females.

Experimental design

For each participant the experimental procedure took two separate days, including 8 rTMS blocks and 8 corresponding Attneave and Curlee's Moving Spot Task test blocks. There were 4 rTMS and Moving Spot Task blocks in one day. One rTMS block included 5 minute 1-Hz rTMS stimulation of the selected brain region. Stimulation was applied to the following areas: left and right dorsolateral prefrontal cortex (DLPFC), left and right occipital cortex (OCC, or V1), left and right occipito-temporal junction (Junction) and left and right sham conditions. The stimulation order was specially grouped to avoid repetitions and exclude the stimulation order artefacts on behavioral results. Each Moving Spot Task test was presented right after a rTMS block containing 10 imagery-task trials. No more imagery-task trials per block were used because the rTMS aftereffect can not last very long. Number of trials with correct responses, corresponding to each TMS condition were assessed. After each trial a subjective visibility scale with 4 gradations from complete invisibility to full visibility was presented where each participant evaluated how clear and vivid his mental imagery was during the imagery test. Correct trials and vividness level were compared.

Moving Spot Task

The Moving Spot Task was chosen because of its informational content: it gives both behavioral data of correct and wrong trials, which in turn can measure task perfomance and accuracy, and also allows for evaluation of subjective experience of vividness and clarity of the mental images underlying covert manipulations with an imagined object. For each participant a grid with 36 cells (6x6) was presented on computer monitor, with a dot (spot) positioned in a randomly selected grid cell. The grid was presented and its presentation parameters controlled by a desktop computer. After 1500 milliseconds necessary for remembering spot position it disappeared and participants closed their eyes, imaging the grating with the spot. Thereafter, commands followed indicating the next position the spot had to be mentally moved within the grid, by steps of one grid cell at a time ("right", "left", "up" or "down"). Thus, the spot had to be mentally moved in the direction specified by the commands which were given ten times with 0.4 seconds interval between the commands. Subjects had to specify the final position the spot arrived and report it. Errors of performance were recorded. The inter-command interval was specially calculated before the main experiment in a pilot study so that in normal conditions people would make mistakes in about 40% of trials (for this calculation the person not included in participant list made several trials with different interval lengths).

TMS

The format of repetitive transcranial stimulation (rTMS) was applied using the Nexstim OY stimulation and neuronavigation system equipped with a figure-of-eight coil for biphasic TMS-stimuolation protocol. Navigation of TMS focus locations vis-à-vis the cortical areas was aided by the MRI based NBS visualization system that can be used online with experiment in real time. The rTMS target locations were indicated on individual MRI brain images, which can be "peeled" to different depths. Momentary locations of TMS focus were displayed on-line. Mapping and navigation was aided by infrared stereo-camera which allows get 3D information from the special reflectors mounted on subjects' head and TMS coil. Before the experiment, individual head size and reference point locations of that particular subject's head-brain were entered to the system by the pencil with similar reflectors as used on TMS coil and subject's spectacles. The rTMS trains were applied 4 times during first day of experimental procedure and 4 times during second day – each time for each brain region. After application of rTMS the behavioral task began. Before the experiment, individual phosphene thresholds (PTs) of stimulation were determined by stimulating the primary visual cortex.

The stimulation intensity used during the experiment was set at 65% of each participant's PT to avoid interference from phosphenes. During the experiment, rTMS was delivered with a frequency of 1Hz over 5 minutes which resulted in 300 stimuli for each condition. Participant also received TMS treatment in a sham regimen where the coil focus is drawn away from the critical location of the scalp and oriented parallel to the scalp. Frontal and occipital TMS conditions were compared.

Behavioral results

Descriptive statistics

Means of correct task performance and visibility ratings for all rTMS conditions and both sham conditions are presented in Table 1. Mean visibility ratings of each participant for each rTMS condition are presented in Table 2 in Appendix.

condition	Mean proportions for correct answers	Standard deviation	Means for vividness ratings	Standard deviations
RPFC	*0.4778*	*0.50230*	*2.5222*	*0.85101*
LPFC	*0.5556*	*0.49969*	*2.5667*	*0.73515*
ROCC	*0.6000*	*0.49264*	*2.5444*	*0.76674*
LOCC	*0.5444*	*0.50081*	*2.3778*	*0.90663*
RJUN	*0.5444*	*0.50168*	*2.7111*	*0.96273*
LJUN	*0.4667*	*0.49023*	*2.5222*	*0.82418*
RSHAM	*0.6111*	*0.49831*	*2.6889*	*0.89499*
LSHAM	*0.4333*	*0.49950*	*2.6444*	*0.78341*

Table 1: Means of correct answers and vividness for all rTMS conditions and sham. RPFC – right prefrontal cortex, LPFC – left prefrontal cortex, ROCC – right occipital cortex, LOCC – left occipital cortex, RJUN – right temporal-occipital junction, LJUN -- left temporal-occipital junction. LSHAM and RSHAM are left and right sham.

Correct task performance

The principal results of this experiment are as follows. As a statistical tool for effect assessment two-way repeated measures ANOVA was applied with rTMS conditions and laterality as factors. Analysis showed no significant effects in correct task performance between rTMS conditions

[F(3,24) = 0.580; p = 0.633]. For better visualization of results number of correct answers of all 9 participants is presented in Figure 1. For exploration of possible tendencies, several post-hoc tests were applied, yet none of the possible effects exist on significant level. It appears that there is also no laterality effect [F(1,8) = 5.025; p = 0.055] for correct task performance. The p value at first sight indicative of a tendency may be accidental, caused by a strangely low level of the results with left-side sham stimulation.

Vividness

According to repeated measures ANOVA, there is no statistical differences in visibility ratings both between rTMS conditions [F(3,24) = 1.188; p = 0.335] and for left-right hemisphere comparison [F(1,8) = 0.948; p = 0.359]. Figure 2 illustrates mean level of vividness ratings.

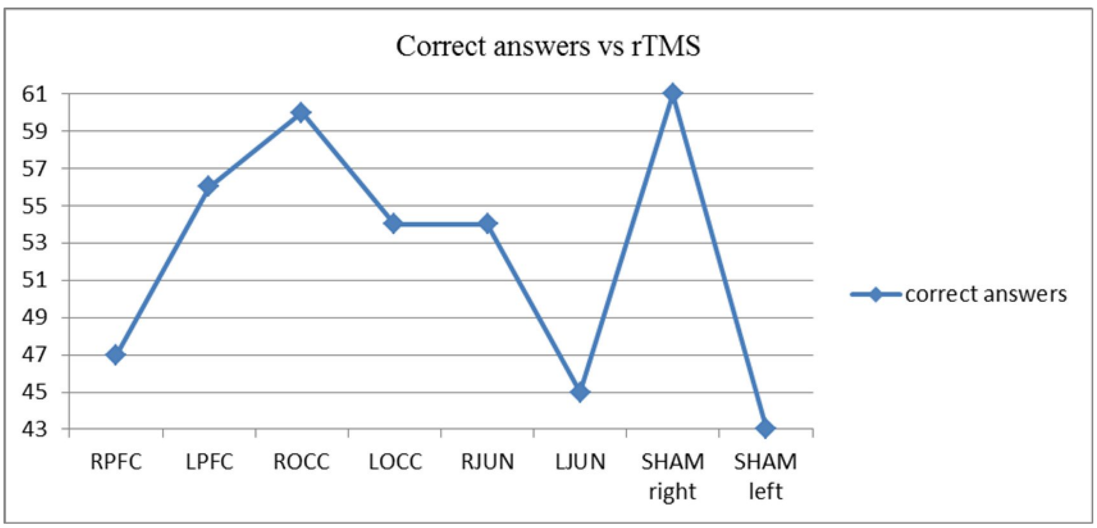


Figure 1:Number of correct answers for each rTMS condition. RPFC – right prefrontal cortex, LPFC – left prefrontal cortex, ROCC – right occipital cortex, LOCC – left occipital cortex, RJUN – right temporal-occipital junction, LJUN -- left temporal-occipital junction.

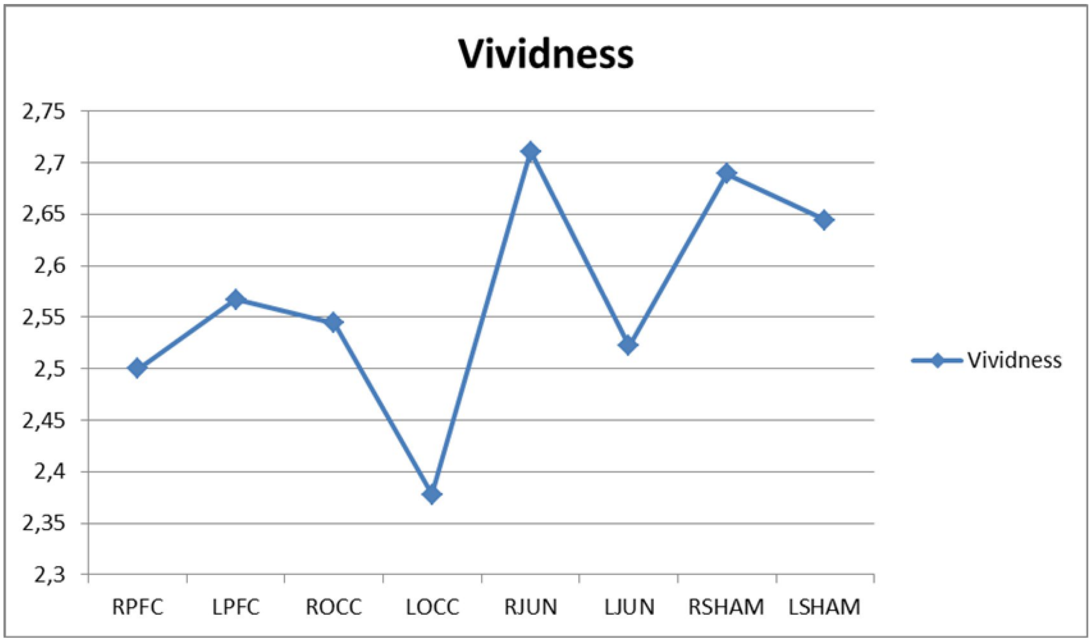
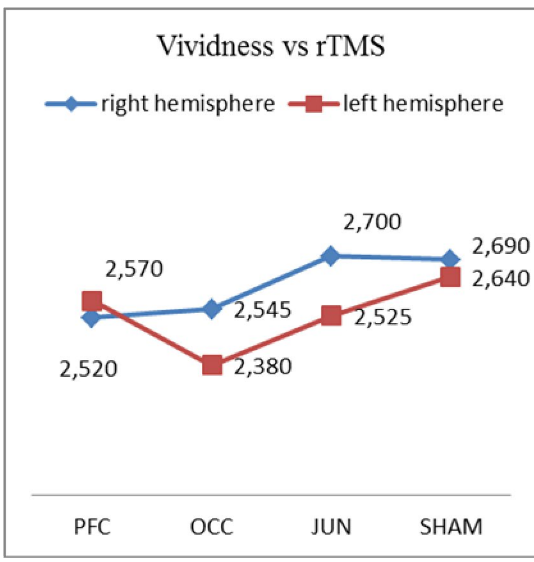


Figure 2: Vividness ratings for each rTMS condition. RPFC – right prefrontal cortex, LPFC – left prefrontal cortex, ROCC – right occipital cortex, LOCC – left occipital cortex, RJUN – right temporal-occipital junction, LJUN -- left temporal-occipital junction.



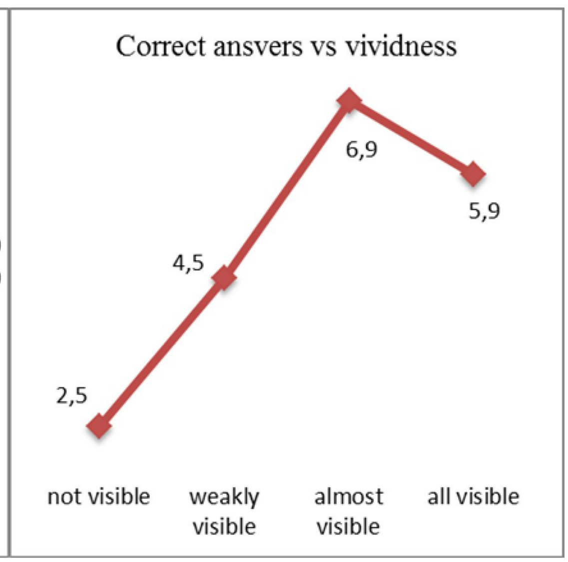


Figure 3: mean vividness ratings in each rTMS condition (varying lateraitly).

Figure 4: mean number of correct answers as a function of subjective vividness ratings.

Correct task performance in relation to vividness

There is a weak positive correlation between correct answers and vividness (r = 0.211[1]; $p < 0.01$). There is a possible tendency observed in Figure 4 that highest correct task performance is connected to vividness level above average ("almost visible"), yet a further increase in vividness may lead to accumulating mistakes would this result be supported by data from more extended studies.

Effects of accumulating experience

There is no significant effect of accumulating experience during two days of experiment neither in correct task performance [$F(1,8) = 1.452$; $p = 0.262$], nor in visibility ratings [$F(1,10) = 0.214$; $p = 0.886$].

Individual differences

There are statistically significant individual differences in mean levels of participants' correct task performance during all rTMS conditions and sham. For testing the significance, one-way ANOVA was applied with participant numbers as factors and correct answers as dependent variable. The results are the following: [$F(1, 8) = 15.154$; $p < 0.0001$] for correct task performance and [$F(1, 8) = 23.088$; $p = 0.0001$] for vividness. This shows that subjects perform the moving spot task with different efficiency.

[1] In this case of two rank-variables both Spearman and Kendall's correlation were used. Kendall's tau coefficient was r = 0,197

Discussion

The lack of statistical significance both for behavioral results and visibility ratings questions the hypothesis and can not support it. There is no statistically significant effect of correct task performance or vividness ratings as dependent on rTMS conditions. In fact, this situation may be due to high individual differences in levels of correct task performance in concert with a relatively small sample size, or perhaps insufficient influence of rTMS, but it also may represent real situation as it is, indicating that the present experimental paradigm is not well suited for studying involvement of the selected cortical areas in executing covert mental operations necessary in imaging.

It may seem that correct task performance should also be impaired by rTMS compared to sham. The absence of this effect can be alternatively explained not only by high individual differences in levels of correct task performance combined with a relatively small sample size, but may be also due to a considerably more substantial effect of the cognitive control mechanisms compared to the effects of rTMS. There may be two possible explanations of such results. First is that rTMS in this experiment made not enough effect. The second is concerning mental imagery itself. In general, it is widely accepted that high-frequency rTMS increases cortical excitability and low-frequency stimulation produces the opposite effect (Chen and Seitz, 2001). In case of this research, low-frequency stimulation (1Hz) was used to decrease cortical excitability, in order to interrupt places of rTMS application. According to one recent review of rTMS influence (Fitzgerald et al., 2006) in 6 experiments using 1Hz stimulation, 5 have reported no change in cortical facilitation\inhibition effect and this could be the case why in the present study effects were absent. However, the cited review analyzed motor-cortex excitability, but our rTMS targets were in different locations for which disruptive effectiveness of 1-Hz rTMS has been repeatedly shown (for references see Karton & Bachmann, 2011; Murd, Einberg, Bachmann, 2012). Nevertheless, perhaps higher frequencies in contrast might have more significant impact, yet in this study higher frequency were not used. Thus, in future research this is one idea to be tested.

In some studies that report significant changes with 1-Hz stimulation (Trojano et al., 2006) 600 TMS stimuli instead of 300 for each condition were used. The use of 300 stimuli in this study has a reason: overall time of one experimental day for each participant would be too long and make them tired.

Another aspect is connected to stimulation intensity. Some researchers report effects with intensity of 100% of subject's motor threshold (Beaken et al., 2011), and here just 65% of phosphene threshold intensity was applied. The reason was occipital stimulation: with higher intensities, phosphenes would interfhere with visualization of imagery.

In an experiment on top-down visuo-spatial processing functional anatomy Aleman et al. (2002) used rTMS protocols with much stronger rTMS treatment than in this experiment: 20 min 2-Hz stimulation with 90% of motor threshold intensity. For reasons mentioned, this experiment could not afford that.

Alternative explanation of the lack of positive results may be the nature of mental imagery. For example, Kosslyn et al. (2002) used rTMS to test occipital cortex excitability during mental imagery and found positive results, but their experimental design proposed extremely high frequency rTMS stimulation (300+ Hz) for a short period of time to obtain activation, not inhibition. It seems logical to assume, that centers responsible for visual perception are involved in imagery. One result in our study is consistent with the "analog" theory of visual imagery: there was a positive correlation between correct responses and vividness ratings.

Earlier in the discussion, we tentatively attributed the lack of effect to the small sample size. Yet, Figure 1 and values of the individual results of the subjects (Tables 1 and 2) show that the directions of the differences between rTMS conditions and sham conditions are haphazard. This suggests that even with a larger sample, but preserving the present experimental protocol the results may nevertheless remain negative.

Conclusion

The lack of behavioral results both for correct performance and vividness can not support nor decline the hypothesis. There is no statistically significant effect of correct task performance and vividness ratings as dependent on rTMS conditions. In fact, this situation may be due to both small sample size, unoptimal parameters of rTMS such as its intensity, number of pulses, etc.

Quite many studies have reported effects of 1Hz rTMS stimulation on cortical activation/inhibition and related behavioral effects, including when moderate rTMS intensities have been used (e.g., Karton & Bachmann; Murd et al., 2012). It may be that while their tasks were different, imagery performance may need different protocols of rTMS esperimets. Higher frequencies could have more significant impact on brain, yet in this study higher frequency could not be used because it rather increases cortical excitability and activation (for example, of visual area) which was not desirable in the present study because of the nature of the hypotheses. The use of 300 stimuli for each condition (which is rather small amount) in this study had a reason that overall time of one experimental day for each participant would be too long and make them tired

In addition to the possible problems with rTMS protocol and sample size it could be assumed that our rTMS design does not affect brain in a proper and strong enough manner, given the task of moving a spot mentally. Alternatively, it could be speculated that perhaps mental imagery itself is not affected by rTMS or even that aforementioned cortical structures do not play a role in this phenomenon. However, given the earlier fMRI and TMS research referred to in the introduction, this conclusion could not be logical and true. As demonstrated in numerous previous experiments, concerning functional anatomy of imagery, occipital cortex and frontal cortex in terms of its top-down regulation mechanisms definitely participates in fully functioning imagery.

To conclude, with the lack of the significant rTMS effect on mental imagery functional system in the present experiment, a new experimental design with higher stimulation durations and/or intensities must be chosen for further investigations of this phenomenon.

Acknowledgments

Author specially thanks his supervisor and the personnel of BachmannLab – especially Renate Rutiku and Carolina Murd -- for support and assistance during all phases of this study. However, for all possible issues or faults remaining in the thesis responsibility remains entirely with the author.

References

d'Alfonso A A L, Aleman A, Kessels R P C et al (2002). Transcranial magnetic stimulation of left auditory cortex in patients with schizophrenia. Effects on hallucinations and neurocognition. Journal of Neuropsychiatry and Clinical Neurosciences, 14: 77-79

Arnsten, A.F.T., Paspalas, C.D., Gamo N.J., Wang , M. (2010). Dynamic network connectivity: A new form of neuroplasticity. Trends in Cognitive Science, 14, 365–375.

Arrington, C.M., Carr, T.H., Mayer, A.R., Rao, S.M. (2000). Neural mechanisms of visual attention: Object-based selection of a region of space. Journal of Cognitive Neuroscience, 12, 106–117.

Attneave, F., Curlee, T. E. (1983). Locational representation in imagery: A moving spot task. Journal of Experimental Psychology: Human Perception and Performance, 9, 20-30.

Bartolomeo, P. (2002). The relationship between visual perception and visual mental imagery: A reappraisal of the neuropsychological evidence. Cortex, 38, 357–378.

Brandimonte, M.A., Hitch, G.J, Bishop, D.V.M. (1992b) Verbal recoding ofvisual stimuli impairs mental image transformations. Memory & Cognition, 20, 449-455.

Brandimonte, M.A., Hitch, G.J, Bishop, D.V.M. (l992c). Manipulation ofvisual mental images in children and adults. Journal of Experimental Child Psychology, 53, 300-312.

Baeken, C., De Raedt, R., Van Schuerbeek, P., Vanderhasselt, M.A., De Mey, J., Bossuyt, A., Luypaert, R., (2010). Right prefrontal HF-rTMS attenuates right amygdala processing of negatively valenced emotional stimuli in healthy females. Behavioural Brain Research, 214, 2, 450-455

Chambers, D., Reisberg, D. (1985). Can mental image be ambiguous? Journal of Experimental Psychology: Human Perception & Performance, 3, 317-328.

Chen, R., Seitz, R.J., (2001). Changing cortical excitability with lowfrequency magnetic stimulation. Neurology 57, 379 – 380.

Corbetta, M., Kincade, J.M., Ollinger, J.M., McAvoy, M.P., Shulman, G.L. (2000). Voluntary orienting is dissociated from target detection in human posterior parietal cortex. Nature Neuroscience, 3, 292–297.

Courchesne, E. (1978). Neurophysiological correlates of cognitive development: Changes in long-latency event-related potentials from childhood to adulthood. Electroencephalography & Clinical Neurophysiology, 45, 468-482.

Craver-Lemley, C., Reeves, A. (1992). How visual imagery interferes with vision. Psychological Review, 99, 633-649.

Deco, G., Zihl, J. (2004). A biased competition based neurodynamical model of visual neglect. Medical Engineering Physics, 26, 733–743.

Denis, M., Kosslyn, S. M. (1999). Scanning visual mental images: A window on the mind. Current Psychology of Cognition, 18, 409-465.

Douglas, K. L., Rockland, K. S. (1992). Extensive visual feedback connections from ventral inferotemporal cortex. Abstracts – Society for Neuroscience, 18, 390.

Finke, R.A. (1989). Principles of Mental Imagery. Cambridge, MA: MIT Press.

Finke, R.A., Slayton, K. 1988. Explorations of creative visual synthesis in mental imagery. Memory and Cognition, 16, 252-257.

Fitzgerald, P.B., Fountain, S., Daskalakis, Z.J. (2006). A comprehensive review of the effects of rTMS on motor cortical excitability and inhibition. Clinical Neurophysiology, 117, 2584–2596.

Frith, C. Dolan, R. (1996). The role of the prefrontal cortex in higher cognitive functions. Cognitive Brain Research, 5, 175-181.

Friedrich, F. J., Egly, R., Rafal, R. D., Beck, D. (1998). Spatial attention deficits in humans: A comparison of superior parietal and temporo-parietal junction lesions. Neuropsychology, 12, 193–207.

Ganis, G., Thompson, W. L., Kosslyn, S. M. (2004). Brain areas underlying visual mental imagery and visual perception: An fMRI study. Cognitive Brain Research, 20, 226-241.

Ganis, G., Shendan, H.E. (2008). Visual mental imagery and perception produce opposite adaptation effects on early brain potentials. NeuroImage, 42, 1714-1727.

Harman, G. (1998). Intentionality. In W. Bechtel & G. Graham (Eds.), A Companion to Cognitive Science (pp. 602-610). Oxford: Blackwell.

Intraub, H., Hoffman, J. E. (1992). Reading and visual memory: Remembering scenes that were never seen. American Journal of Psychology, 105, 101– 114.

Johnson, M. K., Raye, C. L. (1981). Reality monitoring. Psychological Review, 88, 67–85.

Karton, I., Bachmann, T. (2011). Effect of prefrontal transcranial magnetic stimulation on spontaneous truth-telling. Behavioural Brain Research, 225, 209– 214.

Kosslyn, S.M. (1980). Image and Mind. Cambridge, MA: Harvard University Press

Kosslyn, S.M. (1994). Image and Brain: The Resolution of the Imagery Debate. Cambridge, MA: MIT Press.

Kosslyn, S.M., Behrmann, M., Jeannerod, M. (Eds.) (1995). The Cognitive Neuroscience of Mental Imagery. Neuropsychologia special issue (33, #11)

Kosslyn, S. M., Thompson, W. L., Kim, I. J., Rauch, S. L., Alpert, N. M. (1996). Individual differences in cerebral blood flow in area 17 predict the time to evaluate visualized letters. Journal of Cognitive Neuroscience, 8, 78–82.

Kosslyn, S.M., Pascual-Leone, A., Felician, O., Camposana, S., Keenan, J.P., Thompson, W.L., Ganis, G., Sukel, K.E. Alpert, N.M. (1999). The role of Area 17 in visual imagery: Convergent evidence from PET and rTMS. Science, 284, 167-170.

Kosslyn, S.M., Ganis, G., Thompson, W.L. (2003). Mental imagery: Against the nihilistic hypothesis. Trends in Cognitive Sciences, 7, 109-111.

Kosslyn, S. M. (2004). Preface to B. Libet, Mind time: The temporal factor in consciousness. Cambridge, MA: Harvard University Press.

Kosslyn, S.M., Thompson, W.L., Ganis, G. (2006). The Case for Mental Imagery. Oxford: Oxford University Press.

Laeng, B., Teodorescu, D.-S. (2002). Eye scanpaths during visual imagery reenact those of perception of the same visual scene. Cognitive Science, 26, 207-231.

Marzi, C. A., Girelli, M., Miniussi, C., Smania, N., Maravita, A. (2000). Electrophysiological correlates of conscious vision: Evidence from unilateral extinction. Journal of Cognitive Neuroscience, 12, 869–877.

Marzi, C. A., Girelli, M., Natale, E., & Miniussi, C. (2001). What exactly is extinguished in unilateral visual extinction? Neurophysiological evidence. Neuropsychologia, 39, 1354–1366.

McGinn, C. (2004). Mindsight: Image, Dream, Meaning. Cambridge, MA: Harvard University Press.

Miller, E. K., Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. Annual Review of Neuroscience, 24, 167-202.

Miller, B. T., D'Esposito, M. (2005). Searching for ''the top'' in top–down control. Neuron, 48, 535–538.

Miyashita, Y., Chang, H. S. (1988). Neural correlate of pictorial short-term memory in the primate temporal cortex. Nature, 331, 68–70.

Murd, C., Einberg, A., Bachmann, T. (2012). Repetitive TMS over V5/MT shortens the duration of spatially localized motion aftereffect: The effects of pulse intensity and stimulation hemisphere. Vision Research, 68, 59–64.

Oostenveld, R., Praamstra, P. (2001). The five percent electrode system for high-resolution EEG and ERP measurements. Clinical Neurophysiology, 112, 713-719.

Pearson, D. G., Logie, R. H., Green, C. (1996). Mental manipulation, visual working memory, and executive processes. Psychologische Beiträge, 38, 324-342.

Pearson, D. G. (2001). Imagery and the visuo-spatial sketchpad. In J. Andrade (Ed.), Working memory in perspective (pp. 33-59). Hove, UK: Psychology Press

Pinker, S. Finke, R.A. (1980) Emergent Two-Dimensional Patterns in Images Rotated in Depth. Journal of Experimental Psychology: Human Perception and Performance, 6, 244-264.

Rockland, K. S., Saleem, K. S., Tanaka, K. (1992). Widespread feedback connections from areas V4 and TEO. Abstracts – Society for Neuroscience, 18, 390.

Ruff, C. C., Driver, J. (2006). Attentional preparation for a lateralized visual distractor: Behavioral and fMRI evidence. Journal of Cognitive Neuroscience, 18, 522–538.

Sereno, M. I., Pitzalis, S., Martinez, A. (2001). Mapping of contralateral space in retinotopic coordinates by a parietal cortical area in humans. Science, 294, 1350–1354.

Serences, J.T., Shomstein, S., Leber, A.B., Golay, X., Egeth, H.E., Yantis, S. (2005). Coordination of voluntary and stimulus-driven attentional control in human cortex. Psychological Science, 16, 114–122.

Serences, J. T., Yantis, S. (2006). Selective visual attention and perceptual coherence. Trends in Cognitive Sciences, 10, 38–45.

Tanaka, K., Saito, H., Fukada, Y., Moriya, M. (1991). Coding visual images of objects in the inferotemporal cortex of the macaque monkey. Journal of Neurophysiology, 66, 170–189.

Thomas, N.J.T. (1989). Experience and theory as determinants of attitudes toward mental representation: The case of Knight Dunlap and the vanishing images of J.B. Watson. American Journal of Psychology, 102, 395-412.

Trojano, L.,Conson, M., Maffei,R., & Grossi, D. (2006).Categorical and coordinate spatial processing in the imagery domain investigated by rtms. Neuropsychologia, 44(9), 1569-1574.

Wittgenstein, L. (1953) Philosophische Untersuchungen / Philosophical Investigations. (Translated by G.E.M. Anscombe) Oxford: Blackwell.

Wittgenstein, L. (1967) Zettel. Translated by G. E. M. Anscombe. Edited by G. E. M. Anscombe and G. H. von Wright), Berkeley and Los Angeles: University of California Press

Appendix 1

	Pt 1 Mean	Pt 2 Mean	Pt 3 Mean	Pt 4 Mean	Pt 5 Mean	Pt 6 Mean	Pt 7 Mean	Pt 8 Mean	Pt 9 Mean
RPFC	3,3000	2,0000	3,9000	2,1000	2,2000	2,6000	3,0000	1,9000	1,7000
LPFC	2,8000	1,8000	3,9000	2,3000	3,1000	2,0000	3,0000	2,0000	2,2000
ROCC	2,9000	2,0000	3,7000	2,5000	2,5000	2,0000	3,5000	2,0000	1,8000
LOCC	2,9000	2,0000	4,0000	2,4000	1,0000	2,5000	3,0000	2,0000	1,6000
RJUN	2,7000	2,1000	3,8000	2,6000	4,0000	2,1000	3,6000	1,6000	1,9000
LJUN	2,8000	2,0000	3,7000	2,6000	2,4000	2,3000	3,1000	2,0000	1,8000
RSHAM	3,3000	2,0000	3,8000	2,6000	3,5000	2,4000	2,9000	2,0000	1,7000
LSHAM	2,6000	2,4000	3,8000	2,4000	2,7000	2,5000	3,6000	2,0000	1,8000
Total	2,9125	2,0375	3,8250	2,4375	2,6750	2,3000	3,2125	1,9375	1,8125

Table 2: mean visibility ratings of each participant (Pt) for each rTMS condition; RPFC – right prefrontal cortex, LPFC – left prefrontal cortex, ROCC – right occipital cortex, LOCC – left occipital cortex, RJUN – right temporal-occipital junction, LJUN -- left temporal-occipital junction.

Non-exclusive licence to reproduce thesis and make thesis public

I, Dmitri Filimonov, 17.02.89,

1. herewith grant the University of Tartu a free permit (non-exclusive licence) to:

1.1. reproduce, for the purpose of preservation and making available to the public, including for addition to the DSpace digital archives until expiry of the term of validity of the copyright, and

1.2. make available to the public via the web environment of the University of Tartu, including via the DSpace digital archives until expiry of the term of validity of the copyright,

Exploring the functional system of mental imagery by rTMS targeted at different cortical areas

supervised by Talis Bachmann,

2. I am aware of the fact that the author retains these rights.

3. I certify that granting the non-exclusive licence does not infringe the intellectual property rights or rights arising from the Personal Data Protection Act.

Tartu, 26.05.2013