

1 **Title**

2 Intelligent Therapy Assistant (ITA) for cognitive rehabilitation in patients with Acquired Brain Injury

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24

25 **Abstract**

26

27 **Background**

28 This paper presents the design, development and first evaluation of an algorithm, named Intelligent
29 Therapy Assistant (ITA), which automatically selects, configures and schedules rehabilitation tasks for
30 patients with cognitive impairments after an episode of Acquired Brain Injury. The ITA is integrated in
31 “Guttman, Neuro Personal Trainer” (GNPT), a cognitive tele-rehabilitation platform that provides
32 neuropsychological services.

33 **Methods**

34 The ITA selects those tasks that are more suitable for the specific needs of each patient, considering
35 previous experiences, and improving the personalization of the treatment. The system applies data mining
36 techniques to cluster the patients according their cognitive impairment profile. Then, the algorithm rates
37 every rehabilitation task, based on its cognitive structure and the clinical impact of executions done by
38 similar patients. Finally, it configures the most suitable degree of difficulty, depending on the impairment
39 of the patient and his/her evolution during the treatment.

40 **Results**

41 The ITA has been evaluated during 18 months by 582 patients. In order to evaluate the effectiveness of
42 the ITA, a comparison between the traditional manual planning procedure and the one presented in this
43 paper has been done, taking into account: a) the selected tasks assigned to rehabilitation sessions; b) the
44 difficulty level configured for the sessions; c) and the improvement of their cognitive capacities after
45 completing treatment.

46 **Conclusions**

47 The obtained results reveal that the rehabilitation treatment proposed by the ITA is as effective as the one
48 performed manually by therapists, arising as a new powerful support tool for therapists. The obtained
49 results make us conclude that the proposal done by the ITA is very close to the one done by therapists, so
50 it is suitable for real treatments.

51

52 **1. Introduction**

53 Acquired Brain Injury (ABI) is defined as brain damage that suddenly and unexpectedly appears in
54 people's life, being the main cause of disability in developed countries [1]. The World Health
55 Organization (WHO) [2] predicts that by the year 2020 Traumatic Brain Injury (TBI) and stroke, the two
56 main causes of ABI, will be within the top five etiologies considering not only the economic cost, but also
57 costs related to Disability-Adjusted Life Year (DALY), that can be thought of as the number of years of
58 normal life lost by the disability.

59
60 Globally, cerebrovascular disease is the second leading cause of death and the eighth cause of severe
61 disability in the elderly. The WHO estimated that in 2005, stroke accounted for 5.7 million deaths
62 worldwide, and was the predominant cause of disability, afflicting 30.7 million people. Statistical data
63 shows that after a stroke, one third of patients die during the first month, and 40% of people who recover
64 from the acute phase exhibit a high degree of impairment that decreases their independence and quality of
65 life. Only one third of patients recovers their basic functions and can resume a normal life [3].

66
67 The incidence of TBI over industrialized countries is in a range of 200 to 300 per 100,000 habitants,
68 with an average age between 16 to 35 and mostly male [4].

69
70 Consequences of an ABI vary between cases and can cause motor, cognitive and behavioral deficits
71 to the patient, disrupting their daily life activities at personal, social and professional levels. The most
72 important cognitive deficits after suffering an ABI are those related to attention, decrease of memory and
73 learning capacity, worsening of scheduling and solving problems capacity, reduction of abstract thinking,
74 communication problems, and also a lack of conscience of their own limitations. These cognitive
75 impairments hamper the path to functional independence and a productive lifestyle for the person with
76 ABI [1].

77
78 New techniques of early intervention and the development of intensive ABI care have noticeably
79 improved the survival rate. However, despite these advances, brain injuries still have no surgical or
80 pharmacological treatment to re-establish lost functions [5]. In this context, cognitive rehabilitation is
81 defined as a process whereby people with brain injury work together with health service professionals and
82 others to remedy or alleviate cognitive deficits arising from a neurological insult [6].The provision of
83 cognitive rehabilitation thus becomes an essential part of the services to manage the complex disablement
84 provoked by ABI, allowing recovery of the altered functionalities and preventing the aging-related
85 deterioration. This is achieved by taking advantage of the plastic nature of the nervous system [7],
86 optimizing its capability of functional reorganization and stimulating the creation of new activation
87 patterns.

88
89 Despite the existence of empiric knowledge about the benefits of neuropsychological rehabilitation
90 [8], extending it to most potential users becomes difficult due to important limitations. First, the
91 traditional on-site intervention model requires a neuropsychologist supervising the procedure, to
92 administer exercises and cues, based on patient performance. The cost of this process limits the intensity
93 and length of the treatments, compromising sustainability, accessibility and scalability. Besides, the
94 patient is forced to move to the clinical center, making the duration of the treatment conditional to the
95 patient's availability. Finally, in the neuropsychological rehabilitation field there is an absence of clinical
96 practice guidelines to allow a rational extension of these services. Nevertheless, there is sufficient
97 information to support evidence-based protocols and implement empirically-supported treatments for
98 cognitive disability [9].

99
100 Neuropsychological rehabilitation and cognitive stimulation aim to minimize or compensate those
101 cognitive deficits for patients who suffer ABI. Traditionally, treatments consist of exercises with different
102 basis (e.g. cards, puzzles, blocks, images or objects), which are specifically selected from detected
103 deficits after a previous neuropsychological assessment. The use of Information and Communication
104 Technologies (ICTs) to develop tele-rehabilitation and tele-assistance systems allows improving the
105 quality and access to clinical services, helping to break geographical barriers. The main objective of tele-
106 assistance is centered on the patient, facilitating communication at different clinical levels. Moreover, one
107 of the main advantages of using ICTs is the possibility to extend the therapeutic processes beyond the
108 hospital (e.g. patient's home). Finally, a reduction of unnecessary costs and a better costs/benefits ratio are
109 achieved, making possible a more efficient use of the available resources [10-12].

110

111 “Guttmann, Neuro Personal Trainer[®]” (GNPT) [13] is a cognitive tele-rehabilitation platform aiming
112 to provide neuropsychological services by optimizing dedicated time with an asynchronous model,
113 increasing personalization and intensity of treatments. The rehabilitation process is also extended beyond
114 clinical centers, breaking geographical barriers. Besides, it automatically monitors treatments based on
115 established therapeutic criteria, reporting real time results and offering the most suitable therapeutic
116 options, based on the patient's characteristics and evolution. Finally, it allows knowledge extraction for
117 the establishment of clinical practice.

118

119 The aim of this work is to design, develop and evaluate an automatic therapy planning functionality,
120 called Intelligent Therapy Assistant (ITA), to help therapists to configure the patients' treatments in the
121 GNPT platform. In this first study, we have focused on the evaluation of the technical viability and the
122 efficiency of the ITA, trying to demonstrate if the clinical outcomes remain, at least, as good as when
123 using the traditional manual planning in GNPT. Besides, a higher variety in the selection of the
124 rehabilitation tasks is expected, what helps to increase the adherence of the treatment. Decision support
125 systems in medicine have been widely used for the last decades [14], like for example in diabetes care
126 [15], in the prevention of cardiovascular disease [16] or, in general, to improve the quality of medical care
127 [17]. However, there is no evidence in the scientific literature on such systems applied to cognitive
128 rehabilitation processes, neither any algorithm to automatically plan rehabilitation sessions to patients
129 based on the information stored in databases. The decision support system presented in this paper
130 classifies and selects the most suitable tasks for each patient, configuring the optimal input parameters to
131 adjust the difficulty level to each patient's specific needs. Data mining techniques are used to classify
132 similar patients, extracting knowledge from the stored results in the system's database.

133 2. Cognitive rehabilitation using GNPT

134 2.1. Rehabilitation process

135 Figure 1 shows the rehabilitation process followed in Institut Guttmann hospital for the cognitive
136 rehabilitation using GNPT.

137

138 The process starts by assigning a patient to a therapist responsible for the treatment. Then, the
139 therapist has to perform the initial neuropsychological assessment, consisting of a set of validated tests
140 used to evaluate cognitive functions (attention, memory or executive functions). The results of these tests
141 are stored in the system as the PRE neuropsychological assessment (prior to the treatment), and provide
142 the therapists with information to support their treatment decision. The normalization process and the
143 assignment to a cognitive profile are described in the section 2.4.1.

144

145 Usually, treatments consist of 2 or 3 sessions per week, with a total of 60 sessions that last one hour
146 each. The therapist defines these rehabilitation sessions by assigning a set of computerized tasks to a
147 certain day, configuring the input parameters of each task in order to personalize treatments. Once a
148 rehabilitation session is defined, the patient executes the assigned tasks, sending the results back to the
149 server, so therapists can asynchronously see the performance. These results help therapists to select the
150 difficulty level for the next sessions, adjusting treatment to patient evolution.

151

152 The system defines three different ranges of performance according to each task's execution score:

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- 154 • *Therapeutic* range, when the score is between 65% and 85% of correct answers. The patient
155 executes the task with an appropriate difficulty configuration in order to get the best treatment
156 effectiveness.
- 157 • *Infra-therapeutic*, when the score is below 65%. The difficulty level of the task is too high for
158 the patient's capacity and could also lead to frustration.
- 159 • *Supra-therapeutic*, when the score is above 85%. The difficulty level is too low for the patient's
160 capacity and the neurological activation is not being high enough. Could also lead to boredom.

161

162 These ranges are used by the system to improve the effectiveness of the rehabilitation, by
163 automatically re-launching a task when the score of the patient on that task is out of the therapeutic range,
164 re-adjusting the difficulty level. The objective is to have the patient most of the time executing tasks in
165 therapeutic range, trying to avoid the too easy (supra) or too difficult (infra) ranges during the treatment.

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After a patient completes the treatment, the therapist performs the final neuropsychological assessment (POST), which is compared to the PRE one. An improvement of the patient's cognitive capacities is considered when he or she improves, at least, one of the three main cognitive capacities, and does not get worse in any of the others.

172 2.2. Cognitive neuro-rehabilitation platform: "Guttmann, Neuro Personal Trainer[®]"

173 The "Guttmann, Neuro Personal Trainer[®]" (GNPT) is a tele-rehabilitation platform developed by a
174 multidisciplinary research team led by the Neuropsychosocial rehabilitation area and the research
175 office from the Institut Guttmann, together with the Biomedical Engineering and Telemedicine Centre of
176 the Universidad Politécnica de Madrid. The platform constitutes the second generation of the
177 PREVIRNEC tele-rehabilitation platform [18], which started providing cognitive rehabilitation services
178 in 2008.

179
180 GNPT incorporates multiple technological solutions, from telemedicine services to artificial
181 intelligence applied to knowledge extraction (data mining, collaborative environments, and real-time
182 system adaptation for every single patient). The system is conceived as a tool to enhance cognitive
183 rehabilitation, strengthening the relationship between neuropsychologists and patients, and offering
184 treatment personalization, results monitoring, and computerized rehabilitation tasks performance.

185
186 This neuro-rehabilitation platform consists of two main different components: on one hand, a web
187 application for therapies management (see Fig. 2), where the therapists configure and schedule
188 rehabilitation sessions that consist of a set of computerized tasks; and on the other hand, the client
189 application that patients use to execute the scheduled computerized tasks and send the results to the
190 server. The ITA algorithm has been developed as an innovative functionality for GNPT, helping
191 therapists on their treatment selection and configuration in order to schedule a personalized therapy to
192 each patient.

194 2.3. Rehabilitation tasks

195 The rehabilitation content used in GNPT consists of a set of computerized tasks [19], grouped in
196 categories (like ABI), which covers different cognitive functions and subfunctions, as shown in Table I.
197 Therefore, every task has been specifically designed by neuropsychologists to address a cognitive
198 subfunction, in order to obtain a better personalization of the treatment according to the patient's specific
199 needs. In total, GNPT has 95 tasks designed for ABI.

200

Cognitive function	Subfunction
Attention	Sustained
	Selective
	Divided
Memory	Visual
	Verbal
	Working
Executive functions	Scheduling
	Inhibition
	Flexibility
	Sequencing
	Categorization

201 *Table I. Cognitive functions and subfunctions classification for ABI category.*

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204 Additionally, neuropsychologists have defined a set of input parameters for every task (e.g. number
205 of images, presentation speed, or latency time), allowing to configure different difficulty levels.
206 Therefore, the treatments can be adjusted to the patient's specific needs. Besides, they have also defined
207 how the execution result is calculated, based on several performance parameters (e.g. correct and wrong
208 answers, omissions, execution time, etc.) depending on each task. Thus, when a patient performs a task, a
209 score between 0 and 100 is always calculated and assigned to that execution.

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Examples of two computerized neuro-rehabilitation tasks for ABI patients are shown in Fig. 3.

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In order to help the reader to understand how the ITA algorithm works, the Bingo task is going to be used as an example through the paper. In this task the patient is required to click on the numbers appearing on the screen (see example on the right of Fig. 3) and it belongs to the cognitive subfunction “sustained attention”. It has three input parameters, with the following values:

- Dimension of the matrix: “4x4”, “5x5” or “6x6”, representing the number of rows and columns of the bingo card.
- Presentation time: 4, 3.5, 3, 2.5 or 2, meaning the seconds that each number remains on the screen.
- Level: “ordered” or “in disorder”, related to how numbers are spread along the bingo card.

The results defined for this task are the number of correct, incorrect and omitted answers. Thus, the execution score is calculated as the correct answers divided by the total answers, including the numbers omitted.

Figure 4 shows the interface used by therapists to manually adjust the values of the different input parameters.

230 **3. Materials and Methods**

231 **3.1. Clustering of ABI patients**

232 GNPT implements a data analysis module able to filter, analyze and extract knowledge from the
233 information stored in the database, in order to aid neuropsychologists in decision-making processes. The
234 use of data mining techniques to predict the outcomes of cognitive rehabilitation in patients with ABI [20]
235 has been revealed as a powerful tool for obtaining new knowledge to evaluate and improve the
236 effectiveness of the cognitive rehabilitation process. Applying data mining techniques to group patients
237 allows us to determine the most suitable therapies for each case, depending on the results and evolution of
238 other similar patients in previous treatments.
239

240 In particular, a clustering algorithm has been used to group patients with similar characteristics in
241 order to compare treatments and the evolution of similar patients [21]. The data mining and clustering
242 algorithm has been programmed using the Weka tool (University of Waikato, New Zealand), by
243 implementing the Expectation Maximization (EM) clustering technique. This probabilistic clustering
244 technique is based on a statistical model called Mixture that provides the probability for each patient to
245 belong to a certain cluster.
246

247 The clustering module assigns a patient to a cluster, depending on his or her cognitive profile. This
248 profile is calculated using the PRE neuropsychological assessment of the cognitive functions, after a
249 normalization process that takes into account the patient's age and study level. Each test's item has been
250 semantically translated onto the International Classification of Functioning, Disability and Health of the
251 WHO [22], as a common taxonomy to describe patient's cognitive and functional impairment. As a result,
252 the process rates the 11 defined cognitive subfunctions between 0 (normality) and 4 (very severe
253 impairment) for each patient, resulting on a cognitive profile. The process flow is shown in Fig. 5.
254

255 Every time a new patient starts treatment using GNPT the clusters are calculated, considering all the
256 information of patients who have already followed a therapy. So, this approach tries to use all the
257 available knowledge in the system related to the PRE tests and the previous therapies and results.
258

259 In the end, this clustering process allows the system to group patients with similar characteristics, in
260 order to automatically determine which rehabilitation tasks work better for each cognitive profile, taking
261 into account all previous results and improvements done by similar patients in the past. Moreover, this
262 knowledge can be used to learn about the neuro-rehabilitation processes and to improve the designed
263 tasks, modifying the ones that appear not to be appropriate for certain kind of patients.
264

265 **3.2. Intelligent Therapy Assistant (ITA)**

266 The Intelligent Therapy Assistant (ITA) algorithm automatically schedules rehabilitation sessions to
267 patients, considering the assigned cognitive profile to determine which tasks are more suitable for their
268 specific needs. The execution results from previous rehabilitation sessions processed by the ITA help the
269 therapist to efficiently personalize treatments according to the patient's characteristics. Naturally, the
270 suggestions provided by the ITA can always be modified by therapists according to their own clinical
271 criterion and experience.
272

273 In order to determine the suitability grade for each of the 95 different tasks defined in the system for
274 ABI, the ITA rates every task based on the following scoring criteria:

- 275 • *usage score (U)*, considering the number of times that the task has been used in other
276 treatments.
- 277 • *improvement score (I)*, considering the results obtained by similar patients who executed the
278 task.
- 279 • *clinical score (IL&CC)*, as a combination of two different criteria: the *impairment level*
280 *score (IL)*, considering the patient's initial neuropsychological exploration (PRE) results;
281 and a *clinical criterion (CC)*, considering subjective neuropsychologists' experience to
282 determine how good a task is to rehabilitate each cognitive function.
283

284 This scoring process is defined together with a set of variables and coefficients, shown in the
285 equation in Fig. 6, allowing the neuropsychologists to adjust the results calculated by the ITA in order to
286 get more realistic configuration results based on their own clinical experience.
287

288 Once the scoring process is finished, the system rates all tasks according to their Global Suitability
289 Score (GSS). Then, the system splits these ordered tasks into Suitability Quartiles, from most suitable
290 (SQ1) to less suitable (SQ4). Finally, the automatic therapy planning is done by selecting tasks from the
291 Suitability Quartiles, configuring the appropriate difficulty depending on the rehabilitation needs of each
292 patient.
293

294 Figure 6 summarizes the process of assigning the score to every task, rating them into suitability
295 quartiles, and how the difficulty level is selected to personalize treatments.
296

297 A complete description of the algorithm and its scoring criteria is described next.
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299

300 3.2.1. Usage score (U)

301 This first criterion gives a score to the task considering the number of executions done by patients
302 with the same cognitive profile. Thus, the used tasks are ordered and divided into quartiles. The algorithm
303 then assigns a score to each task, giving a 4 to the tasks that belongs to the most used quartile, and 1 to the
304 less used quartile, while a 0 is given to the not used tasks.
305

306 Consequently, those tasks that have been used more times for similar patients, receive a higher score,
307 rewarding the previously scheduled tasks in GNPT by all the therapists.
308

309 3.2.2. Improvement score (I)

310 This second rule rates tasks taking into account the improvement of similar patients who executed the
311 task on the subfunction that particular task was designed for (e.g. sustained attention for the task Bingo).
312 Besides, this rule also considers the improvements that similar patients who executed the task had on the
313 other cognitive functions apart of the one it was designed for (e.g. in the case of the Bingo task, that
314 would be memory and executive functions).
315

316 Additionally, thanks to the coefficients defined in the algorithm, neuropsychologists can adjust this
317 rating to promote those tasks that help patients not only to improve the subfunction they were defined for
318 but also the other cognitive functions.
319

320 3.2.3. Impairment level score (IL)

321 This score takes into account the patient's previous impairment level (PRE) for every subfunction and
 322 function, taking the normalized value of the neuropsychological assessment (from 0 meaning normality to
 323 4 meaning very severe impairment).

324
 325 The algorithm gives a higher score to those tasks designed for the patient's most impaired functions.
 326 On the other hand, if the scoring task is defined for a cognitive function that has less affectation, it
 327 receives a lower score.

328
 329 Using this rule the ITA tries to reward those tasks that belong to the patient's more damaged
 330 cognitive functions, because patients need to rehabilitate these impaired functions more than the less
 331 impaired ones.

332

333 *3.2.4. Clinical criteria score (CC)*

334 This score determines, from 0 to 4, the suitability of every task to each defined subfunction in ABI.
 335 This fourth rule is based on the clinical experience of the neuropsychologists of the Institut Guttmann,
 336 who have determined how good is every neuro-rehabilitation task defined in GNPT for the treatment of
 337 all the defined 11 subfunctions.

338

339 Therefore, a task that has been classified for a certain subfunction can also have a high score for the
 340 treatment of other subfunctions, due to their suitability to rehabilitate cognitive capacities in other
 341 subfunctions and functions. For example, the Bingo task receives a 4 for sustained attention, 2 for
 342 selective attention and 1 for divided attention, while receiving a 0 for all the remaining subfunctions.

343

344 *3.2.5. Clinical score (IL&CC)*

345 This score combines the two previous ones, since they are the most subjective criteria of the
 346 algorithm. It also has a coefficient that allows the algorithm to give more or less importance to this
 347 combined rule compared to the usage and improvement scores, which are more objective rules.

348

349 Table II shows an example of the clinical score for the Bingo task, with a particular patient's
 350 impairment level and the clinical criteria defined for that task. The Clinical Score is calculated
 351 multiplying both subfunction values, obtaining the final score adding them up. So, the Bingo task would
 352 receive 19 points according this combined rule.

353

Cognitive function	Subfunction	Patient's Impairment Level (IL)	Clinical Criteria for Bingo (CC)	Clinical Score
Attention	Sustained	3	4	12
	Selective	2	2	4
	Divided	3	1	3
Memory	Visual	2	0	0
	Verbal	1	0	0
	Working	3	0	0
Executive functions	Scheduling	1	0	0
	Inhibition	0	0	0
	Flexibility	1	0	0
	Sequencing	2	0	0
	Categorization	0	0	0
			Final Clinical Score (IL&CC)	19

354 *Table II. Clinical Score example for the Bingo tasks and a patient's impairment level*

355

356

357 *3.2.6. Global suitability score*

358 Once we have all tasks rated according to the previous three scores, we get the Global Suitability
 359 Score (GSS) as a weighted sum of those values. As we can see, thanks to the different coefficients (kx)
 360 the algorithm's punctuation result can be adjusted to give more or less weight to each of the defined
 361 criteria.

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$$GSS = (U \times ku) + (I \times ki) + (IL \& CC \times kc)$$

Finally, the system splits all the tasks into suitability quartiles (SQ1, SQ2, SQ3, and SQ4). Then the ITA is ready to automatically create rehabilitation sessions, by randomly assigning tasks from the different four suitability quartiles, until the maximum duration of the session is reached (by default, a rehabilitation session lasts one hour). To do this, the following order is followed: 3 tasks from SQ1, 2 tasks from SQ2, 2 tasks from SQ3 and 1 task from SQ4, and so sequentially. As a result, the algorithm is rewarding tasks from SQ1, but without looking down on the rest of tasks that belong to the other quartiles.

373 3.2.7. Difficulty Quartiles

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Due to the fact that every computerized task used in GNPT has a set of input parameters to configure the difficulty level, the system assigns a weight to each parameter value, from 0 to n, where 0 means less difficulty. So, each possible parameter values configuration is classified into the Difficulty Quartiles (DQ). The goal is to generate combinations of values to schedule either easy or difficult tasks, adjusting the sessions to the patient's specific needs. The ITA determines which DQ has to be selected when a task is assigned to a certain rehabilitation session, based on the patient's PRE impairment level.

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The ITA schedules sessions in blocks of ten, so for the next ten sessions both the PRE neuropsychological assessment and the results that the patient has already obtained during the treatment are taken into account. This second adjustment criterion parameter is based on the Mean Execution Result for a certain Subfunction (MERS) of the task, which calculates the average result of every already executed task for each subfunction. Thus, the ITA adjusts the difficulty level of the scheduled tasks considering the evolution of the patient, as follows:

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- If MERS is in infra therapeutic range ($MERS < 65\%$) the algorithm adds one to the PRE normalized value for that subfunction, considering that the patient needs easier tasks to rehabilitate that function.
- If MERS is in the therapeutic range ($65\% < MERS < 85\%$) the ITA subtracts one to the PRE value for that subfunction, considering that the patient is positively evolving and so can do more difficult tasks.
- If MERS is in the supra therapeutic range ($MERS > 85\%$) the ITA subtracts two to the PRE value for that subfunction, considering that the patient can do even more difficult tasks.

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This modification considering the MERS comes after an evaluation of the first ITA version, where these patient's execution results were not taken into account. In that previous version, the algorithm scheduled a complete treatment set (normally 60 sessions) instead of blocks of ten. Clinicians saw that the ITA's proposal did not adjust to the patient's evolution during the treatment. As a result, the previous ITA version scheduled tasks at the end of the treatment with a difficulty level lower than the suitable one, so the MERS modification was introduced in the second version.

403 3.3. Evaluation

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GNPT system is running at the Institut Guttmann Hospital in clinical routine, so specific ethical approval is not required to carry out this study. Nevertheless, clinical data usage is aligned with the Declaration of Helsinki, and every treated patient signs the informed consent to participate in the program.

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The aim of this evaluation is to evaluate the technical viability and to measure the impact on the efficiency and clinical outcome. So, to evaluate the ITA algorithm, the present study compares the results of the historic manual configuration of sessions performed by therapists to the results once they had the ITA functionality available in the GNPT platform. The ITA has been used for 18 months by 28 different therapists (12 therapists belonging to the Institut Guttmann and 16 therapists from other clinical centers). In total, 582 patients have received treatment using the algorithm presented here, 126 using the first version and 456 using the second one. This means 20,127 rehabilitation sessions automatically scheduled with 92,813 executed tasks. Considering manual planning done by therapists, 1,210 patients have completed treatment, with 44,989 rehabilitation sessions and a total of 286,870 executed tasks.

So, the assessment of the ITA algorithm is focused in the following three outcome parameters:

420 3.3.1. *Selected tasks for rehabilitation sessions*

421 In order to compare which tasks are selected for rehabilitation sessions, the number of times that each
422 of the 95 available ABI tasks has been selected has been studied. This will let us know if there are
423 significant differences between the tasks manually selected by therapists compared to those automatically
424 selected by the ITA. A higher variety for the ITA is expected, since the amount of information that a
425 therapist can manage is limited, and they usually schedule the ones that they know the most.
426

427 3.3.2. *Difficulty level selected*

428 The evaluation criteria for assessing the difficulty level configured by the ITA, has been to measure
429 the number of tasks executed in therapeutic range by patients. As it is explained in section 2.1, the system
430 always tries to have patients most of the time executing tasks in therapeutic range, trying to avoid the too
431 easy (supra) or too difficult (infra) ranges during the treatment, and so increasing the effectiveness of the
432 treatment.
433

434 At this point, the two versions of the algorithm have been analyzed separately, as we wanted to see
435 the benefits of the improvements introduced in the second one. As it is explained before, the first version
436 of the algorithm scheduled 60 sessions at a time, setting the difficulty level considering just the PRE
437 neuropsychological assessment results. On the other hand, the second version scheduled blocks of ten,
438 taking into account not only the PRE results, but also the patient's evolution to adjust the difficulty of the
439 following rehabilitation sessions.
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441 3.3.3. *Improvement of the cognitive capacities*

442 A study comparing the improvements achieved by patients after completing treatment has also been
443 carried out. The objective is to see if there are significant differences between the cognitive capacities
444 improvements for those patients that received manual treatment compared to those who received it using
445 the ITA algorithm. Thus, differences between the clinical outcomes will be analysed, letting us to know if
446 the introduction of the ITA into GNPT has undesirable consequences.
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448 So, in order to see the improvements after treatment, a comparison between the PRE and the POST
449 neuropsychological assessment is done, being able to determine the evolution for each cognitive function
450 and subfunction. To carry out the study, we have used a sample of 746 brain injury patients for manual
451 treatment (64% men), while 141 patients have been selected for ITA treatment (55% men). All of them
452 where adults between 16 and 55 years old, with a complete PRE and POST neuropsychological
453 assessment that allows us to see the improvements on the cognitive capacities after completing treatment.

454 **4. Results**

455 The results of the first outcome parameter are presented, showing the number of times that each task
456 is selected for a rehabilitation session. Next, how the ITA configures the difficulty level of the
457 rehabilitation tasks is compared, in order to assess which method adjusts better the difficulty according
458 to the cognitive affectation level. Finally, a comparison between the improvements of the cognitive
459 capacities after completing treatment is shown, in order to assess the clinical outcomes achieved by the
460 ITA.

461 **4.1. Selected tasks for rehabilitation sessions**

462 As it is said before, GNPT has 95 different rehabilitation task for treating ABI patients. Figure 7
463 shows the ITA results considering the number of times that each of these 95 tasks has been selected for a
464 rehabilitation session. In order to compare the tasks manually selected by therapists to those automatically
465 selected by the ITA, results have been normalized to the total number of tasks scheduled, not only the
466 executed one, but also all the selected tasks to be assigned to a rehabilitation session (399,409 for manual
467 planning and 190,197 for ITA planning). So, we can compare the frequency of selection of a task for a
468 rehabilitation session.
469

470 Figure 7a represents a selection of the most selected ones by therapists, while Figure 7b represents
471 the less used ones by therapists. The y-axis represents the number of times that a task is selected to be
472 assigned to a rehabilitation session, normalized to the total of scheduled tasks, so both data can be

473 compared. On the other hand, the x-axis represents the identification number of the task in the database,
474 so each pair of columns represents a same task.

475

476 Besides, there is statistically significant difference (p -value < 0.001) between the manual and the ITA
477 selection of tasks, ensuring that there are differences between the tasks selected by therapists to those
478 ones selected by the ITA

479

480 **4.2. Difficulty level selected**

481 In order to assess how appropriate is the difficulty level selected to the assigned tasks, the number of
482 tasks executed in therapeutic range has been studied (the results are shown in Fig. 8). This graph
483 compares the manual planning done by therapists to the automatic one done by the ITA. Besides, the ITA
484 results are shown distinguishing between the two versions of the algorithm. Remember that the first
485 version only considered the patient's PRE assessment results to configure the difficulty level of the
486 scheduled tasks, while the second one also added the patient's evolution during treatment to determine the
487 most suitable difficulty configuration.

488

489 In order to see if there are significant differences between these results, statistical analysis have been
490 done. After doing the chi-square test for the three samples, it shows a p -value < 0.001 , so we can ensure
491 that there are significant differences between the results obtained by the three methods.

492

493 **4.3. Improvement of the cognitive capacities**

494 The results of the patients' improvement after completing treatment are shown in Fig. 9. As it is
495 described before, the improvement of the cognitive capacities is calculated comparing the PRE and POST
496 neuropsychological assessment. Once we have this comparison, we consider that a patient improves their
497 cognitive capacities if, at least, he or she improves one main cognitive function and get not worse in any
498 of the others.

499

500 Regarding the statistical study, p -value is equal to 0.3484, showing that there is not significant
501 differences between the improvements achieved by each method.

502 **5. Discussion**

503 In this study the Intelligent Therapy Assistant (ITA) algorithm has been evaluated, as an integrated
504 functionality in the "Guttmann, Neuro Personal Trainer[®]" (GNPT) tele-rehabilitation platform. The ITA
505 has been used during 18 months as an automatic tool for the selection and scheduling of therapies for
506 cognitive rehabilitation.

507

508 Looking at the results for the selected tasks assigned to rehabilitation sessions we see that there are
509 some "favorite" tasks for therapists when planning those sessions; and also the opposite, where some
510 tasks are rarely used to treat patients (Fig. 7). Considering that the results of the executed tasks are quite
511 similar, we can say that the ITA is selecting some tasks that are not taken into account by therapists. The
512 same way, the ITA is not giving so much importance to those "favorite" tasks, so we can think that many
513 times therapists select those tasks that they know or like more, and not only those which would work
514 better for the specific needs of the patient. This more equal distribution is achieved thanks to the
515 Improvement and Clinical Scores implemented in the algorithm, compensating the Usage one. So, the
516 ITA also considers the information regarding tasks that could not be properly executed by patients,
517 neither those executions that did not turn into a clinical improvement. This procedure should allow us to
518 refine when a task is selected for a rehabilitation session, beyond the implicit knowledge of the clinicians
519 and their different preferences (knowledge of a task, aesthetic preferences, etc.). Furthermore, the ITA
520 also incorporates the theoretical preferences chosen by consensus of the therapists regarding the
521 suitability of each exercise to rehabilitate each one of the cognitive domains defined in the system (e.g.
522 visual memory or sustained attention). Theoretically, this should lead to a generalization and offer to the
523 patients more varied and better accepted treatments. In this way, the main objective of the ITA and what
524 we try to demonstrate in this work, is the possibility to elaborate a therapeutic plan taking into account all
525 the theoretical premises agreed by clinical consensus. Thus, we offer to the patient more varied exercises
526 and keep, at least, the same level of efficacy than the manual planning, but with lower associated costs

527 and less dependent to the expertise of the therapist (clinical expertise, knowledge of the system,
528 knowledge of the rehabilitation tasks...).

529
530 Considering the percentage of tasks executed in therapeutic range comparing therapists (23.34%) to
531 ITA v2 (28.11%) (Fig. 9), we can ensure that the difficulty selection procedure performed by the ITA is
532 as good as the one used by therapists. Actually, if we see the results from the two versions of the
533 algorithm, we see that the second one achieves the best therapeutic range percentage. Furthermore, it is
534 desirable to avoid the supra therapeutic range, as we would be trying to treat problems that the patient
535 does not have. Considering this, the second version of the ITA has a 65.37% of executed tasks in infra
536 and therapeutic range, while the manual procedure has 59.96% and the ITA v1 57.06%. So, we can
537 guarantee that the new characteristics introduced to the second version sensibly improved the results,
538 since the algorithm considers not only the initial PRE assessment to determine the difficulty level of the
539 tasks, but also the patient's evolution during the treatment. However, both therapists and ITA results are
540 quite low, so a deeper study on how GNPT configure the difficulty level has to be carried out to improve
541 the number of tasks executed in therapeutic range. Besides, the different therapeutic ranges are not based
542 on any empiric evidence, but only on general assumptions about which are the generally accepted results
543 desirable to be performed by patients [23]. In this way, we are already planning a deeper study to evaluate
544 this hypothesis.

545
546 This previous analysis have been done to demonstrate if the ITA algorithm correctly selected the
547 possible parameters values when assigning a task to a rehabilitation session, trying always to have the
548 patient executing tasks in therapeutic range, where the rehabilitation is more efficient. But the final stage
549 of our study is to analyze the differences between the improvements that patients experiment after
550 completing GNPT treatment, comparing those ones treated using the traditional manual planning to those
551 treated using the ITA algorithm. Figure 10 represents the improvement percentage results, where it is
552 shown that there is no significant difference (with a p-value = 0.3484) between the two treatments
553 methods. These results make us conclude that the proposal done by the ITA is very close to the one done
554 by real therapists, so it is suitable for real treatments. However, there is no evidence demonstrating that an
555 improvement in cognitive functions turns into an improvement in Activities of the Daily Living (ADL).
556 In this regard, we plan to introduce ADL questionnaires to assess how the improvement of cognitive
557 functions benefits patient's quality of life and to introduce this outcome in the proposal done by the ITA.

558
559 Besides, the time saved for therapists is quite significant, because they do not need to invest time
560 searching, selecting and configuring tasks, just click a button and wait until the intelligent and automatic
561 process finishes and then verify the proposal and modify those tasks and configurations that they do not
562 consider appropriate. After analysing the time expended by therapists in Institute Guttmann using both
563 methods, we have seen that the mean time used for manual planning is about thirty minutes per ten
564 sessions, while by using the ITA the time is reduced to approximately 5 minutes. So, the reduction of
565 time turns into a considerable increase of the efficiency of the procedure. This functionality could also be
566 a good support for a novel therapist, who does not have a high knowledge of every GNPT rehabilitation
567 task, helping them to select the more appropriate tasks for each specific patient.

568
569 Looking at the clustering process implemented, we have described how the system dynamically
570 calculates all the clusters when a new patient starts the treatment, instead of assigning a new patient to an
571 already calculated cluster. This way the system ensures that all the clusters are the most suitable to group
572 patients according their cognitive profile, adapting the process to the new patients coming. However,
573 since the variables taken into account to define the clusters are not many, and the amount of patients
574 included in the process is considerably high, we presume that the number of calculated clusters might be
575 tending to stabilization. So, further research must be done in the future, trying to add new clinical
576 variables and also to study the different cognitive profiles defined by the process and their stability. Then,
577 if the clusters are eventually stable, the clustering process might be changed by a classification model.

578
579 Besides, another new work is being done, trying to cluster patients based on their results and
580 evolution during treatment. In the coming future, this work will allow us to define new variables to
581 predict how a patient will evolve during the treatment, or even just after the PRE results, by using a
582 prediction model.

583 6. Conclusions

584 This paper presents the design and first evaluation of an algorithm called Intelligent Therapy
585 Assistant (ITA). This new algorithm automatically plans rehabilitation sessions for patients suffering
586 ABI, who are receiving treatment using the cognitive neuro-rehabilitation platform “Guttmann, Neuro
587 Personal Trainer[®]” (GNPT). The ITA assigns a score to the computerized neuro-rehabilitation tasks,
588 grouping them into suitability quartiles depending on how good they are for the patient's specific needs.
589

590 The ITA is presented as a new powerful support tool for therapists. By managing the high amount of
591 stored data and applying data mining techniques, the ITA extracts information related to the task's
592 suitability to treat each patient depending on his or her cognitive profile. The algorithm has been used for
593 18 months, with promising results. The improvements achieved by patients in their cognitive capacities
594 after completing treatment using the ITA algorithm are also very similar to the results obtained by using
595 the manual planning. These results make us conclude that the proposal done by the ITA is very close to
596 the one done by real therapists, so it is suitable for real treatments.
597

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606

607

608 **Competing interests**

609 The authors declare that they have no competing interests.

610

611

612 **Authors' Contributions**

613 **J. Solana** has contributed to the design and implementation of the assistant; to the integration into the
614 tele-rehabilitation platform; to the evaluation of the obtained results; and to the interpretation of the
615 results.

616 **C. Cáceres** and **P. Chausa** have contributed to the design of the algorithm; and have supervised the
617 development and evaluation of the assistant.

618 **A. García** has contributed to the design of the assistant; to the clinical validation; and to the analysis and
619 interpretation of the results.

620 **E. Opisso** and **T. Roig** have contributed to the conception and design of the assistant; and the definition
621 of the evaluation methodology.

622 **J.M. Tormos** has contributed to the conception and design of the assistant; the definition of the
623 evaluation methodology; and has coordinated the research work from the clinical point of view.

624 **E.J. Gómez** and **E. Menasalvas** has contributed to the conception and design of the system; has
625 supervised the technical evaluation; and has coordinated the research work from the Biomedical
626 Engineering point of view.

627 **J. Solana**, **C. Cáceres** and **P. Chausa** wrote the first draft of the manuscript. All authors have revised it
628 critically and have approved the final version before submission.

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- 694

695 **Figure legends**

696

697 *Figure 1. Rehabilitation process followed using NPT*

698 Diagram illustrating the rehabilitation process followed at the Institut Guttmann using Neuro
699 Personal Trainer

700

701 *Figure 2. Main menu of the user interface for therapists, with all the functionalities implemented*

702 The figure shows an example of the user interface that the therapists see when accessing the
703 system for managing treatments. Each hexagon gives access to a main functionality, like the reports
704 module, or the communication one.

705

706 *Figure 3. Neuro-rehabilitation tasks examples*

707 The figure shows two examples of rehabilitation tasks used in NPT, for treating working
708 memory (left), and sustained attention (right).

709

710 *Figure 4. Input parameters configuration*

711 Example of interface used to configuring the input parameters of a task, used by therapists to
712 configure the difficulty level when scheduling rehabilitation tasks.

713

714 *Figure 5. Clustering process diagram*

715 Diagram illustrating the different phases of the process followed by the system to assign a patient
716 to a certain cluster, depending on the patient's neuropsychological assessment and the normalization
717 process that takes into account both the age and study level.

718

719 *Figure 6. ITA algorithm diagram*

720 Diagram illustrating the different scoring criteria and phases used to determine the most suitable
721 tasks to the patient's specific needs. Then, both the impairment level and the previous tasks results
722 are used to configure the tasks' difficulty level.

723

724 *Figure 7. Tasks selected to treatments comparing traditional manual planning to ITA one*

725 Blue bars represent the traditional manual planning done by therapists, while red bars show the
726 ITA planning. The left one represents a selection of the most selected ones by therapists, while the
727 right one represents the less used ones by therapists. The y-axis represents the number of times that a
728 task is selected to be assigned to a rehabilitation session, normalized to the total of scheduled tasks,
729 so both data can be compared. On the other hand, the x-axis represents the identification number of
730 the task in the database.

731

732

733 *Figure 8. Execution results tasks ranges comparing manual to ITA planning*

734 This graph compares the manual planning done by therapists to the automatic one done by the
735 ITA. Take into account that the ITA results are shown distinguishing between the two versions of the
736 algorithm: the first version only considered the patient's PRE assessment results to configure the
737 difficulty level of the scheduled tasks, while the second one also added the patient's evolution during
738 treatment to determine the most suitable difficulty configuration.

739

740 *Figure 9. Patient's improvement comparison between manual and ITA planning*

741 This figure shows the percentage of patients who improve their cognitive capacities after
742 completing treatment, comparing the traditional manual planning to the automatic ITA one.