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ANAGRAM PROBLEM-SOLVING AND LEARNING IN ANTERIOR PREFRONTAL CORTEX

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We utilized Near-Infrared (NIR) spectroscopy to closely investigate the activation change in anterior prefrontal cortex (aPFC) during verbal anagram problem-solving and learning. We used a parametric design of anagram-solving with three difficulty levels and evaluated anagram skill with two sets of subjects and protocols. The first protocol was a one-time evaluation of untrained subjects ($n = 10$) and the second protocol evaluated subjects over 6 weeks of training ($n = 6$). The untrained subjects in the first protocol demonstrated blood oxygenation corresponding to neuronal activation in the aPFC in response to medium and hard difficulty levels of the stimuli, while the easy anagram task deoxygenated the aPFC bilaterally, corresponding to deactivation. Higher performers have more aPFC activation than lower performers in the medium difficulty level anagram-solving task. Six weeks of training in the second protocol showed that training reduced oxygenation in aPFC. In particular, subjects with lower baseline skill in anagram production showed a larger reduction in oxygenation where true performance gains occurred (medium difficulty) and smaller reduction where the performance gains were limited (hard anagrams).

Association of the aPFC activation with the difficulty of the complex task suggests that aPFC is a part of a circuit for execution of task performance. In addition, more use of aPFC by untrained high performers suggests that the role of the aPFC is to increase efficiency of a problem-solving task. Thus, the NIR spectroscopy showed that the aPFC is a key structure in the circuit implementing the development of anagram skill.

Keywords: Anagram; anterior prefrontal cortex; hemoglobin; NIR; oxygenation; training effects; difficulty.

1. Introduction

The prefrontal cortex (PFC) has become the anatomical *sine qua non* of complex, higher-level problem-solving.[1–7] In problem-solving processes, holding, transforming, and organizing information is well known through imaging studies in the PFC.[8] In addition, rule discovery, the development of algorithms for solution/action, and the emergence of insight are core features of problem-solving and learning.[8,9]

The judgment and decision-making functions of orbito and medial PFC are also important for problem-solving processes.[10] Any specific model of learning must characterize the neuro-anatomical correlates in PFC throughout the whole learning process — from novice status to the development of expertise and task mastery through practice. During unpracticed performance of most tasks, there is some degree of supporting activation in intentional and control areas of PFC and this is sometimes called "scaffolding".[11] The "scaffolding" area has been found to include anterior prefrontal cortex (aPFC),[1] anterior cingulated, and cerebellum in verbal tasks. This "scaffolding" neural circuit drops off as one becomes familiar with the task. Though "scaffolding" neural circuit is generic for most tasks,[12] complexity of the task and other factors may play a role for the extent of the function. We intend to find factors which influence the activity of the aPFC during unpracticed complex verbal performance of solving anagrams and to find the extent of reduction of the aPFC in trained anagram task for "scaffolding" effects.

Anagrams are a complex verbal problem. Anagram solutions resemble insight problems since they involve a sudden shift in subjective experience that brings sudden, unpredicted awareness of a solution since speed-accuracy decomposition studies have shown that prior to reaching a solution, partial information is not available.[13] The effects of practice on the neural representation of complex problem-solving and mechanisms such as insight have not been studied extensively but the effects of simple, brief motor practice[14] and training on a complex motor skill[15] have been studied. It is unclear whether brain activation associated with (1) obtaining a solution or (2) insight at the point of early, novice experience is identical to a solution or insight obtained after extensive practice.

To examine the role of aPFC in complex insight-based problem-solving and, in particular, to test for practice-related brain activation changes in aPFC, we administered word anagrams task during collection of Near Infrared Spectroscopy (NIRS). In humans, NIRS has been demonstrated to show mental and sensory-motor tasks in humans through detection of oxygenation changes.[16–18] Also, NIR optical mapping technology has been developed[19–21] for the assessment of many cortical activities (for example, Matsuo *et al.*[22]). Brain activity studies using fMRI and NIR simultaneously show that both technologies measure similar cortical activations through hemodynamic information.[23] The NIR device detects light migrated through brain tissue carrying information of blood volume and tissue oxygenation through a mechanism similar to fMRI. As opposed to other imaging technologies, the NIR device is portable, easy-to-operate, cost-efficient, and safe. Thus, it has potential use in a classroom setting for tracking the effectiveness of teaching through the collection of information on brain states that reflect the learning progress, the consolidation of knowledge, and the development of solution algorithms or insight.

As a parametric cognitive stimulation, we used word anagrams of varying difficulty levels. In protocol 1, anagrams were given to 10 untrained subjects and in protocol 2, anagrams were practiced daily over a 6-week period by a sample of high-school students. The parametric design allowed us to concurrently examine: (1) the brain's response to varying levels of difficulty and (2) extensive periods of practice. We hypothesized that in this age group, the easy 3-letter anagram is an automatic task. Therefore, it does not engage the high executive function in scaffolding and therefore is suitable for a control condition. We also hypothesized that an increase in aPFC activity would be associated with "scaffolding" of anagram problem-solving of increased difficulty level. In addition, a decrease in aPFC activation would be associated with practice for all difficulty levels due to the redistribution of the circuit (no "scaffolding" brain activity). The latter is in line with the reduction in attention resource demands (arousal, effort, and strategy) and changes in cognitive mechanisms (formation of a solution algorithm, more automatic memory retrieval, and reduced working memory) that should result from skill development. Also, due to the linguistic nature of the anagram task, we expected greater overall activity from left prefrontal regions. Since aPFC is very active in the resting condition,[24] we used 3-letter anagrams as a control for the protocol 2. In order to verify this control condition, we compared the 3-letter anagrams with the baseline in protocol 1 and showed a reduction of aPFC activity during the 3-letter anagram-solving task, thus we used the 3-letter anagram as a control condition of protocol 2.

2. Material and Methods

2.1. *Subjects*

The first protocol consisted of 10 right-handed undergraduate student volunteer subjects (aged 18 to 22 years, 5 males and 5 females) recruited from the University of Pennsylvania and Drexel University. The second protocol consisted of 6 right-handed volunteer subjects (aged 16 to 18 years, 3 males and 3 females) recruited from the summer program at the University of Pennsylvania and were healthy senior high-school students with high academic achievements from local Philadelphia schools. Both protocols were approved by the Institutional Review Board of the University of Pennsylvania.

2.2. *Apparatus*

An NIR optical mapping device was utilized to acquire data on the aPFC activation. The instrument was a modification of the previous brain mapping device.[25] The probe consisted of two sets of lasers or light emitted diodes (LED emitting 735 or 780 and 830 or 850 nanometer wavelengths of light) and two sets of 4 to 8 silicon diodes detectors. Placed on the forehead, the probe covered both the right and left aPFC prefrontal cortices with one set of lasers/LEDs in the middle and 4 or 8 detectors surrounding the source in right and left sides (Fig. 1(c)). The source and detector were placed 3 cm apart to optimize the signal from the gray matter of the aPFC. The sources and detectors covered the left and right areas by 6 cm. The circled points in the figure represent the midpoint between each detector and

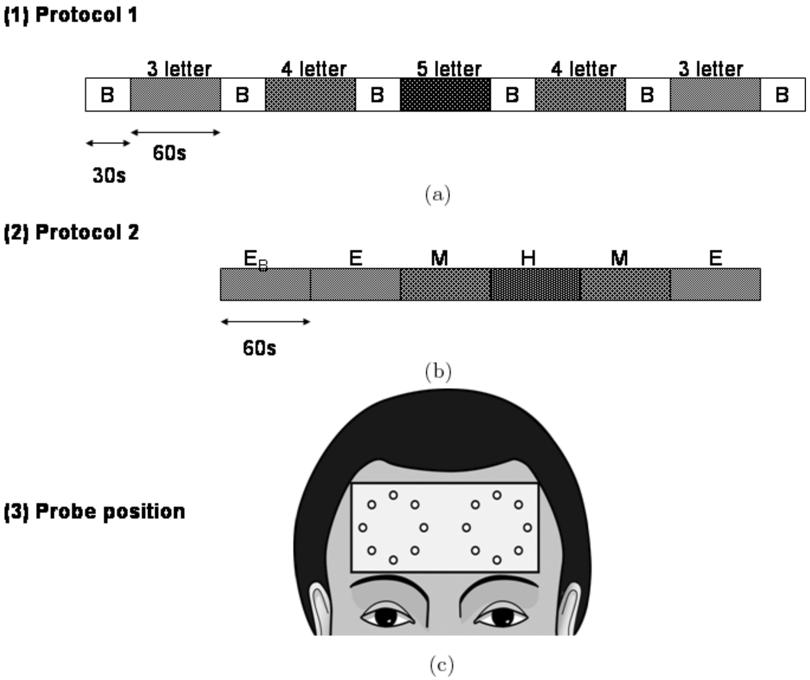


Fig. 1. Experimental set-up. (a) In the protocol 1, baseline task was between anagram-solving tasks, consisting of 3, 4, 5, 4, 3-letter anagram-solving; (b) For protocol 2, 2 minutes of 3-letter anagram (easy) was followed by medium, hard, medium and easy anagram (E = easy, M = medium, H = hard) and (c) Schematic of the probe location. The open circles indicate midpoint between source and detector under which the cortical activation was monitored.

the adjacent light source (i.e., the center of each voxel). These voxels were located in the aPFC (lower voxels, BA10, and higher voxeles BA 9/10). This location can also be translated into the EEG areas of Fpz (Fp1, Fp2), AFz (AF7, AF3, AF4, AF6), and Fz (medial F5, F3, F1, F2, F4, F6), which represent the most anterior leads in the International 10–20 electrode system.

The diffusion optical spectroscopy has been described extensively elsewhere.[26] Briefly, it is the amount of injected light from each wavelength migrating to each of the detectors carrying quantitative information of oxy- and deoxy-hemoglobin changes and was recorded on a PC. Using the observed signals (i.e., the amplitudes of the two wavelengths of light), changes in brain oxygenation were calculated for right and left aPFC in μM from the difference in oxyhemoglobin and deoxyhemoglobin (HbO_2–HbR) using the modified Beer–Lambert law with differential path length factors (DPF).[27]

2.3. *Procedure*

Anagrams are sets of scrambled letters requiring subjects to rearrange the letters to identify meaningful words. To produce anagrams for use in this experiment, we used computerized software (with a random number generator) to scramble the letters of selected words in a random fashion. The words utilized were of strong familiarity in the English language, with the majority of words having a rate of occurrence of 50 per million in terms of formal frequency of occurrence ratings.[28] For all protocols, easy anagram consisted of 3-letter anagrams. In protocol 1, we attempted to show brain activity relative to baseline task, where subjects see a non-anagram task consisting of no-vowel letters for 30 seconds so that subjects immediately know it is not an anagram task (Fig. 1(a)). Letters have a different color code on a PC monitor and subjects have to advance to the next letters by typing the same keys as they do in the anagram-solving task. The anagram was then presented until subjects decided by typing a key of choice, depending on whether the anagram was solvable or not. The sequence of the anagram task was 3-letter, 4-letter, 5-letter, 4-letter, and 3-letter anagrams with the baseline task in between. Once they pressed the key, the next anagram was presented and this procedure was repeated for 1 minute followed by the next baseline task for 30 seconds.

For protocol 2, we compared the first minute of 3-letter anagrams to each anagram task. Subjects did 2 minutes of the 3-letter anagram, followed by 1 minute of a medium, a hard, a medium, and a 3-letter anagram (Fig. 1(b)). This was the same sequence as protocol 1, but without a baseline period in between. Each scrambled word was then written on a card. A set of these cards was placed in a small cardholder with one card on each page. Subjects were instructed to hold the cardholder in their hands while attempting to rearrange the letters. Upon solving each problem, subjects were instructed to immediately advance the card and begin working on the next anagram. For protocol 2, the difficulty level of the task was manipulated by varying the number of letters in the anagrams. For all the six subjects, the easy difficulty level was comprised of three-letter anagrams. To attempt to have all subjects performing anagrams of similar difficulty during the medium and hard conditions, the number of letters comprising each of these difficulty levels was determined using each subject's subjective assessment of his or her performance on a few practice trials. Two subjects classified themselves as "low-performers". For these two subjects, the medium and hard difficulty levels consisted of 4- and 6-letter anagrams, respectively. The other four subjects classified themselves as "high-performers". For the four high performers, the medium and hard conditions consisted of 5- and 7-letter anagrams, respectively. The behavioral record of number of anagram solved per minute in medium and hard anagram did not show statistical differences between "low performer" and "high performer" groups.

Protocol 1 took 9.5 minutes, on average for the 10 subjects who did one time, and for protocol 2, six subjects performed for 6 weeks, with each experimental session consisting of 6 minutes of continuous anagram-solving. For each 6-minute session, the same experimental paradigm was used (see Fig. 2(b)). Each subject completed at least one session per day for six weeks. Thus, each subject finished a minimum of 30 anagram sessions in 6 weeks.

2.4. *Data analysis*

The NIRS device started baseline measurements by watching non-vowel letters in protocol 1 and 3-letter anagrams in protocol 2 in order to produce quantitative oxygenation values. The initial minute of the easy anagram task (E_B in Fig. 1(b)) was selected as the baseline measure. Oxygenation measures were expressed as the difference between the experimental oxygenation measure and the baseline measure. That is, the oxygenation measure reflects the change in hemoglobin oxygenation (HbO_2–Hb) during the three difficulty conditions relative to their baselines. In protocol 2, the oxygenation changes in the three difficulty conditions were expressed relative to the first easy-baseline (E_B). For example, the oxygenation measure for the easy condition reflects the difference in hemoglobin oxygenation between the easy (E) and easy-baseline (E_B) conditions.

In order to assure that the NIR oxygenation signals of these differences come from the brain, we also measured a non-brain reference tissue volume near the brain. In particular, we placed two sets of probes on the cheek bilaterally. This volume of tissue carries oxygenation changes in the skin as well as motion noises. The cheek signals were used to eliminate these artifacts from non-brain origin by subtracting them from the overall signals taken from the probes located on the aPFC. Most of the times, there were only high-frequency motion artifacts recorded from the cheek signals.

To examine the role of aPFC in "scaffolding" in protocol 1, the relationship between brain oxygenation and behavior outcome was examined. The number of correct answers per minute from each level of anagram difficulty was used as a performance outcome. We observed great differences between the outcomes of high performers and low performers and were able to separate them into two groups, high ($n = 4$) and low performance ($n = 6$). We were then able to compare the aPFC activity of the two groups in protocol 1 using ANOVA model (SPSS). The aPFC was separated into 4 locations (left upper (BA 9/10), left lower (BA10), right upper (BA9/10), and right lower (BA10) for these 2 group comparisons.

To examine learning effects over time, two time periods were identified for protocol 2. The initial and final 2 weeks of anagram training were selected as the "initial-training" and the "final-training" periods. Within each period, each subject had a total of 600 (12 scans/minute × 5 minutes/day × 10 days) scans per voxel. Of these, 240 were collected under each of the easy- and medium-anagram conditions, respectively. The remaining 120 scans were collected under the hard-anagram condition. Within each period, 8 voxel-level means were averaged to calculate left and right aPFC oxygenation means at each anagram-difficulty level. The means from the "final-training" period were then subtracted from those from the "initial-training" period to obtain a measure of learning across time periods. These differences were used as the dependent variable in a within-subjects ANOVA model to estimate the effects of learning (initial-training vs. final-training), difficulty (3 levels: easy, medium, and hard), as well as laterality (left or right hemisphere).

The within-subject ANOVA model was fit using PROC GLM (SAS Institute, Cary, NC, Release 8.01). The mean number of anagrams solved per minute was used as a behavioral measure of learning. The difference in the average number of anagrams performed per minute between periods (final–initial) was also calculated for each subject. The score difference was then used as the dependent variable in a Poisson regression model to test for learning (2 levels) and difficulty (3 levels) effects. The Poisson regression model was fit using PROC GENMOD (SAS Institute).

3. Results

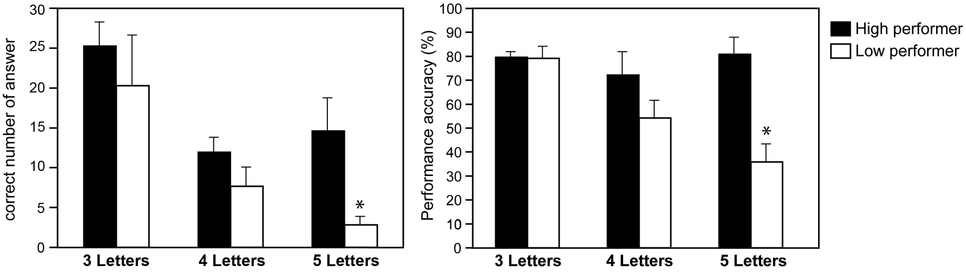
3.1. *The aPFC activity with anagram-solving on novice subjects–The first protocol*

3.1.1. *Behavioral outcomes*

Anagrams consisting of greater numbers of letters (5, 4, and 3 in the order) required more time to solve and fewer numbers of anagram solutions per minute, indicating that difficulty does increase in the progression of 3, 4, and 5-letter anagrams. In addition, the subjects could be divided into 2 significant groups in the 5-letter anagram-solving task in protocol 1. Figure 2 illustrates the two groups: (1) higher performers ($n = 4$), who solved more anagrams and (2) those who solved fewer anagrams (lower performers, $n = 6$). The two groups differed significantly in their accuracy profile during 5-letter anagram-solving, 70%–80% and below 40% accuracies with higher and lower performers respectively, as well as in correct number of answers per minute, 15 and 3 anagrams per minute with high and low performing subjects, respectively.

3.1.2. *The effect of difficulty of anagram solution on aPFC oxygenation*

In general, there is a negative linear relationship of aPFC oxygenation with the task difficulty. The linear regression analysis showed a significant relationship between



(a) (b)

Fig. 2. Behavioral outcomes of the anagram-solving task in protocol 1. (a) Left, correct number of answers are plotted against 3, 4, and 5-letter anagrams and (b) Right, performance accuracy (correct answers/all answers) is plotted against 3, 4, and 5-letter anagrams. Black bar: high performer; white bar: low performer.

aPFC oxygenation (Y) and the correct number of solutions per minute (X) in each group, $Y = -0.06X + 1.22\,(p < 0.05)$ in high performers, and $Y = -0.05X + 0.55$, ($p < 0.05$) in low performers.

The aPFC was deoxygenated (deactivation) with the 3-letter anagram-solving task in both high and low performers bilaterally, about -0.1 to $-0.5\,\mu$M in the designated four areas compared to the baseline condition (Fig. 3, bottom). With the hard 5-letter anagram task, aPFC was oxygenated (activation) bilaterally in both groups about 0.3 to $0.6\,\mu$M on average (Fig. 3, top) compared to the baseline. There was no statistical difference between high and low performers in the degree of oxygenations (activations) in the 3 and 5-letter anagram-solving tasks. On the other hand, during 4-letter anagram-solving tasks, the two groups showed significantly different responses in the aPFC (Fig. 3, middle). The high performers had oxygenation in the left aPFC and a part of right BA10, while low performers did not show oxygenation compared to the baseline task, but, the oxygenation level was still higher compared to that of the 3-letter anagram task.

The aPFC oxygenation during the 4-letter anagram-solving task in low performers (Fig. 4(a)) and high performers (Fig. 4(b)) were plotted in the MRI images. These plots subtracted control condition (3-letter anagram-solving). The activity of the high performer and corresponding oxygenation used more aPFC and left brain. The lower portion of aPFC showed left dominant in the high performer but a higher

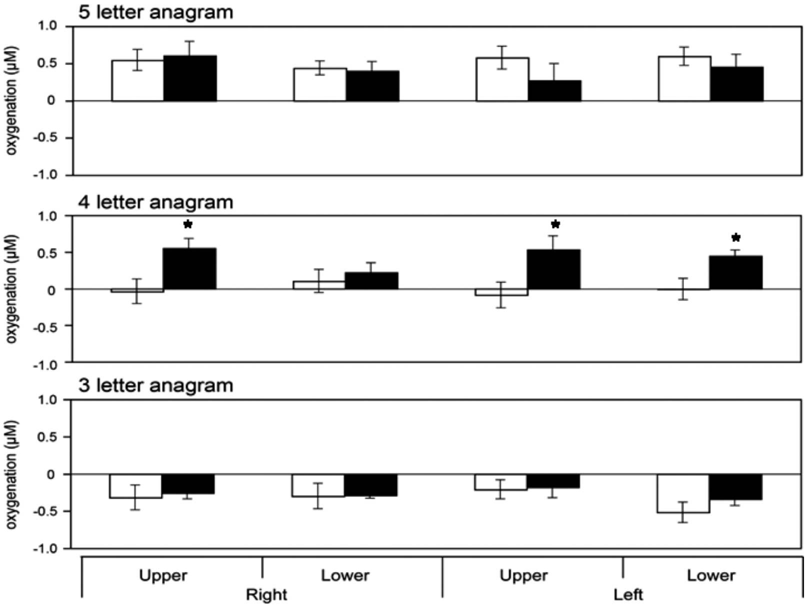
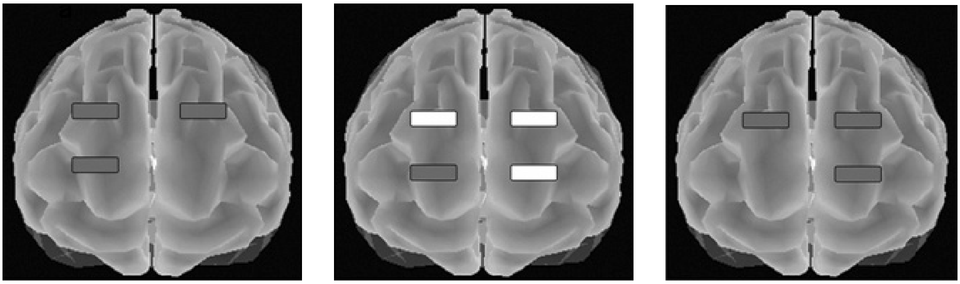


Fig. 3. aPFC responses to 3, 4 and 5-letter anagram-solving tasks. There are bilateral deactivations with 3-letter anagram-solving and bilateral activations with 5-letter anagram-solving tasks. In the 4-letter anagram-solving task (middle), the low (white bar) and high (black bar) performers differed in the degree of activation.



(a) (b) (c)

Fig. 4. Illustrating aPFC activation during 4-letter anagram task (compared to 3-letter anagram task). (a) Low performers; (b) high performers; and (c) differences of aPFC activity between high and low performers (b–a). White and gray bars indicate approximately 0.8 μM and 0.4 μM oxygenation, respectively.

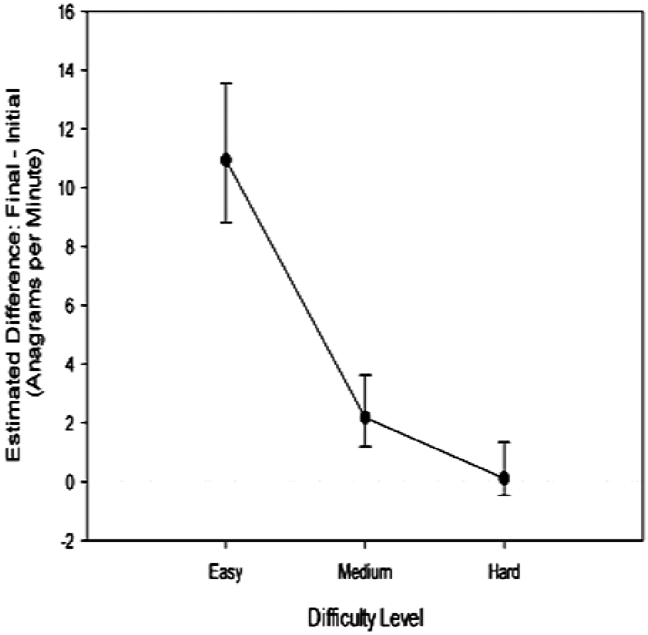
portion had bilateralism. The high performer used dorsal anterior PFC more than the low performer. In the low performer's aPFC, the right hemisphere was fully used compared to the left aPFC. This suggests that the left aPFC is not fully engaged in low performers. Thus, the results showed the left dominance in aPFC is responsible for high anagram performance in untrained subjects (Fig. 4(c)).

3.2. *The effects of long-term training (6 weeks) on aPFC activation–The second protocol*

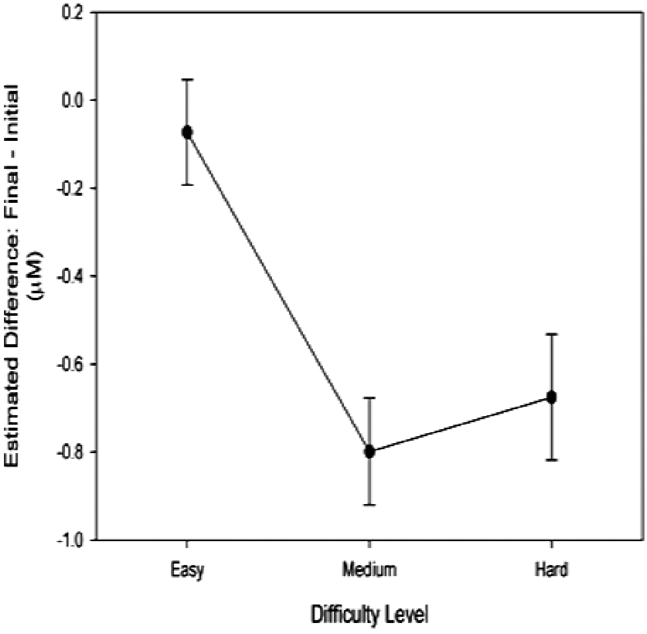
3.2.1. *The effect of long-term training on behavior outcomes*

Determination of the behavioral effects of training was accomplished by estimating the overall mean change in anagrams completed per minute during the initial and final training periods. A Poisson regression model was utilized. The overall estimate of the mean difference in anagrams solved from initial to final training was 2.49. This estimate was significantly greater than zero ($\chi^2(1) = 23.4$, $p < 0.001$), indicating that overall performance increased with training.

The test for effect of difficulty level was also significant ($\chi^2(2) = 92.4, p < 0.001$). As shown in Fig. 5(a), the difference between initial and final training periods decreased as the anagram tasks became more difficult. Overall estimates of the increase in the number of anagrams solved were computed using weighted least squares. Across subjects, the number of anagrams solved increased from initial to final training by almost 11 anagrams per minute for the easy condition. Similarly, average increases of 2.2 and 0.1 anagrams per minute were estimated for the medium and hard conditions, respectively. The estimate for the hard condition was not significantly greater than zero ($\chi^2(1) = 0.08$, $p = 0.77$). Pair-wise comparisons of these estimates revealed that the performance outcome differed significantly across all difficulty levels. Thus, the improvement in performance declined with anagram difficulty.



(a)



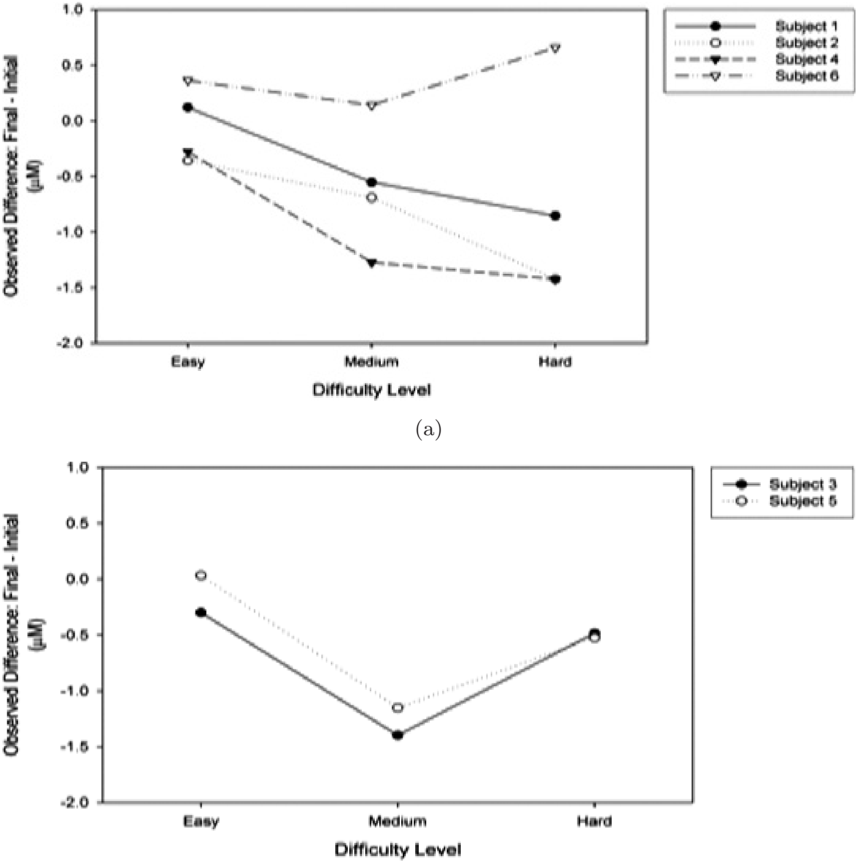
(b)

Fig. 5. Estimated differences: (a) in the number of anagrams solved per minute and (b) in aPFC oxygenation across each of the three difficulty levels. Error bars denote 95% confidence intervals.

3.2.2. *aPFC oxygenation outcome*

The test for an effect of learning on aPFC oxygenation was conducted by estimating the overall mean of the ANOVA model. The estimate for the overall mean difference in oxygenation from initial to final was $-0.516\,\mu$M. This estimate was significantly less than zero ($t_{272} = -13.68$, $p < 0.001$), indicating that prefrontal oxygenation decreased with training. The test for evidence of effect of difficulty level was also significant ($F_{2,272} = 39.19$, $p < 0.001$).

Estimates of the oxygenation difference for each of the three difficulty levels are shown in Fig. 5(b). Pair-wise comparisons of these estimates were then performed using Fisher's LSD post-hoc test. The pair-wise differences between the easy-medium and easy-hard conditions were statistically significant ($t_{272} = 8.37$, $p < 0.001$; $t_{272} = 6.36$, $p < 0.001$). However, the estimate from the medium-hard



(a)

(b)

Fig. 6. Observed oxygenation differences across difficulty levels for each. (a) High performer and (b) low performer.

comparison was not significant ($t_{272} = -1.29, p = 0.20$). Thus, the activation change between initial and final periods for the medium and hard conditions differed from that of the easy condition, but did not differ from each other.

Initial-final oxygenation difference by difficulty level is shown for low and high performers (see Figs. 6(a) and 6(b), respectively). It is important to note that for low performers the medium anagrams elicited a larger oxygenation decrease than the hard ones, likely indicating that more learning took place during the medium (i.e., 4-letter) conditions (Fig. 6(b)).

Also of interest was whether the left hemisphere was more active than the right. Based on the above ANOVA, the main effect of hemisphere was significant ($F_{2,272} = 2.49, p = 0.023$), indicating that the relationship between hemisphere and oxygenation was significant for at least one subject. Since the hemisphere effect was nested within individual subjects, the test for hemispheric differences was investigated on an individual subject level. Although five out of six subjects had larger (i.e., less negative) oxygenation differences in the left hemisphere, only the laterality test for subject 3 was statistically significant. Despite the lack of statistical significance across all subjects, the overall trend was clear. A larger decrease in oxygenation occurred in the right hemisphere when comparing the initial with the final period of training. This suggests that the learning effect was greater for the right hemisphere.

4. Discussion

We demonstrated the role of the aPFC in a "scaffolding" network using complex verbal tasks of anagram-solving in both untrained subjects (protocol 1) and in trained subjects (protocol 2) with NIRS. The aPFC activity increased with task difficulty in the untrained subjects. Further, the aPFC activity was reduced in response to training. In addition, untrained subjects, especially better performers, used more of the left aPFC, demonstrating the importance of the "scaffolding" circuitry in the initial efforts in protocol 1. Further, during the 2-week training period of protocol 2, all the subjects were able to develop the highest initial "scaffolding" activity of aPFC. Association of the aPFC activation with the difficulty of the complex task suggests that aPFC is a part of a circuit for execution of task performance. In addition, more use of aPFC by untrained high performers suggests that the role of the aPFC is to increase efficiency of a problem-solving task.

With regard to aPFC responses to easy anagram-solving (3-letter anagrams), deoxygenation was apparent in the bilateral area of BA10 and the BA9/10 border of the aPFC, showing deactivation. This is contrasted with the area of aPFC activation with more difficult anagram-solving in untrained subjects as well as those in the initial training period of protocol 2. This area of aPFC has been noted as one of the highest activity regions in the brain in the resting state.[29] The deactivation of BA10 has been noted during goal-oriented tasks[30] and this study confirms deactivation during easy 3-letter anagram-solving. Subjects can automatically solve them without aPFC effort in word retrieval. Previous studies also suggested that the medial PFC plays a role in the instantiation of aspects of the multifaceted "self" in the resting state or default state of aPFC.[29] Frith has shown that the PFC, including the aPFC, was responsible for the "theory of mind".[31] The aPFC has been noted as a part of cerebellar-tharamo-PFC circuitry.[32] This circuitry is known for an automatic search system which looks at environments and "sniffs" for events which match up temporally and conditionally (with search patterns and criteria). This search for "problems" (search patterns, error signals, templates, and clues as to what unconditional associations to find) can be a part of the default state of the aPFC and responsible for higher-resting brain activity. In addition, the "scaffolding" function described by Petersen[11] is similar in terms of searching for problems and finding criteria for comparisons with memory resources.[32]

In anagram-solving, specific activation in the aPFC is presumed to arise out of a series of demands for attention (stimuli) requiring cognitive operations for the problem-solving task. First, a goal state is developed where an internal referent or target state is determined by the instructions. Second, an algorithm is formed to create a series of subgoals to link or associate the current stimulus input (anagram) with the response (target state). The arrival of a match between input and target state is not immediate and is preceded by a long trial-and-error process of creating internal steps that manipulate the input. Thus, the anagram-solving task is complex enough to activate the "scaffolding" circuit, where attentive control for problem-solving and searching demand are easily triggered by the stimuli.

Untrained high performers activated the aPFC more than untrained low performers in the medium difficulty anagram-solving task. Both untrained high and low performers showed bilateral activation of the aPFC, but high performers showed more use of the left aPFC in BA10, which could be due to better use of the aPFC leading to better performance. Thus, this finding agrees with the use of "scaffolding" circuitry in the aPFC together with the fact that more difficult anagram-solving requires more activation of the aPFC, demonstrating that the aPFC is responsible for participation in the untrained anagram-solving task. It is not surprising to see more engagements in the left aPFC due to the verbal retrieval function in the task.

It is also noteworthy that during the initial phase of training (2 weeks of 10 sessions) in protocol 2, all subjects experienced the highest aPFC activation as compared to the untrained status in protocol 1 where only the high performers activated this region. This may mean that the scaffolding function is a trainable function and that the more use of "scaffolding", the better the performance results in anagram-solving. Initially, and for the 2 weeks of training, the subjects were still increasing use of "scaffolding" until some time later when the circuit was no longer necessary to establish the problem-solving task for redistribution of the circuit.[12]

Although our data cannot parse out activation associated with each step in problem-solving, our data demonstrate that anterior prefrontal cortex (Brodmann areas 9, 10) plays an important role in sudden insight problem-solving tasks. Anagram-solving involves a goal state, where a target state is determined by the instructions and creation of a series of subgoals to link the current stimulus input (anagram) with the response (target state) and eventual arrival of a match between input and target state, after a trial-and-error process of creating internal steps that manipulate the input. During this stage, phonetic encoding, syllabification, metrical structures, and even semantics come into play as the actual input is manipulated. It is also likely that phonologic or visual-spatial working memory processes in inferior and superior prefrontal cortex, respectively, are in high demand due to the need to hold the letters in mind while undertaking a strategy. Over the course of processing, an approximation of the final target is achieved through recursive movements in the word formation algorithm. Next, the match between input and response comes abruptly via insight, involving selection of the target word from the mental lexicon. Finally, articulatory commands are issued and the solution is expressed. A state of learning is demonstrated when solution times drop and the learning results from efficient search strategies (e.g. taking advantage of letter-pair frequencies in English), increased likelihood of automatic memory retrieval (e.g. access to learned letter patterns more quickly), reduced working memory (e.g. chunking the input letters into larger phoneme units more quickly), and process deletion whereby smaller steps in the production algorithm are subsumed by larger ones.[33–35] As these changes take place, there is less need for the algorithm-building skills of wider regions of prefrontal cortex rather than aPFC, explaining the learning-related decrease in activation in these areas, including the area where working memory (BA45/46) is obtained.

Despite 6 weeks of training, however, it is not likely that anagram performance was achieved automatically. This is one reason why prefrontal cortex activation remained, though at a reduced level, even after highly practiced, mastered performance set in.

Learning-related changes in prefrontal cortex have been observed in previous studies[36,37] with this area clearly a marker for early declarative learning where attentive processes dominate. The primary reason for this is the prefrontal cortex's role (dorsolateral section, in particular) in working-memory[38–40] where the manipulation of stored information aids the development of a learning algorithm. Other studies have specifically shown that in response to practice, the role of prefrontal cortex is reduced. For instance, Jansma *et al.*[41] used a verbal Sternberg task to examine the potential shift in activation association with practice and found a reduction in left dorsolateral prefrontal cortex, right superior frontal, right frontopolar area, and supplementary motor areas. Also, Anderson *et al.* showed reductions in left dorsolateral prefrontal and left posterior parietal cortex in response to practice of difficult algebra problems.

Differences in processing time are often taken to reflect transformation in the way information is handled. For instance, some have argued that reductions in processing time reflect the movement from serial to parallel processing of the information and that, in cognitive neuroscience terms, this shift may reflect a change in the neural circuit carrying out the task.[43–45] Therefore, the reduction in processing time that we observed in anagram production following training may suggest that the associated prefrontal change, i.e., reduced oxygenation, reflects alteration in the underlying neural circuit implementing the anagram skill at higher levels of task mastery. An fMRI study by Tracy *et al.*[15] suggested that, following training on a motor task where high skill (but not automaticity) was achieved, there was still a significant shift in the brain circuit involved toward posterior regions engaged in "non-executive" task monitoring. This shift was characterized by reduction in frontal cortex activation. Thus, training short of automaticity can initiate activation of a new brain circuit and one of the key features of this shift may be reduced frontal activation (see Damasio and Damasio[46]; Raichle[47]).

The involvement of other structures outside the frontal cortex is crucial to anagram success, since frontal lobe activation is part of a larger neural network. Some of these brain processes include activation of primary letter-detection mechanisms in striate and extra-striate cortex, phonemic-unit recognition processes in occipitotemporal cortex, and word recognition/access in these same areas. During anagram-problem-solving, covert speech in Broca's area or the cerebellum are likely.[48] Also, depending on the strategy, phonemic or semantic processes could be called upon, as well as other possible regional involvements such as inferior parietal activation as a result of spatial manipulation of letter position. Note, however, that the location of the NIRS system dictated a bias toward brain activation arising from prefrontal processes and not in these other areas.

In our study, the PFC showed a second pattern of responsiveness. That is, oxygenation levels increased with anagram difficulty level. The relationship was clearly non-linear as the hard and medium difficulty anagrams triggered the same degree of reduction in oxygenation. A relationship between difficulty in language tasks and prefrontal brain function has been shown previously by Gur *et al.*[49] utilizing a comprehension task. Our data, however, showed that in terms of prefrontal response, there is an interaction between difficulty and training such that the effective reduction in activation brought about by learning is less for easier than for more difficult items. This may simply be due to the fact that less learning occurred for the easier anagrams because of ceiling effects (i.e., performance was already at very strong levels and only limited improvement was possible). Another possibility is that reduced oxygenation levels in the prefrontal cortex represented a selective response to difficulty as it interacts with learning and for low performers the medium anagrams elicited a larger oxygenation decrease than the hard anagrams. This is precisely the pattern one would expect under conditions of stronger (medium anagrams were mastered) and weaker (hard anagrams remained too difficult) learning. Activation with 4-letter anagrams may suggest that the frontal cortex is most responsive to tasks when the subject is in the middle of the learning curve in terms of skill acquisition. That is, if the task is too easy (e.g. 3-letter anagram) or too hard (e.g. anagrams with 5-letters or more) frontal lobe activity is reduced. In the case of an "easy" task, strategy and executive resources are minimally required; in the case of a "harder" task, no reliable strategy may exist and no increment in resources would be helpful. Indeed, our data show such a pattern. For the 3- and the 5-letter anagrams, high and low performers showed little difference in frontal activation, suggesting that for easy or hard tasks the frontal lobe is insensitive to differences in skill level. Only for the middle difficulty level (4-letter anagrams) did the high and low performers differ. Thus, the frontal cortex may show some attunement to middle ground effort and moderate levels of difficulty where both the strategies and resources devoted to the task are effective and where the learner (such as our high-performer group) is optimized to take advantage of the functions.

In addition, our data revealed a bias in activation toward the left side, yet there were considerable individual differences in laterality, i.e., the group data did not hold for all individuals. It is possible that these differences in laterality reflect different solution strategies, with a left-hemisphere activation bias associated with a greater phonemic strategy and a right-hemisphere bias associated with a greater imagery or spatial strategy that relied on manipulating the spatial positions of the letters in the "mind's eye." Regardless of these potential individual differences, however, there was a clear reduction in right-sided activity with learning, suggesting that right prefrontal activation may be providing an important clue to the nature of the more advanced solution algorithms. Work has suggested an association between high-imagery anagrams and higher activity of right hemisphere.[50] The anagrams, however, were equally imaginable at both the start and the end of training, leaving open the reason for the training effect. Although, our data is not the first to implicate the right prefrontal cortex in complex problem-solving (for instance, Cavalli *et al.*,[51] found that the right-hemisphere damage diminished anagram skill), it is the first to suggest that right prefrontal involvement in anagrams, whether from imagery activity or spatial manipulation, decreases with training and the development of strong skill.

Finally, the left side remained active after 6 weeks of training, suggesting that its engagement represented a constant in problem-solving and this may be related to linguistic search processes (whether they be serial or parallel) or the presence of working memory (e.g. articulatory loop[52]). This constancy says, in effect, that for each anagram item, no matter the level of skill, a pool of letters had to be held in mind (verbal working memory) and manipulated.

In conclusion, the data make clear that the NIRS system is sensitive to insight-oriented problem-solving procedures such as anagrams. The data also shows that the prefrontal cortex is responsive to extensive training and level of difficulty. And, the interaction between training and difficulty results in a greater reduction in oxygenation when greater performance gains are achieved and greater learning occurs. We also provide preliminary evidence suggesting that the prefrontal cortex may be attuned to middle ground effort and moderate levels of difficulty where both the strategies and resources devoted to the task are effective and where the learner has acquired some skill and is ready to take advantage of these functions. There were also indications that strong learning effects were obtained in the right-prefrontal cortex, suggesting that changes in this region may be crucial to developing an advanced, highly-skilled solution algorithm. It must be acknowledged that although we observed a small section of the full functional anatomical circuit implementing the anagrams, it is clear that NIRS has strong sensitivity to a key structure in this circuit (i.e., prefrontal cortex). Therefore, as a result, it offers great potential as a practical technology in cognitive rehabilitation and classroom learning.

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