

	<b>M3W • Maintaining and Measuring Mental Wellness</b>	07/14/2015
---	--	------------

<b>Project</b>	
Reference:	AAL-2009-2-109
Short Name:	M3W
Full Name:	Maintaining and Measuring Mental Wellness
Website:	<a href="http://m3w-project.eu">http://m3w-project.eu</a>

### D33 - Report on data analysis and evaluation

<b>Document</b>			
WG / Task:	WG1	Deliverable number:	D33
Issued by partner:		Confidentiality status:	Public
Due date:		Acceptance date:	31/08/2017
Document status:	Final	Pages:	24

Authors	Name	Organization/Unit
	Enikő Slrály, MD	Semmelweis University
	Gábor Csukly, MD, PhD	Semmelweis University

#### Document History

Date	Affected	Description of change	Author	Status
16/07/2015		Perusal; content incl.	P. Breuer	Pre-final
31/08/2015		Formatting	P. Hanák	Final

Approval	Name	Organization/Unit

	<p align="center"><b>M3W • Maintaining and Measuring Mental Wellness</b></p>	<p align="center">07/14/2015</p>
---	--	----------------------------------

**Content**

Acronyms..... 3

1 Introduction..... 4

2 Course of cognitive training ..... 5

    2.1 Games used in the cognitive training program ..... 6

        2.1.1 Games developed in the M3W project ..... 7

        2.1.2 Games form the domain 'www.kognitiv.hu' ..... 10

3 Assessments ..... 14

    3.1 Computer based tests ('Cogstate' Battery) ..... 14

        3.1.1 Chase Test Task ..... 14

        3.1.2 Identification Task ..... 14

        3.1.3 One Card Learning Task ..... 14

        3.1.4 One Back Learning ..... 14

        3.1.5 Two Back Learning ..... 14

        3.1.6 Set Shifting Task ..... 15

        3.1.7 Continuous Paired Associated Learning Task ..... 15

        3.1.8 Social Emotional Cognition Task ..... 15

        3.1.9 Groton Maze Learning Task ..... 16

        3.1.10 Groton Maze Test Delayed Recall ..... 16

    3.2 'Paper and Pencil' tests ..... 16

        3.2.1 Addenbrooke's Cognitive Examination and Mini Mental State Examination (ACE and MMSE) 16

        3.2.2 Rey Auditory Verbal Learning Test (RAVLT) ..... 17

        3.2.3 Trail Making test, Part A and Part B (number connection) ..... 17

4 Participants..... 18

5 Results ..... 19

6 Discussion ..... 21

7 Conclusion ..... 22

8 References..... 22

	<b>M3W • Maintaining and Measuring Mental Wellness</b>	07/14/2015
---	--	------------

## Acronyms

Acronym	Description
<b>ACE</b>	Addenbrooke's Cognitive Examination
<b>AD</b>	Alzheimer Disease
<b>CNS</b>	Central Nervous System
<b>GDS</b>	Geriatric Depression Scale
<b>GLM</b>	General Linear Model
<b>MCI</b>	Mild Cognitive Impairment
<b>MMSE</b>	Mini Mental State Examination
<b>MRI</b>	Magnetic Resonance Imaging
<b>PAL</b>	Paired Associates Learning
<b>RAVLT</b>	Rey Verbal Learning Test
<b>SD / Std Dev</b>	Standard Deviation
<b>STAI</b>	Spielberger State and Trait Anxiety Inventory
<b>TMT</b>	Trail making Task

 <p>MAINTAINING AND MEASURING MENTAL WELLNESS <b>M3W</b></p>	<p><b>M3W • Maintaining and Measuring Mental Wellness</b></p>	<p>07/14/2015</p>
---	---	-------------------

## **1 Introduction**

Neuroplasticity is the nervous system's ability to reorganize its structural contacts and functions in response to extrinsic and intrinsic stimuli (Ruge et al, 2012). It's functional role is significant. Plasticity is related in time and influenced by environment and mental conditions such as motivation and concentration. Some of the mechanisms of neuroplasticity are functional changes or modifications of neurons inner qualities or structural changes such as changes in numbers or localization of synapses. (Johnston 2009).

There are several ways of examining neuroplasticity, which includes morphological, cell- and molecular biological and electro-physical methods as well as MR imaging. The later method helped to describe neuroplasticity in different parts of the brain caused by different stimuli. Structural MRI revealed experience based responses in adult brain structure. A good example of this is the enlarged hippocampus volume of the taxi drivers in London. The alteration is supposedly related to navigation while driving, the extent of the volume enlargement correlates with time the drivers spent navigating in the streets of London (Maguire et al., 2000).

Plasticity associated with learning and memory, motor skills, recovery of neural circuits following an injury are all likely to be connected with the activity-related changes in the neural circuits and/or synapses. This can be similar to the changes observed in animal models (Sweatt 2001; Johnston et al., 2003). The changes of synapses, the changes of dendritic spikes in size, shape and numbers and neural circuits are responsible for new memories and for long term changes in circuits responsible for sensory and motor skills.

This plasticity gives the scientific background to theories that suggest that cognitive training may slow down mental decline.

The issue is very current all over Europe as the amount of aged people within the society is rising fast and the tendency is to increase further in the future. It is well known that the chance of dementia is increasing with age and more and more people are involved in mental decline. As currently there is no efficient cure for dementias, slowing their progress and early diagnosis is of utmost importance. As the importance of prevention has grown, more and more focus was given to mild cognitive impairment (MCI), which is considered to be a preceding stage of dementia.

	<p align="center"><b>M3W • Maintaining and Measuring Mental Wellness</b></p>	<p align="center">07/14/2015</p>
---	--	----------------------------------

As a definition MCI means memory problems with retained everyday activity, memory loss shown by neuropsychological tests, retained global cognitive functions and exclusion of dementia (Petersen, 2004). During our study we considered 1 standard deviation, age and education adjusted alteration as diagnostic value. According to long-term follow-up studies, those participants who performed worse on the neuropsychological tests had an increased risk for developing dementia later (Blackwell et al., 2004; Gomar et al., 2011). Diagnosis of MCI is based on these empiric data and accordingly indicates a population at risk, not etiologic connection.

Screening the population at risk is backed by literature data, according to which treatment during the pre-dementia prolongs this phase and also prolongs the time when the patient is able to take care of themselves (Budd et al., 2011). During early treatment of MCI cognitive training gets more emphasis to medical treatment according to literature. (Gates et al., 2011; Emery, 2011; Rosen et al., 2012; Verghese et al., 2003).

In the study changes of neuropsychological test results of patients with mild cognitive disorder were examined in correlation with cognitive trainings.

## **2 Course of cognitive training**

Participants were examined by the Addenbrooke's Cognitive Examination (ACE), the Mini Mental State Examination (MMSE), the Geriatric Depression Scale (GDS) and the State and Trait Anxiety Inventory (STAI) to exclude dementia and depression and to determine anxiety. The possession of global cognitive functions was determined by the ACE, dementia was excluded by the result on the MMSE (adjusted for age, gender and education), severe depression was excluded by a 10 + result in GDS, and anxiety was evaluated by the STAI. The cut off scores of the tests were based on age and education adjusted standardized data.

Following the exclusion of dementia, the Rey Auditor Verbal Learning test (RAVLT) was carried out at baseline, which examines delayed recall and learning capacity. Also the Trail making A and B tests were done, in order to assess concentration and executive functions.

Besides the above mentioned paper-based tests, computer tests were also done at baseline: the parts of 'Cogstate' test package (<http://www.'Cogstate'.com/go/research>) related to mild cognitive disorder and a Pair Associated Learning test, developed by the authors. Based on

	<b>M3W • Maintaining and Measuring Mental Wellness</b>	07/14/2015
---	--	------------

these neuropsychological tests participants were categorized as healthy controls and subjects with MCI.

After baseline testing, the participants were involved in a four week cognitive training program.

For 4x5 days, all patients had to spend 1 hour playing the cognitive games, in order to improve attention, memory and executive functions. All types of games are used every day.

For the games and the corresponding neuropsychological functions see **Table 1** and the following descriptions.

<b>Table 1 Games and neuropsychological functions to improve</b>			
<b>M3W games</b>	<b>cognitive function</b>	<b>kognitiv.hu games</b>	<b>cognitive functions</b>
<b>Hashi</b>	executive functions	<b>Flasher</b>	visuospatial memory
<b>Rotate</b>	executive functions	<b>Jeweler</b>	visuospatial thinking/ mental rotation
<b>Corsi</b>	visuospatial memory	<b>Odd one Out</b>	executive function (recognizing rules)
<b>Connection</b>	executive functions	<b>Suspicious guy</b>	working memory
<b>Sudoku</b>	executive functions	<b>New take-off</b>	visuospatial memory
<b>Planargame</b>	executive / visuospatial thinking		
<b>Memory</b>	visuospatial memory		
<b>Gopher</b>	attention / psychomotor speed		

### *2.1 Games used in the cognitive training program*

Below is a detailed description of the games that have been used in the cognitive training programme.

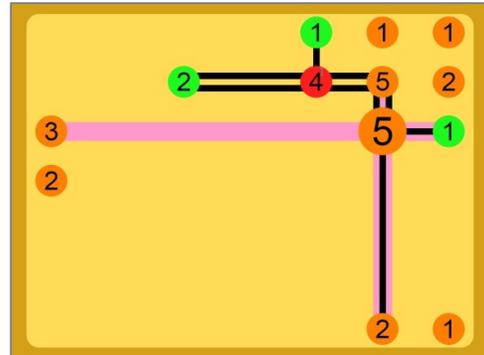
While in the beginning of the training program there were not enough games for training memory functions in the M3W project, games from the domain 'www.kognitiv.hu' were also used.

## 2.1.1 Games developed in the M3W project

### 2.1.1.1 Hashi

**Hashi** is a bridge-building puzzle.

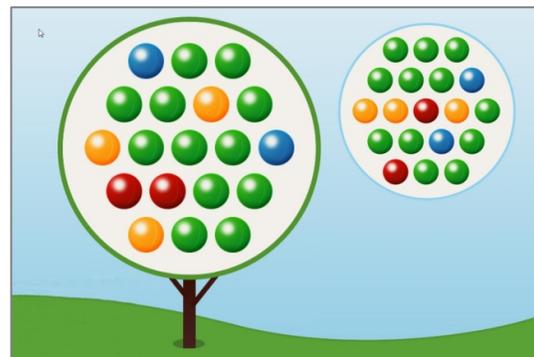
- The objective is to connect islands with bridges enabling to walk from any island to others.
- Each puzzle is an arrangement of numbered islands (represented by circles) in a rectangular area.
- The number in an island equals to the total number of bridges connected to it.
- No more than two bridges may connect neighbour islands. Bridges can be vertical or horizontal only. Bridges cannot cross islands or other bridges.
- You may click on an island, then click several times on the colour bars to build or remove bridges represented by lines. First click on the colour bar: one bridge, second click: two bridges, third click: bridges removed, and so on.
- You can change the difficulty level, and switch on or off the state indication for the islands in the Settings.



### 2.1.1.2 Rotation

**Rotation** is a game to improve executive functions

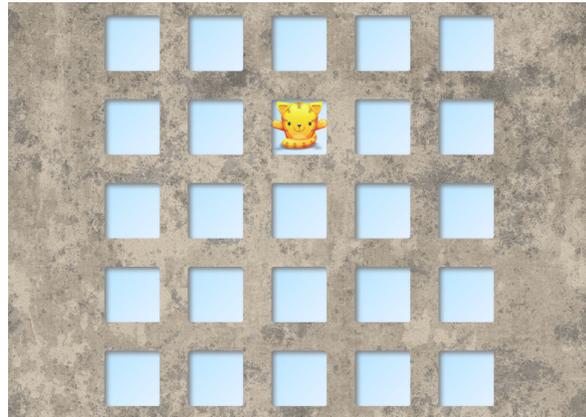
- The objective is to make the big circle look like the small one by rotating the balls.
- You can click on a ball to rotate the six surrounding balls clockwise.
- Nothing happens if you click on a ball that is not in the middle of six other balls.
- If you solve the task you may go to the next level.
- You can change the base colour of the colour scheme, the difficulty level and the number of balls in the Settings.



### 2.1.1.3 Recall Order

**Recall Order** is a game to improve visuospatial memory

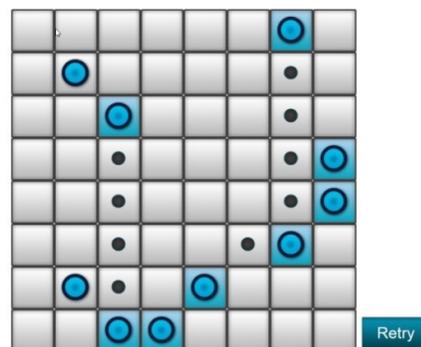
- This game is a variant of the Corsi Block-Tapping Test that assesses the visuospatial short term working memory. It requires you to remember and reproduce a sequence of block positions.
- You have to observe the order of blocks that get marked with an image for a moment, and then reproduce that order or its reverse by clicking on the blocks.
- The game has several levels. At the first level, the sequence consists of two marked blocks. The number of marked blocks increases on every level.
- Advancing to the next level requires two correct responses out of three on the same level. The game goes on until a certain level fails.
- You can change the board size, the recall order, the start level and the image category in the Settings.



### 2.1.1.4 Connection

**Connection** is a game to improve executive functions

- The game's board is divided into squares. The size of the board can be set to 6x6, 8x8, 10x10 or 12x12 squares.
- You will also see circles in some fields.
- You may connect two neighbouring circles by clicking on them in any order. Straight connecting lines may be horizontal, vertical or diagonal.
- Your task is to connect all circles by one line while each circle can be passed only once.
- You can change the board size and the number of circles in the Settings.



2.1.1.5 *Sudoku*

**Sudoku** is a logic-based number-placement puzzle. It is played on a grid containing 9x9 cells. At the start of a game, some of the cells already contain digits between 1 and 9.

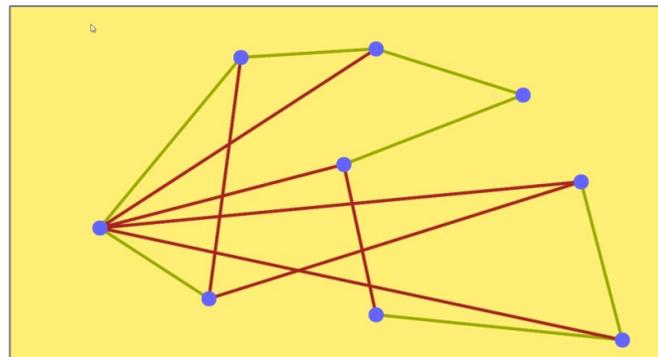
- Your task is to fill the grid with digits so that each column, each row and each block (a sub-grid of 3x3 cells) that compose the grid contain all of the digits from 1 to 9. Every row, column and block (subgrid of 3x3 cells) must contain one of each digit.
- Drag and drop the digits from the top row to fill the empty cells, or overwrite previously entered numbers.
- You may turn on and off note and eraser modes by clicking on the images in the lower corners.
- In note mode, you may drag numbers into the cells to remind yourself of the possibilities. In eraser mode, you can empty a cell by dragging a eraser over it. If both note and eraser modes are on, you can delete notes by dragging numbers into the cells.
- You can change the difficulty level in the Settings.



2.1.1.6 *Planargame*

**Planargame** is a remake of the puzzle game Planarity.

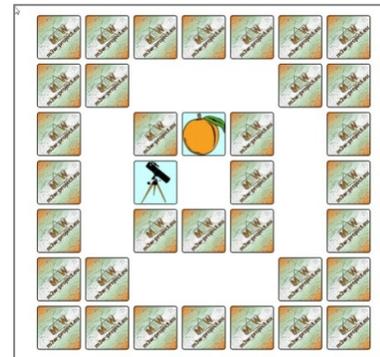
- The game is played by dragging and dropping the nodes of a graph to rearrange them such that no lines cross.
- If Highlight is enabled in the Settings, crossing lines are marked red.
- When there are no crossings left, the game is solved, and you may go to the next level.
- You can change the difficulty level, and enable or disable the highlighting of crossing lines in the Settings.



*2.1.1.7 Find the Pairs*

In the popular **Find the Pairs** (also known as Memory) game, the player has to remember the images on card faces.

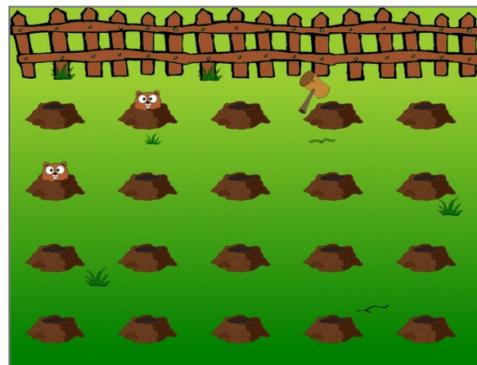
- Your task is to turn over pairs of matching cards.
- In the beginning of the game, cards are laid face down. Two cards can be flipped face up in each turn by clicking on them. If they match, they disappear.
- The fewer moves you make the higher your score.
- You can change the turning speed and the number of the cards, and enable or disable the switching of the cards in the Settings.



*2.1.1.8 Gopher*

The simple game **Gopher** is to improve and assess visuomotor speed.

- There are two game modes: limited and limitless.
- The task in the two modes is the same; you have to beat upon the head of the gophers by clicking on them as fast as you can.
- In the limited mode you have to fight against the gophers for about 15 seconds.
- In the limitless mode you have to fight against the gophers as long as you let any of them escape. In this mode the game will be harder and harder.



**2.1.2 Games form the domain 'www.kognitiv.hu'**

*2.1.2.1 Flasher*

The game **Flasher** is to improve short-term visual memory

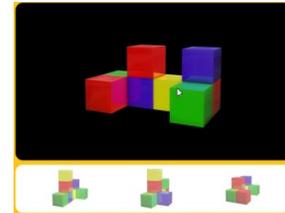
- First there are 2 symbols on the screen you should memorize
- Afterwards you have to reproduce the previously seen symbols by changing the shape and color of the symbols on the next screen



2.1.2.2 *Jeweler*

The game **Jeweler** is to improve mental rotation

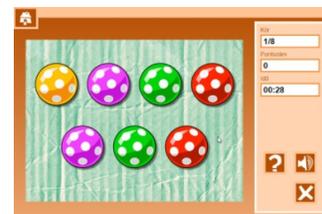
- There is a 3D object on the centre of the screen
- You have to select the exact match for this object from the 3 other objects on the bottom of the screen



2.1.2.3 *Odd One Out*

The game **Odd One Out** is to improve executive functions

- There are 6 figures on the screen
- You have to pick the 'odd one out' by establishing the rule



2.1.2.4 *Suspicious Guy*

The game **Suspicious Guy** is to improve working memory

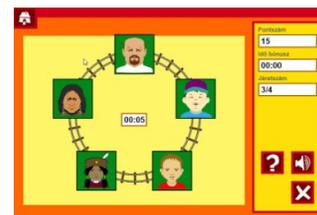
- There are faces appearing on the center of the screen after each other
- You have to respond by a button press if you saw the same face one or two faces before



2.1.2.5 *New Take-off*

The game **New Take-off** is to improve visual and working memory

- There are faces appearing around the centre of the screen, and you have time to memorize them
- In the next round the same faces and an additional one, the "new take-off" are displayed. You have to pick the "new take-off".



	<b>M3W • Maintaining and Measuring Mental Wellness</b>	07/14/2015
---	--	------------

**Table 2/a Results of the first round by game**

<i>Cognitive Game</i>	<i>Group</i>	<i>No of Subjects</i>	<i>Mean Score</i>	<i>Standard Deviation</i>	<i>p value</i>
"Jeweler"	Control Group	277	192.1	47.1	<0.0001*
	Training Group	29	151.7	50.5	
"Suspicious Guy"	Control Group	193	66.9	15.8	0.003*
	Training Group	24	56.7	12.3	
"Odd One Out"	Control Group	10	116.1	44.0	0.48
	Training Group	23	105.5	36.4	
"New Take-off "	Control Group	259	67.6	39.6	0.37
	Training Group	26	60.3	35.8	
"Flasher"	Control Group	233	46.7	15.1	0.008*
	Training Group	30	38.9	16.0	

\* (p < 0.05 ) significant

**Table 2/b Average results of all rounds by game**

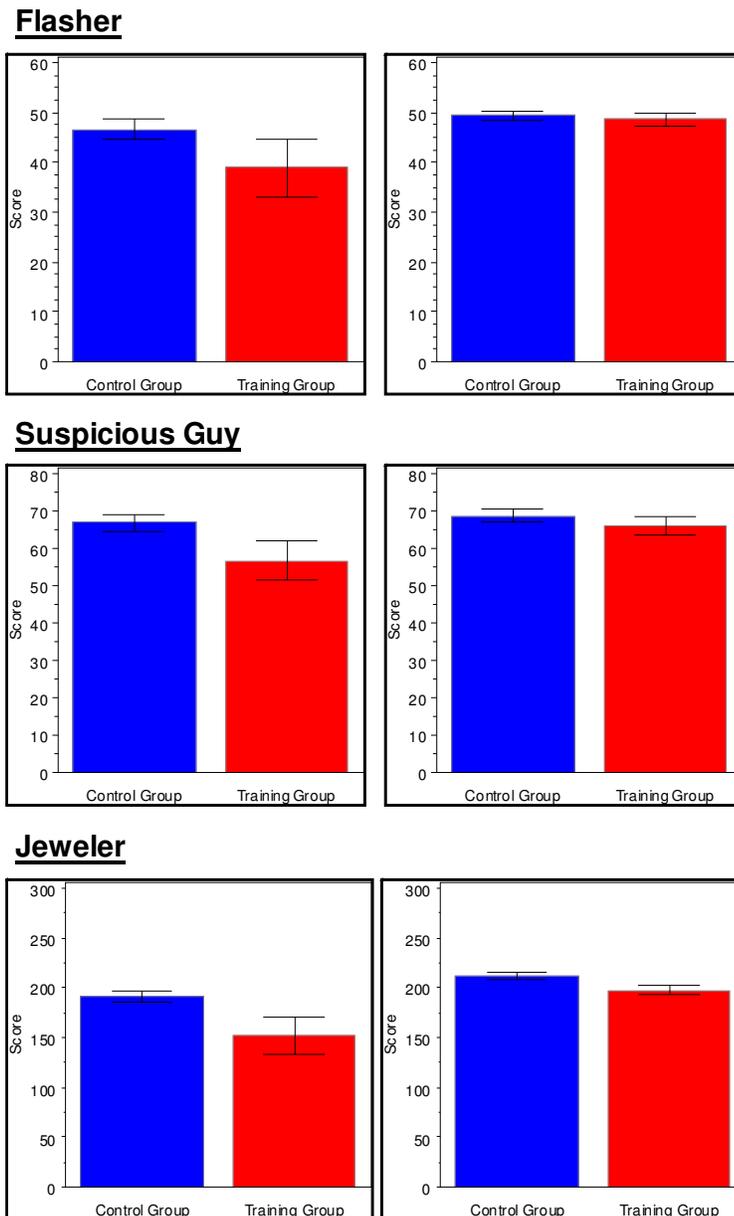
<i>Cognitive Game</i>	<i>Group</i>	<i>Rounds played (by group)</i>	<i>Mean Score</i>	<i>Standard Deviation</i>	<i>p value</i>
"Jeweler"	Control Group	931	212.5	51.5	*ns.
	Training Group	439	197.4	46.6	
"Suspicious Guy"	Control Group	306	68.8	16.3	*ns.
	Training Group	149	66.1	14.5	
"Odd One Out"	Control Group	138	141.7	33.2	*ns.
	Training Group	487	143.4	38.1	
"New Take-off "	Control Group	727	53.3	36.0	*ns.
	Training Group	383	53.9	33.0	
"Flasher"	Control Group	683	49.4	13.0	*ns.
	Training Group	339	48.7	11.8	

\*ns = not significant (p>0.05)

The results of the games from 'www.kognitiv.hu' are summarized in the **Table 2/a** and **Table 2/b**, where the results of the training group (n=32) are compared to the results of other (younger) players from the internet (n~300). It is interesting to note that in the first round, younger players from the internet outperformed elderly participants from the training group in games such as the 'Jeweler', 'Suspicious Guy', or 'Flasher' assessing both executive and memory functions (**Table 2/a and Figure 1**). However, at the end of the training course the

difference between the groups (average results in all rounds) has vanished as a possible result of the training (**Table 2/b and Figure 1**).

**Figure 1**



After the 4 week training program the 'Cogstate' test battery had been repeated to detect changes in cognitive functions.

 <p>MAINTAINING AND MEASURING MENTAL WELLNESS <b>M3W</b></p>	<b>M3W • Maintaining and Measuring Mental Wellness</b>	07/14/2015
---	--	------------

### **3 Assessments**

For the computer based and the 'paper and pencil' neuropsychological tests see the following short descriptions.

#### *3.1 Computer based tests ('Cogstate' Battery)*

##### **3.1.1 Chase Test Task**

The subject is shown a 10 x 10 grid of tiles on a computer touch screen. The subject is asked to tap the blue tile in the top left corner of the grid with the stylus pen. As the target moves, the subject 'chases' it by tapping on the tiles, one at a time. The subject cannot move diagonally and cannot skip a tile. If the subject makes a mistake, they must go back to the last correct tile.

##### **3.1.2 Identification Task**

Examined cognitive domain: visual attention/ vigilance

The card will flip over so it is face up. As soon as it does this the subject must decide whether the card is red or not.

##### **3.1.3 One Card Learning Task**

Examined cognitive domain: visual attention /visual memory

Each time a card is revealed, the subject must decide whether he/she has been shown that card before in this task and respond by pressing the "Yes" or "No" key.

##### **3.1.4 One Back Learning**

Examined cognitive domain: attention/working memory

A playing card is presented face up in the centre of the screen. The subject must decide as each card is presented whether it is identical to the one just before.

##### **3.1.5 Two Back Learning**

Examined cognitive domain: attention/working memory

A playing card is presented face up in the centre of the screen. The subject must decide as each card is presented whether it is identical to the one just before.

	<b>M3W • Maintaining and Measuring Mental Wellness</b>	07/14/2015
---	--	------------

### **3.1.6 Set Shifting Task**

A playing card is presented in the centre of the screen. At the start of this task, the subject literally has to guess whether the card is the ‘target’ or ‘correct’ card. The subject is being asked to determine whether the card contains a target stimulus dimension (a color or a number).

As the subject makes their guesses, the software provides feedback and will not display the next stimuli until a correct response has been made. For example, if the subject wants to guess that a card is correct he/she presses “Yes”. If the guess is correct, the card will flip over. If the guess is incorrect, the subject will hear an error sound and the card will not flip over, indicating that the card does not contain the target stimulus dimension. In this case the subject would guess again (e.g. choose “No” to indicate that the card is ‘incorrect’). In this way, the subject is taught that a specific dimension of the card (either a colour or a number) is ‘correct’.

When the subject has made their way through a set of cards, the ‘target’ or ‘correct’ stimulus dimension changes, either to the opposing example within the same dimension (e.g., from red to black – intra-dimensional shift) or to a different dimension of the stimuli altogether (e.g., from colour to number – extra-dimensional shift). The subject is not told when these intra-dimensional or extra-dimensional ‘set-shifts’ occur, and they must re-learn the new target ‘rule’ to proceed through the task. There are multiple set-shifts within the task, and the order of these set-shifts is pseudo-randomized to create multiple alternate forms of the task.

### **3.1.7 Continuous Paired Associated Learning Task**

In this task, the subject must learn and remember the pictures hidden beneath different locations on the screen. The subject must tap the target on the central location to begin. As each picture to be learned is revealed, the subject must tap each location and remember where the picture was located

The pre-task on-screen instructions ask: “In what locations do these pictures belong”

Now the same pictures will be presented in the centre of the screen, and the subject must tap on the peripheral location where that picture previously appeared.

### **3.1.8 Social Emotional Cognition Task**

In this task, the subject will see a number of pictures on the screen. One of these pictures will be different to the others in some way. The subject must decide which one of the pictures is different then must tap that picture as quickly as they can.

	<b>M3W • Maintaining and Measuring Mental Wellness</b>	07/14/2015
---	--	------------

### **3.1.9 Groton Maze Learning Task**

The subject is shown a 10 x 10 grid of tiles on a computer touch screen. A 28-step pathway is hidden among these 100 possible locations. The start is indicated by the blue tile at the top left and the finish location is the tile with the red circles at the bottom right of the grid. The subject is instructed to move one step from the start location and then to continue, one tile at a time, toward the end (bottom right).

The subject moves by touching a tile next to their current location with the stylus. After each move is made, the computer indicates whether this is correct by revealing a green checkmark (i.e. this is the next step in the pathway), or incorrect by revealing a red cross (i.e. this is not the next step in the pathway, or the subject has broken a rule, see below). If a choice is incorrect (i.e. a red cross is revealed), the subject must touch the last correct location (i.e. the last green checkmark revealed) and then make a different tile choice to advance toward the end.

While moving through the hidden maze, the subject is required to adhere to two rules. Firstly, the subject cannot move diagonally or touch the same tile twice in succession. Secondly, the subject cannot move backwards along the pathway (e.g. move back to a location that displayed a green tick, but from which they have since moved on from).

The subject learns the 28-step pathway through the maze on the basis of this trial and error feedback. Once completed, they are returned to the start location and repeat the task, usually 4 more times, trying to remember the pathway they have just completed.

### **3.1.10 Groton Maze Test Delayed Recall**

The 10 x 10 grid of tiles is shown again on the computer screen. The subject is asked to reproduce the pathway that he/she learned at the start of the 'Cogstate' battery. The subject completes this delayed recall trial once.

## *3.2 'Paper and Pencil' tests*

### **3.2.1 Addenbrooke's Cognitive Examination and Mini Mental State Examination (ACE and MMSE)**

The MMSE is a standard test; its effectiveness was proven by several studies, as a useful method in differentiating between subjects with dementia and healthy controls (Crum et al, 1993). The majority of the previous studies used the cut off score of 26 for dementia. The subtasks of the test assess orientation, central executive function, rapid association formation, verbal identification ability and the ability to analyze and synthesize.

The Addenbrooke's Cognitive Examination (ACE) was used to assess the global cognitive performance, including orientation, attention, memory, verbal fluency, verbal and visuospatial skills (Alexopoulos et al., 2010).

### 3.2.2 Rey Auditory Verbal Learning Test (RAVLT)

The *Rey Auditory Verbal Learning Test* (RAVLT) was used for the detailed assessment of memory functions based on Petersen criteria. Rey test evaluates verbal learning and memory (Rey, 1958). A list of 15 words (list A) should be repeated by the subject immediately. This test is repeated 5 times. Then another list of 15 words (list B or interference list) is presented once that should be recalled. Then list A should be recalled without repeating, and then this task is repeated after 30 minutes.

### 3.2.3 Trail Making test, Part A and Part B (number connection)

The *Trail Making test, Part A and Part B* (number connection) (Retain et al., 1955; Tombaugh et al., 2004) is used to evaluate selective attention, cognitive flexibility and executive functions. In Part A, randomly distributed numbers should be connected in numerical order, while in Part B randomly distributed numbers and letters are displayed. The subject is instructed to connect them in a pre-defined order. The time required to complete the test is the dependent variable. Part A of TMT measures attention and executive functions, while Part B is also affected by cognitive flexibility.

The results of the neuropsychological tests are shown in **Table 3**.

**Table 3 Results of neuropsychological tests**

Neuropsychological Test	N	Mean	SD	minimum	maximum
<b>ACE Total Score</b>	31	90.3	17.3	72	99
<b>Mini Mental State Score</b>	30	28.8	0.9	27	30
<b>Rey Auditory Verbal Learning Test 1-5</b>	30	51.2	9.0	31	72
<b>Trail Making Test A Time (sec)</b>	29	43.0	14.3	21	77
<b>Trail Making Test B Time (sec)</b>	26	85.8	37.6	39	192
<b>Geriatric Depression Scale Score</b>	31	4.1	3.3	1	11
<b>STAI Score</b>	31	36.8	10.3	22	61

## 4 Participants

The study included 32 participants (66% female), aged between 49 and 74 (the mean age was 64.7).

Patients with record of stroke or head injury with loss of consciousness were excluded from the study. Patients with epilepsy or active phase psychiatric disorder, or drug or alcohol abuses and those who suffered with dementia were also excluded.

According to the neuropsychological tests there were 20 healthy subjects and 12 participants with MCI. For demographic data of the participants see **Table 4**.

<b>Table 4 Demographics</b>		
	<b>frequency</b>	<b>percent</b>
<b>Gender</b>		
female	20	62.5
male	12	37.5
<b>Education</b>		
eight classes (primary school)	1	3.57
locational school	1	3.57
high school graduation	3	17.86
university/collage degree	26	71.43
postgradual	1	3.57
<b>Place of living</b>		
Budapest	25	89.29
other city	3	10.71
missing data	4	12.5
<b>Work status</b>		
employee	7	22.58
retired	14	45.16
disabled	1	3.23
missing data	9	29.03

**Table 4 Demographics**

**Maternity status**

single	2	7.14
married	12	42.86
in relation	2	7.14
divorced	4	14.29
widow/widower	8	28.57
missing data	4	12.5

**Computer/internet use**

never	1	3.57
just computer	1	3.57
both	26	92.86
missing data	4	12.5

Average time spent with cognitive training and average number of games started during the study are summarized in **Table 5**.

**Table 5 Average time spent with cognitive training**

<b>Training</b>	<b>N</b>	<b>Mean</b>	<b>Std Dev</b>
Days	32	13.3	6.8
Hours	32	9.3	8.4
Number of Game Plays (started)	32	47.4	29.1

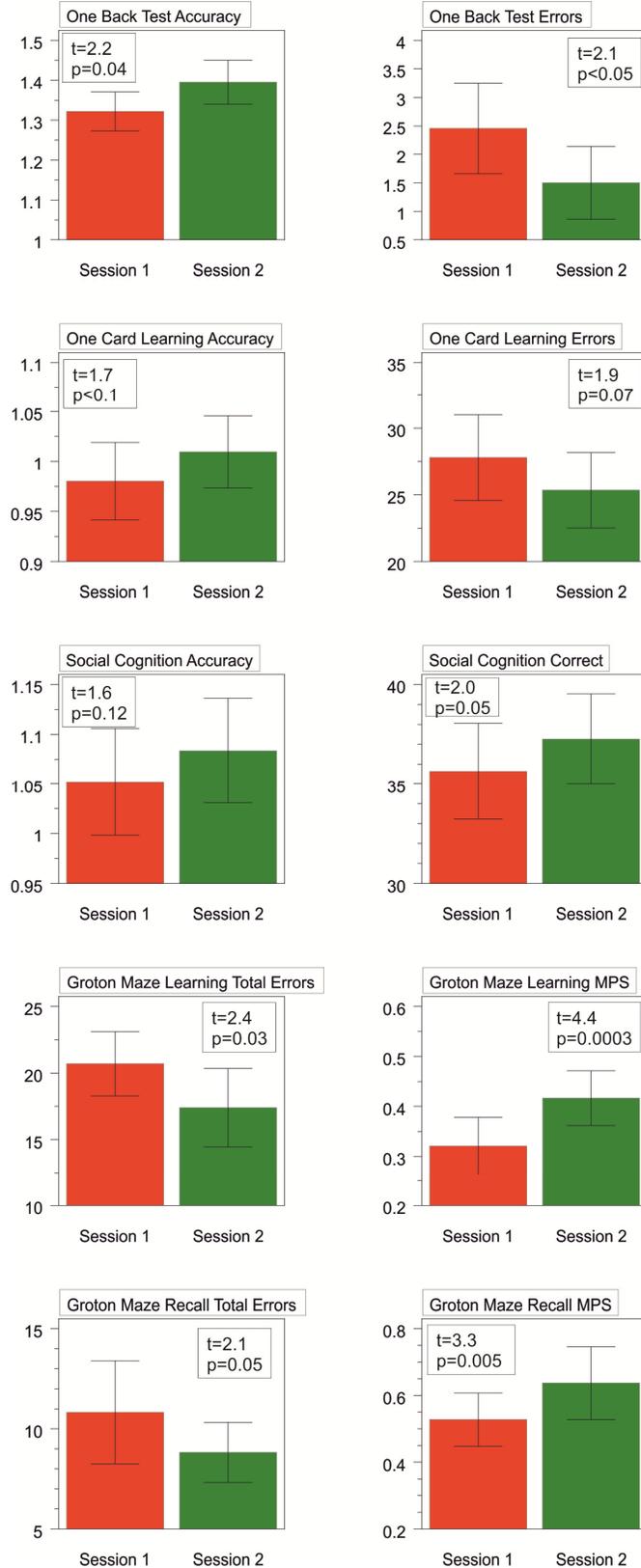
## 5 Results

Performance on the neuropsychological tests at baseline and after cognitive training have been analyzed by paired t-tests.

The change in cognitive performance was evaluated by the primary outcome measures of the 'Cogstate' test battery (**Figure 2**).

There was a significant ( $p < 0.05$ ) or a marginally significant ( $p < 0.1$ ) improvement among the participants by the end of the training in the following tests: One Card Back, One Card Learning (marginally significant), Groton Maze Task and Social Emotion Task (**Figure 2**).

**Figure 2**



	<p align="center"><b>M3W • Maintaining and Measuring Mental Wellness</b></p>	<p align="center">07/14/2015</p>
---	--	----------------------------------

The primary outcomes measure of the *One Card Learning Test* was the arcsine transformation of the correct answers, which was significantly improved. The number of errors was also decreased by 2 following the training. With *One Back Learning Test* the number of errors was decreased by 1 on average, furthermore there was also a significant increase in the number of correct answers. With *Groton Maze Test* the primary outcomes measure was the total number of errors. The number of total errors was significantly decreased at level one and during the delayed recall. With *Groton Maze Test* and with the delayed recall of the test there was a significant increase in the correct moves /second also. There was also a significant increase in the performance with the *Social Emotion Test*, where we evaluated the rate of transformed correct answers and total number of errors as primary outcome measures (**Figure 2**).

The improvements in cognitive performance were between 0.3 and 0.6 in terms of Cohen's d, which corresponds to a medium effect size.

While there was also a trend of improvement in the *Identification Task*, the *Two Back Learning Task*, the *Continuous Paired Associates Learning Task*, the *Chase Task*, and in the *Set Shifting Task*, the performance change was not significant after training relative to baseline.

## 6 Discussion

We examined the cognitive changes of 32 participants as a result of a four week cognitive training. In order to evaluate the cognitive changes a widespread and internationally accepted test battery was used. To compare the cognitive performance before and after training also the primary outcome measures for each respective cognitive tests are assessed, what are the most efficient for the evaluation of the given cognitive function.

The games used for the cognitive training are intended to improve the following functions: visuospatial memory, working memory, executive functions (recognizing rules, planning / execution) attention and psychomotor speed.

A significant medium effect size increase was observed in visuospatial memory, in executive functioning (*Groton Maze*), in working memory (*One Back Test*), in visuospatial memory (*Groton Maze Recall*), in attention (*One Back Learning Task*), visuomotor speed (*Groton Maze Task and Recall*) and also in social cognition.

	<b>M3W • Maintaining and Measuring Mental Wellness</b>	07/14/2015
---	--	------------

As the participants didn't play other games or didn't do any extraordinary mental activity relative to their everyday activity before trial, the increase in the tests were supposedly the result of the training.

In other tests measuring working memory (*Two Back Task*), attention or other executive functions (*Set Shifting Task*) no improvement was observed. A possible explanation to this is the relative good performance at baseline, which is a result of the following:

- 1.) active workers among the participants;
- 2.) almost all participants used computer and internet daily even before the study;
- 3.) most importantly the high frequency of other cognitive activities among participants such as cross puzzles might have boost the baseline performance.

It would have been interesting to look at the improvements as a function of these factors, but the study sample (m=31) was too low for such analyses. However this theory is further supported by the experience that during the trainings a repeated feedback from participants was that games without increasing difficulty levels had become too easy after a while. Finally it should be mentioned, that the real training time (9 hours and 20 minutes in average) was significantly less than the expected (20 hours altogether) (**Table 5**).

## 7 Conclusion

The cognitive games developed in the framework of the M3W project were found to be effective in improving cognitive performance in elderly subjects.

## 8 References

Alexopoulos, P., Ebert, A., Richter-Schmidinger, T., Schöll, E., Natale, B., Aquilar, C.A., Gourzis, P., Weih, M., Perneczky, R., Diehl-Schmid, J., Kneib, T., Förstl, H., Kurz, A., Danek, A., Kornhuber, J. (2010) Validation of the German revised AKV for detecting MCI, mild dementia in AD and frontotemporal lobar degeneration. *Dement Geriatr Cogn Disord*, 29:448-456

Blackwell, A.D., Sahakian, B.J., Vesey, R., Semple, J.M., Robbins, T.W., Hodges, J.R. (2004) Detecting dementia: Novel neuropsychological markers of preclinical Alzheimer's disease. *Dement Geriatr Disord*, 17:42-48

	<p align="center"><b>M3W • Maintaining and Measuring Mental Wellness</b></p>	<p align="center">07/14/2015</p>
---	--	----------------------------------

Budd, D., Burns, L.C., Guo, Z., L'italien, G., Lapuerta, P., (2011) Impact of early intervention and disease modification in patients with predementia Alzheimer's disease:a Markov model simulation. Clinicoecon Outcomes Res, 3:189-195

Chen, K.H.M.,Chuach,L.Y.M.,Sim,S.K.Y.,Chee,M.W.L. (2009) Hippocampal region-specific contributions to memory performance in normal elderly.Brain and Cogn, 72:400-412

Crum, R.M., Anthony, J.C., Bassett, S.S., Folstein, M.F. (1993) Population based norms for the Mini-Mental State Examination by age and educational level. Am Med Assoc, 269:2386-2391

Emery V.O.B. Alzheimer disease: are we intervening too late? (2011) J Neural Transm, 118:1361-1378

Folstein, M.F., Folstein, S.E., Mc Hugh, P.R. (1975) „Mini-Mental State.” A practical method for grading the cognitive state of patients for the cilnician. Psych Res,12:189-198

Gates, N.J., Sachdev, P.S., Fiatarone Singh, M., Valenzuela, M. (2011) Cognitive and memory training in adults at risk of dementia: A systematic review. BMC Geriatrics, 11:55

Geffen, G.M. Rey Auditory Verbal Learning Test In: Strauss,E., Sherman, M.S., Spreen, O. A compendium of neuropsychological tests. Oxford University Press, Oxford, 2010. pp. 776-810

Gomar, J.J., Bobes-Bascaran, M.T., Conejero-Goldberg, C., Davies, P., Goldberg, T.E. (2011) Utility of combinations of biomarkers, cognitive markers, and risk factors to predict conversion from mild cognitive impairment to Alzheimer disease in patients in the Alzheimer's Disease Neuroimaging Initiative. Arch Gen Psychiatry, 68:961-969

Johnston MV. Plasticity in the developing brain: Implications for rehabilitation. Dev Disabil Res Rev 2009; 15: 94-101.

Maguire EA, Gadian DG, Johnsrude IS, Good CD, Ashburner J, Frackowiak RS, Frith CD. Navigation-related structural change in the hippocampi of taxi drivers. Proc Natl Acad Sci U S A 2000; 97: 4398-403.

Petersen, R.C. (2004) Mild cognitive impairment as a diagnostic entity. J of Intern Med, 256:183-194

	<b>M3W • Maintaining and Measuring Mental Wellness</b>	07/14/2015
---	--	------------

Reitan, R.M. (1955) The relation of the Trail Making Test to organic brain damage. J Consult Psychol,19:393-394

Rey, A. (1958) L'examen clinique en psychologie. Paris: Presse Universitaire de France

Rosen, A.C., Sugiura, L., Kramer, J.H., Whitfield-Gabrieli, S., Gabrieli J.D. (2012) Cognitive training changes hippocampal function in mild cognitive impairment: A pilot study. J Alzheimers Dis, 26:349-357

Ruge D, Liou LM, Hoad D. Improving the potential of neuroplasticity. J Neurosci 2012; 32: 5705-6.

Speilberger, C.D., Gorusch, R., Lushene, R. (1970) STAI manual for the State Trait Anxiety Inventory.Orlando, F.L.:Consoulting Psychologist Press

Sweatt JD. The neuronal MAP kinase cascade: a biochemical signal integration system subserving synaptic plasticity and memory. J Neurochem 2001; 76: 1–10.

Tombaugh, T.N. (2004) Trail making test A and B :Normative data stratified by age and education. Arch Ciln Neuropsychol,19,203-214.

Vergheze, J., Lipton, R.B., Katz, M.J., Hall, C.B., Derby, C.A., Kuslansky, G., Ambrose, A.F., Sliwinski, M., Buschke, H. (2003) Leisure activities and the risk of dementia in the elderly. N Engl J Med, 348:2508-2516

Yesavage, J.A. (1988) Geriatric Depression Scale. Psychopharmacol Bull, 24:709

<http://www.'Cogstate'.com/go/research>