(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
4 September 2014 (04.09.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/131090 A1

(51) **International Patent Classification**:
A61B 5/16 (2006.01) *G09B 3/00* (2006.01)
G09B 7/00 (2006.01)

(21) **International Application Number**:
PCT/AU2014/000191

(22) **International Filing Date**:
28 February 2014 (28.02.2014)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:
2013900705 1 March 2013 (01.03.2013) AU
2013903014 9 August 2013 (09.08.2013) AU

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(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,

[Continued on next page]

(54) **Title**: SYSTEM AND METHOD FOR ASSESSING IMPULSE CONTROL DISORDER

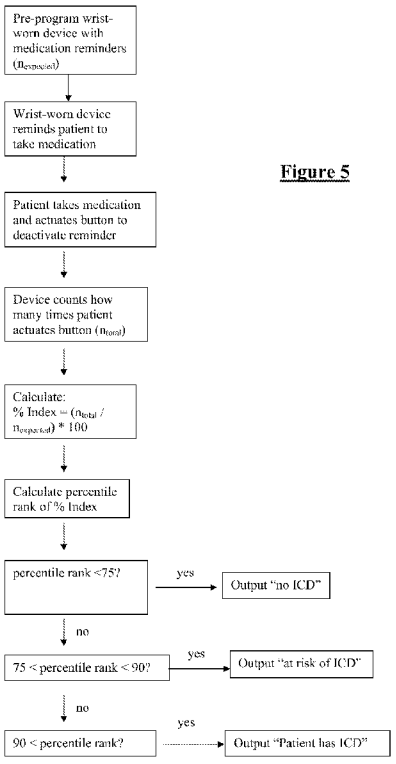

Figure 5

(57) **Abstract**: A method of assessing the likelihood that an individual has impulse control disorder. The individual is provided with an actuator, and instructed to actuate the actuator as an acknowledgement of when the individual has completed a reward task. Actuation of the actuator is monitored and recorded. An automated diagnosis of ICD is produced and output, wherein a greater degree of actuation of the actuator by the individual is taken to indicate a greater likelihood that the individual has impulse control disorder.

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EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

SYSTEM AND METHOD FOR ASSESSING IMPULSE CONTROL DISORDER

Cross-Reference To Related Applications

[0001] This application claims the benefit of Australian Provisional Patent Application No. 2013900705 filed 1 March 2013, which is incorporated herein by reference, and also claims the benefit of Australian Provisional Patent Application No. 2013903014 filed 9 August 2013, which is incorporated herein by reference.

Technical Field

[0002] The present invention relates to a system and method for remotely monitoring individual behaviour, and in particular to a system and method configured to isolate ICD-like behaviour and remotely monitor ICD-like behaviour.

Background of the Invention

[0003] Impulse control disorder, or ICD, is a class of psychiatric disorders characterized by impulsivity, namely the failure to resist a temptation, urge or impulse. ICD involves pathological behaviour (impulsive-compulsive behaviours (ICBs)) which can include one or more of impulsive gambling, impulsive eating, impulsive buying, impulsive sexual behaviour, impulsive cleaning, Internet addiction, punding, hobbyism, hoarding, kleptomania, impulsive smoking, impulsive medication use, and/or one or more of a large number of other impulsive behaviours.

[0004] Dopamine agonists used for the treatment of Parkinson's disease (PD) are known to cause impulse control disorder, amongst other causes.

[0005] Diagnosing ICD can be difficult due to the secretiveness of many of the behaviours, and /or due to the need for the individual to self-report the existence and/or severity of the behaviour. Presently, ICD behaviour is evaluated in the clinical environment, requiring highly trained and astute professionals, and ICD diagnosis and treatment is thus relatively expensive. Clinical evaluation of ICD nevertheless can be imprecise as the individual's inhibitions in the clinical environment may motivate the individual to mask symptoms, and also because the clinician often relies on subjective self-reporting and patients often fail to report ICBs due to embarrassment and/or a lack of awareness of the relationship between PD and ICD.

[0006] Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is solely for the purpose of providing a context for the present invention. It is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present invention as it existed before the priority date of each claim of this application.

[0007] Throughout this specification the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

[0008] In this specification, a statement that an element may be "at least one of" a list of options is to be understood that the element may be any one of the listed options, or may be any combination of two or more of the listed options.

Summary of the Invention

[0009] According to a first aspect the present invention provides a method of assessing the likelihood that an individual has impulse control disorder, the method comprising:

providing the individual with an actuator, and instructing the individual to actuate the actuator as an acknowledgement of when the individual has completed a reward task;

monitoring and recording the actuation of the actuator;

producing an automated diagnosis of ICD, wherein a greater degree of actuation of the actuator by the individual is taken to indicate a greater likelihood that the individual has impulse control disorder; and

outputting the automated diagnosis of whether the individual has impulse control disorder.

[0010] According to another aspect the present invention provides a non-transitory computer readable medium for assessing the likelihood that an individual has impulse control disorder, comprising instructions which when executed by one or more processors causes performance of the following:

processing records of actuation of an actuator by an individual, the individual having been instructed to actuate the actuator as an acknowledgement of when the individual has completed a reward task;

producing an automated diagnosis of ICD, wherein a greater degree of actuation of the actuator by the individual is taken to indicate a greater likelihood that the individual has impulse control disorder; and

outputting the automated diagnosis of whether the individual has impulse control disorder.

[0011] According to another aspect the present invention provides a computer program product comprising computer program code means to make a computer execute a procedure for assessing the likelihood that an individual has impulse control disorder, the computer program product comprising computer program code means for carrying out the method of the first aspect.

[0012] In some embodiments of the invention, the task of actuating the actuator is made salient to the reward task from the perspective of the individual. An individual having ICD is more likely to display ICD-like behaviour by repetitively actuating the actuator if the actuator is considered salient to the reward task. The reward task may be pleasurable; favourable or desirable to the individual. Notably, the present invention does not require that the performance of the task itself is monitored; rather, the diagnostic configuration provided by the present invention provides for a separate actuator which the individual is motivated to actuate as an acknowledgement of completion of the reward task. Such embodiments of the present invention then monitor for the presence or absence of ICD-like behaviour in relation to the actuator, but not necessarily in relation to the reward task.

[0013] Assessment of a degree of actuation of the actuator is in some embodiments made by comparison to an expected degree of actuation of the actuator. For example, the user might be instructed or expected to actuate the actuator once upon completion of a reward task, whereby actuation of the actuator more than once is taken to indicate a greater likelihood that the individual has impulse control disorder. For example, in some embodiments if the user actuates the actuator moderately more than expected, such as by a number of times which is more than 40% more than the expected degree of actuation, an output may be generated to indicate that the user is at risk of ICD. In some embodiments if the user actuates the actuator significantly more than expected, such as by a number of times which is more than 65% more than the expected degree of actuation, an output may be generated to indicate that the user has ICD. Thus, in monitoring for a greater degree of actuation of the actuator, some embodiments may monitor for

actuation of the actuator beyond what is required or has been instructed in order to complete the reward task.

[0014] The actuator may be a button, dial, lever, questionnaire tick-box, or any sensor or input device responsive to a motor response of the individual. For example the actuator may be a button of a device which reminds the individual to take medication, wherein the device is configured to remind the individual to take medication when required, and wherein pressing the button once deactivates the reminder to indicate that the medication has been taken. A user pressing the button more than once can then be taken as indicating a greater likelihood that the individual has impulse control disorder. The device may be body-worn such as a wrist-worn alarm device, or may be located separately to the individual such as a smart phone, tablet device or personal computer configured to generate reminders to the individual.

[0015] Preferably, the individual is given the impression that the actuator is for an alternative purpose and is not informed that their actuation of the actuator is being monitored beyond that alternative purpose. In such a state of mind any ICD-like behaviour of the individual is more likely to manifest in an uninhibited manner in relation to the actuator, and to be realised as an impulsive actuation pattern which can be monitored in a less inhibited, more automated and less costly manner than is provided by clinical evaluation. Moreover, a person suffering ICD is less likely to take excessive medication as a result of having ICD, for example, but in contrast is likely to actuate an actuator many times without reason particularly if the actuator is presented as being salient to the task of taking medication.

[0016] Notably, the present invention thus provides for the measurement of impulse behaviour in PD by monitoring user activity on device controls which provide other functions. This avoids the need for a patient to self-report ICD behaviour nor undertake a self-assessment, and thus avoids the inaccuracy of such reporting and self-assessment.

[0017] This automated system may in some embodiments give the chance to see an ICD risk as it develops, and possibly before conventional ICD behaviour actually occurs.

[0018] Upon generation of an indication that a user has ICD or is at risk of ICD, some embodiments may in turn provide for an intervention or therapy to be applied. For example an alert for a medical practitioner may be output to prompt the practitioner to adjust existing dosages of medicines and/or to prescribe and/or administer new medicines or therapies.

Brief Description of the Drawings

[0019] An example of the invention will now be described with reference to the accompanying drawings, in which:

Figure 1 illustrates configuration of a wrist-worn device with a reminder schedule to assist a patient to take their medication;

Figure 2 illustrates generation of an alarm reminding the patient to take a dose of medication;

Figure 3 illustrates the patient actuating a button of the wrist-worn device to indicate that the medication has been taken and to deactivate the alarm reminder;

Figure 4a illustrates a typical distribution of impulsive behaviour of a sample of 109 individuals;

Figure 4b illustrates the distribution of a study group of 11 persons and the discrimination of ICD made possible by the present invention;

Figure 5 is a flowchart illustrating the process of one described embodiment of the invention;

Figure 6a is a sample output from one day of wrist-worn data logger recording for a patient with low Response Ratio, while Figure 6c is a sample output from one day of wrist-worn data logger recording for a patient with high Response Ratio; Figure 6c is a scatterplot of Response Ratio of patients grouped by medication doses; Figure 6d is a plot of QUIP score against Response Ratio; and

Figure 7a is a segment of a wrist-worn data logger record from a patient with ICB and high dyskinesia scores; Figure 7b is a segment of a wrist-worn data logger record from a patient without ICB and having low dyskinesia scores; Figure 7c shows histograms of median dyskinesia score in the 30 minutes either side of expected or unexpected responses, for the High RR group, the False Negative Group and the low RR Group, respectively.

Description of the Preferred Embodiments

[0020] Example 1:

[0021] The Parkinson's Kinetigraph (PKG) of Global Kinetics Corporation Pty Ltd was used to provide a remote monitoring system and user actuator. Each patient was provided with a wrist-worn data logger. Each wrist-worn data logger was programmed to remind the respective patient when to take their levodopa medication (Fig 1).

[0022] When it is time for the patient to take their levodopa medication, the wrist-worn data logger will vibrate and a light will flash for 10 seconds (Fig 2).

[0023] The individual was instructed that, once they had taken the prescribed medication, they should press the button on the wrist-worn device to deactivate the reminder. The wrist-worn data logger continues to remind the patient to take their medication until they have confirmed that you have done so, by pressing the button (Fig 3). User confirmation is effected by the user holding their thumb in the thumb groove on the top of the wrist-worn data logger for three seconds, at which time the light will come on. The user then needs to promptly remove their thumb immediately after the light comes on, because, if the user's thumb holds the thumb groove for more than 5 seconds the light will extinguish and the wrist-worn data logger will not deactivate the reminder nor record the time at which the medication was taken. Thus, actuation of the button is unlikely to occur without intent. The three second period and five second period can in other embodiments be reconfigured to any other suitable time.

[0024] The wrist-worn data logger records the number of times the button is actuated by the user.

Patient	**ICD clinical assessment**						**response**			
	Current	**Anytime**	**Hobbys punding etc**	**Score**	**ACE**	**UPDRS III**	**Expected**	**Total**	**% Index**	**%tile rank**
A	None	None	None	0	87	15	50	51	102	27.7
B	None	None	None	0	96	7	50	63	126	66.6
C	None	Buying	Cleaning (not current)	3	89	16	40	49	123	60.7
D	None	None	Painting	1	91	14	20	34	170	90.2
E	None	Sex	None	2	94	18	60	55	92	15.7
F	Eating	Eating Buying	Internet chat	6	94	33	70	97	139	75.2
G	Gambling	Gambling	None	5	90	29	70	103	147	81.8
H	Eating (sometimes)	Eating	Computer	6	91	26	50	186	372	99
I	Gambling/Sex	Gambling/Sex Buying	None	5	87	9	60	110	183	91.2

J	Gambling Buying	Gambling Buying	Sewing	6	98	23	70	243	347	98.8
K	Gambling Buying	None	None	5	93	15	40	145	363	99

Table 1

[0025] Eleven patients, denoted "A" to "K" in the first column of Table 1, were clinically interviewed to populate the 2nd to 4th columns of Table 1. The patients self-reported whether they were currently experiencing ICD behaviour (2nd column), whether they had in the past experienced ICD behaviour (3rd column), or whether they had any current hobbies or punding behaviour (4th column). To produce the 5th column ("Score"), the existence of a current ICD behaviour in Column 2 attracted a score of 3, the existence of an ICD behaviour at any time in the past in column 3 was scored as a 2, while the existence of any hobbies or punding in the 4th column was scored as a 1. These scores were summed to provide the ICD score in the 5th column of Table 5.

[0026] Each patient was clinically rated using the Addenbrookes Cognitive Examination, as indicated in the 6th column of Table 1, to screen for dementia.

[0027] The 7th column of Table 1 shows the clinically determined Unified Parkinson's Disease Rating Scale (UPDRS) score for each patient (Part III, motor examination).

[0028] The 8th column of Table 1 shows the expected number of responses from each patient via the wrist-worn data logger. This corresponds to the number of occasions upon which the patient was instructed to take medication during the monitored period. For example, patient A's prescription required that the patient take 50 doses of L-dopa during the monitored period, and so the patient was expected to press the button once on each occasion in order to deactivate the reminder and to indicate that that particular dose of medication had indeed been taken.

[0029] The 9th column of Table 1 shows the actual total number of times that each individual pressed the button during the monitored period. The 10th column of Table 1 shows the ratio of the 9th column to the 8th column, expressed as a percentage. In the 10th column, a percentage of about 100 is consistent with no ICD-like behaviour, as this corresponds to the user pressing the button once for each instance of medication, as they have been instructed to do. A percentage greatly exceeding 100 is consistent with ICD behaviour, as the user has been given no reason to

press the button more than once for each dose of medication. Most persons not having ICD display a % Index of less than about 140%.

[0030] The 11th (right-most) column of Table 1 provides a percentile rank indicating where that patient fits within a reference distribution of patients. The reference distribution was obtained from 109 Parkinson's disease subjects who were not known to have ICD, and who were clinically assessed to obtain the reference distribution, shown in Figure 1a. In the reference distribution the percentiles are as follows: 50th = 114; 75th = 138.75; 90th = 166.65; 95th = 209.25; 99th = 364.86. An alternative reference distribution may be suitable in other embodiments.

[0031] The results shown in Table 1 were statistically assessed using a Fishers exact and comparing the number of patients above the 75th percentile with an ICD score greater than 3 (i.e. 4 or above). This returned a statistical p-value of 0.08, providing a good indication that monitoring the individual's actuation behaviour in relation to a reward gives some ability to diagnose ICD. This p-value is particularly encouraging given the small sample size (n = 11) of the study shown in Table 1, and larger studies are expected to improve the statistical strength of the merits of the described technique. Additionally from clinical experience of Patient "D" it is believed that this patient may have under-reported past and present ICD behaviours, which may help to explain this outlier point in Figure 4b. Apart from patient D, Figure 4b shows that all patients clinically assessed as currently having ICD are correctly diagnosed by the automated technique of the present invention as either "at risk" of ICD (75^{th}-90^{th} percentile) or "highly likely" to have ICD (above 90^{th} percentile). Moreover, using Receiver Operator Curves and comparing ICD Score (5^{th} column of Table 1) to percentile rank (11^{th} column of Table 1) gives a $p < 0.0001$.

[0032] Accordingly, the described technique enables an automated diagnostic to be provided. Where the percentile rank (11^{th} column of Table 1) is between the 50^{th} and 75^{th} percentile, (i.e when the individual's percentage response index (10^{th} column of Table 1) is between 114% and 139%), the individual may be given an automated diagnosis of being "at risk" of ICD. This can be used to alert a clinician to the possibility that the individual has or is developing ICD, potentially at an early stage of the disorder before strong symptoms arise. Moreover, where the percentile rank (11^{th} column of Table 1) is above the 75^{th} percentile, (i.e when the individual's percentage response index (10^{th} column of Table 1) is above 139%), the individual may be

given an automated diagnosis of "likely having" ICD. Notably, the described technique thus permits monitored users to be diagnosed as "not having", being "at risk", or "likely having" ICD, with good statistical accuracy, and without the need for expensive and subjective clinical appointments.

[0033] Example 2:

[0034] The Parkinson's Kinetigraph (PKG) of Global Kinetics Corporation Pty Ltd was used to provide a remote monitoring system and user actuator, in a similar manner as described for Example 1 above in relation to Figures 1 to 3. Additionally, if at times other than the pre-programmed medication times the subject places their thumb on the wrist-worn data logger for 3 seconds, this triggers a brief (1 s) vibration and is recorded as a "redundant response". The timing of both correct responses associated with a reminder, and redundant responses not associated with a reminder, was recorded.

Percentile	Age	Durat'n	LED	UPDRS 1	UPDRS 2	UPDRS 3	UPDRS 4	UPDRS Total	ACE -R	SCOPA -COG	BDI	BIS/ BAS	STAI	AS
Low RR														
25th	51	6	525	0	6	7	2	17	91	26	6	66	53	5
50th	73	10	728	2	8	14	4	33	96	28	7	70	63	7
75th	76	14	1000	3	13	23	7	40	97	32	10	77	86	11
High RR														
25th	64	14	654	1	11	9	6	33	86	23	8	73	60	3
50th	69	16	1207	3	12	19	8	44	91	30	15	77	77	7
75th	75	22	2100	5	17	28	10	53	95	32	21	79	105	17
False Neg														
25th	61	5	682	1	13	14	3	32	84	22	8	63	78	8
50th	64	9	1090	2	14	18	6	39	94	29	10	72	82	11
75th	75	13	1791	4	20	40	8	73	94	35	13	79	98	14

Table 2

[0035] To obtain the data shown in Table 2, a blinded examiner administered the Starkstein Apathy scale and the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's disease (QUIP). QUIP scoring was made into a numerical scale by scoring Category A as six, Category B as five and Category C as four if they were current and as three, two and one respectively if they were some time in the past. The United Parkinsons Disease Rating Scale (parts 1-4), the SCOPA Cog, the Addenbrooke's Cognitive Assessment - Revised (Australian Version) were all

performed in the "on" state. Anti-Parkinson's Medications including the total levodopa equivalent dose (LED) and dopamine 2 receptor agonist use, age and age of onset of disease were all recorded. Further, patients were instructed to complete the Beck Depression Inventory (BDI), BIS/BAS (Behavioural Inhibition Scale/Behavioural Activation Scale) and State Trait Anxiety Inventory (STAI) in isolation. The BDI was used to assess whether the subject suffers from depression and the STAI used to indicate the presence of state and/or trait anxiety. The BIS/BAS questionnaire was scored using the BIS/BAS scale (reverse scoring apart from questions 2 and 22) and the total score was split into four parts; BIS, BAS drive, BAS fun seeking and BAS reward responsiveness.

[0036] Based on the instructions given, Figure 6a illustrates a typical patient's response over the course of one day. In particular, Figure 6a gives an example of the output from one day of wrist-worn data logger recording from a patient who was prescribed 6 doses of levodopa/day. The upper set of dots 606, and the lower set of dots 608, represent the dyskinesia and bradykinesia (respectively) score, which was calculated every 2 minutes, with greater severity of each symptom being represented by increasing distance from the middle of the graph. The horizontal lines indicate the respective median, 75th percentile and 90th percentile of controls. The vertical lines 602 indicate the times at which medications were prescribed, and the diamonds 604 represent when the taking of medication was acknowledged by the patient. This patient reflected in Figure 6a provided a second acknowledgment to the 6:00 am dose, shortly after the first acknowledgement (circled), thus providing 7 acknowledgments for 6 doses. The response ratio (RR) for this patient was thus 116% (100x7/6).

[0037] As expected, each reminder (indicated by vertical bars 602) is closely followed by a respective acknowledgment from the user (diamond markers 604). This subject received six reminders in the day shown, and gave seven acknowledgements, one acknowledgement per reminder with the exception that two acknowledgements followed the 06:00 AM reminder. In contrast, another patient's response profile is shown in Figure 6b. In response to seven reminders (612) in the day shown, the subject in Fig 6b provided thirty five acknowledgments (614) when only seven were required. This is represented as a Response Ratio (RR), namely the actual number of responses recorded, expressed as a percentage of the number expected. Thus the RR for the patient in Fig 6a was 116%, whereas the response ratio for the patient in Fig 6b was 500%. The patient response also includes an automated dyskinesia score (606) and an automated bradykinesia (608) score, each produced repeatedly over the course of the day in

accordance with the teaching of International Patent Publication No. WO 2009/149520, each score being shown as a dot or point in the response profile. A greater deviation of the dyskinesia scores above the midline indicates stronger dyskinesia, and a greater deviation of the bradykinesia scores below the midline indicates stronger bradykinesia. It is notable that the subject of Figure 6b had many more dyskinesia scores at higher levels with many at the upper levels of the graph (e.g. 10:00 am to 11:00 am), as compared to the subject of Figure 6a.

[0038] In this study described here as Example 2, the recording for each patient was taken over 10 days so the RR was calculated for the whole 10 days that the wrist-worn data logger was worn. The median RR in 108 subjects who had worn the wrist-worn data logger in the past 6 months was 116, and the 75th percentile was 136. Twenty three percent of patients who took 4 or less doses of levodopa/day had RR scores over the 75th percentile, whereas the RR in patients taking 5 or more doses/day was 63 percent ($p<0.5$ χ^2 test). This indicates that high RRs are more common in patients with wearing off (i.e. more frequent levodopa dosing), as shown in the scatterplot of Fig 6c.

[0039] The possibility that the increased RR may represent a form of ICB was investigated by examining the relationship between RR and QUIP, BIS/BAS, STAI and Starkstein AS scores in twenty-five subjects. Six subjects were previously identified as having ICBs, but who had not previously worn the wrist-worn data logger. Nineteen subjects were selected by an unblinded assessor from the 108 subjects who had recently worn the wrist-worn data logger because they either had a high RR (>137: n=7) or because their RR was less than 137 (n=12). A second assessor, who was blinded to the selection process, administered the scales and questionnaires and arranged for all subjects to wear a wrist-worn data logger. The QUIP score was plotted against the RR score obtained from the report of the type shown in Figures 6a and 6b. Fig 6D is a plot of the QUIP score (y axis) plotted against the RR (X axis). Two groups are apparent: False Negatives (640: n=6), and a Correlated Group (all other dots: n=19). The grey shaded area represents people whose RR was less than 137% and whose ICB score was 7. In seventeen subjects there was a strong correlation ($r^2=0.79$) with QUIP scores but six were clear outliers and fell into False negative group (540). Thus, the RR was a good predictor of the severity of ICB, as measured by QUIP in 75% of subjects (correlated group) but 25% were false negatives: they had high QUIP scores but a RR within the normal range.

[0040] Because ICBs have been associated with development of dyskinesia, we examined dyskinesia scores in the False Negative Group, a high RR Group (RR>136) and a low RR group (RR<137). First the median of the 2 minute dyskinesia scores 706 from the wrist-worn data logger in the 30 minutes either side of each Response was calculated. Fig 7A is a segment of the daily wrist-worn data logger record from a person with ICB, with diamond markers showing expected responses and unexpected responses as indicated. Note that in this example, the 2 minute dyskinesia scores 706 are mostly high indicating relatively severe dyskinesia. Furthermore, the median dyskinesia score was calculated in the first valid (expected) response after a reminder and after other (unexpected) responses that led to increased RRs. The median dyskinesia scores of both expected and unexpected responses in the False Negative Group and the low RR subjects were below the median of controls. In comparison, the dyskinesia scores in the 30 minutes either side of expected responses in the correlated group were high, but were significantly higher still in the period surrounding unexpected responses.

[0041] In contrast, Fig 2B shows a segment of the daily wrist-worn data logger record from a person without ICB, showing an expected response (diamond marker 722) and unexpected responses (diamond markers 724). Note that in this example, the 2 minute dyskinesia scores 726 are below the median for controls.

[0042] Fig. 7C shows histograms of the median dyskinesia score in the 30 minutes either side of expected and unexpected responses in the High RR group, the False Negative Group and in the low RR Group, respectively. The histogram bars represent the median and 75th percentile values for the subjects in each group. The median dyskinesia score in control (i.e. non PD) subjects is shown as a dotted line. Note that median dyskinesia scores of both expected and unexpected responses in the False Negative Group and the low RR subjects were below the median of controls. On the other hand, while the dyskinesia scores associated with expected responses in the correlated group were high, they were significantly higher still in the period surrounding unexpected responses. The P value associated with each expected and unexpected response is shown.

[0043] The False Negative Group 640 tended to have higher Starkstein Apathy scores than the Correlated Group (p=0.06 Mann Whitney) and a less significant trend toward higher STAI (p=0.15 Mann Whitney) and lower BIS/BAS scores (p=0.16 Mann Whitney). Taken together this suggests that the False Negative Group are indeed a separate entity who have ICBs without

dyskinesia and have higher Apathy but lower impulsivity than might otherwise be expected of subjects with ICBs.

[0044] The duration of PD in the High RR group was significantly longer (medians 16 v 10 years: $p<0.05$ Mann Whitney) and the BDI scores (medians 15 v 7 years: $p<0.05$ Mann Whitney) significantly higher than the low RR group (Table 2). The values for the False Negative subjects fell between the other two groups and did not reach significance (Table 2). There was a trend for the high RR group to have worse UPDRS, ACE-R, SCOPA COG, STAI and AS scores and to take more LED, but none reached statistical significance (Table 2). The values in the False negative group were in general intermediate between the other two groups. One third of the Low RR group (4 out of 11) were on DA2 receptor agonists whereas 2 out of 8 of the High RR subjects and 5 out of 6 of the False negatives were on DA2 receptor agonists.

[0045] The median dyskinesia score from the wrist-worn data logger obtained from 10 days of recording in the time between 9:00 and 18:00 was significantly higher in the high RR group than in the low RR and False Negative groups ($P<0.05$: Kruskal Wallis) as was the UPDRS IV scores ($P<0.05$: Kruskal Wallis). The median dyskinesia score in the False Negative Group was intermediate between the Correlated and non ICB groups.

[0046] Fig 6D indicates that the False Negatives are outliers, lying well outside the confidence limits of the other subjects, and the data presented above point to grounds for regarding the outliers as a separate entity 640. In this context it is possible that the three red dots marked by asterisk in Figure 6d, which fall outside the confidence limits, are incipient members of the False Negative Group 640. Most of the subjects in the study were questioned about the reasons that they used the reminders excessively. Many were unaware that they had responded excessively and those were aware could not provide an explanation. All were adamant that they did not use it to indicate increased consumption of medications. When the False Negative group 640 are excluded, there was high level of agreement between the QUIP and RR Index in detecting ICBs ($p=0.0012$: Fishers exact and free-marginal *kappa* value of 0.79).

[0047] The study of Example 2 shows that a high RR index is a sensitive test for the presence of ICBs. That is, subjects with a High RR will almost always have ICBs. The question of whether the failure to detect the False Negative Group 640 indicates reduced selectivity or more likely, a separate form of ICBs, is discussed further in the following. Subjects with high RR/QUIP scores in the correlated group had higher median dyskinesia scores over the ten days

while wearing the wrist-worn data logger. The finding that the UPDRS IV was higher in this group also reflects the greater sensitivity of continuous objective measurement of dyskinesia with the wrist-worn data logger in evaluating dyskinesia.

[0048] The finding that dyskinesia scores are high in the 30 minutes either side of an expected response is consistent with knowledge that ICBs are more likely to occur in the "on" state, in those at risk of ICBs. However, it is illuminating that the dyskinesia scores at the time of unexpected responses are higher still, which raises the possibility that the unexpected responses reflect a disturbance in the reward related processes. It may be that the behaviours examined in this study, consisting of a tactile stimulus followed by ingestion of medications that cause excessively elevated levels of DA in the striatum, lead to enhanced 'learning' of an acknowledgement response. In turn, the Response has taken on a salience similar to that of a cue in a conditioned stimulus in associative learning. It has been demonstrated in some subjects that striatal dopamine may contribute to the attribution of Pavlovian incentive values to cues that signal reward, thus making them valuable in their own right, and so individuals with a propensity to this form of reward learning, where "incentive salience" is assigned to reward cues, are at risk of the cues driving the behaviour. However, where the cue does not carry this incentive salience, striatal dopamine does not play the same central role in the associative learning.

[0049] Example 2 thus indicates that the Correlated Group represents a group with abnormally high levels of striatal dopamine, for whom the Response has gained salience in its own right. The elevated RR is a marker for ICBs because it is a marker of the risk of propensity to abnormally assign "incentive salience" to reward cues. Conversely, the False Negative group 640 may represent a different form of ICB, such as a group with prefrontal pathology in which changes occur in the function of frontal circuitry associated with the overvaluing of drug reinforcers, the undervaluing of alternative reinforcers, and deficits in inhibitory control for drug responses, where dopamine may play less of a role.

[0050] Thus, in some embodiments, the invention may be applied in conjunction with a dyskinesia score. The dyskinesia score may be generated for example in accordance with the teaching of International Patent Publication No. WO 2009/149520, the content of which is incorporated herein by reference, and in particular the dyskinesia score may be generated as taught at pages 7-10 or pages 16-19 of that disclosure, for example. In such embodiments, the validity of an ICD diagnosis may be improved if resulting from a period in which dyskinesia is

also present, as unnecessary additional actuations which occur during dyskinesia are more likely to be a result of ICD. Such embodiments are advantageous in that the same wrist-worn device may be used both to obtain accelerometer data to produce the dyskinesia score, and to provide alarms to the user in accordance with its existing purpose of improving the medication regime, and to gather the actuation rate information to obtain the automated ICD diagnosis. Using the dyskinesia score as an added input, in addition to the actuation data, has been found to improve the discrimination accuracy of the automated ICD diagnosis.

[0051] In further embodiments, the ICD diagnosis may further be made responsive to the timeframe in which the actuations of the user occur. In particular, ICD behaviour typically occurs sooner after the wrist-worn device issues the medication reminder than other infrequent and unrelated behaviours. Thus, detected actuations of the button which occur shortly after the reminder may be taken in such embodiments to give a stronger indication of ICD, whereas actuations of the button which do not occur soon after the reminder may be given less weight as being indicative of ICD. The time frame of interest after the reminder may for example be a period of between 5 and 60 minutes after the reminder, and may be in clusters that follow quickly after each other in the following 60 minutes.

[0052] The present invention may be particularly applicable to Parkinson's disease patients, as the taking of medication is a rewarding task and so the patient is strongly motivated to comply with instructions around taking medication.

[0053] Nevertheless, it is to be appreciated that the present invention may be applied in other applications. For example a reformed smoker may be reminded to apply a nicotine patch as a reward task, and may be instructed to press a button each time they do so to deactivate the reminder. Pressing the button is thus made salient to the reward task. Once again, a response rate which significantly exceeds 100% may be used as a marker of ICD. Alternatively, the actuator may be the lid of a container of cigarettes, whereby opening or closing of the lid is monitored, and is salient to the reward task of smoking.

[0054] In another embodiment the present invention may be applied to an impulsive gambler, who may be alerted whenever they have lost a predefined increment of money while gambling, and be required to press a button to deactivate the alert, thus making the pressing of the button salient to the reward task of gambling.

[0055] It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the invention as shown in the specific embodiments without departing from the spirit or scope of the invention as broadly described. The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive.

CLAIMS:

1. A method of assessing the likelihood that an individual has impulse control disorder, the method comprising:

providing the individual with an actuator, and instructing the individual to actuate the actuator as an acknowledgement of when the individual has completed a reward task;

monitoring and recording the actuation of the actuator;

producing an automated diagnosis of ICD, wherein a greater degree of actuation of the actuator by the individual is taken to indicate a greater likelihood that the individual has impulse control disorder; and

outputting the automated diagnosis of whether the individual has impulse control disorder.

2. The method of claim 1 wherein the task of actuating the actuator is made salient to the reward task from the perspective of the individual.

3. The method of claim 2 wherein the reward task is pleasurable; favourable or desirable to the individual.

4. The method of any one of claims 1 to 3 wherein performance of the task itself is not monitored.

5. The method of any one of claims 1 to 4 wherein the actuator is at least one of a button, dial, lever, questionnaire tick-box, or a sensor or input device responsive to a motor response of the individual.

6. The method of claim 5 wherein the actuator is a button of a device which reminds the individual to take medication, wherein the device is configured to remind the individual to take medication when required, and wherein the button deactivates the reminder to indicate that the medication has been taken.

7. The method of claim 6 wherein the device is body-worn.

8. The method of claim 6 wherein the device is located separately to the individual.

9. The method of any one of claims 1 to 8 further comprising generating an output that the individual is at-risk of ICD when the user actuates the actuator by an amount which is moderately more than expected, and generating an output that the individual has ICD when the user actuates the actuator by an amount which is significantly more than expected.

10. A non-transitory computer readable medium for assessing the likelihood that an individual has impulse control disorder, comprising instructions which when executed by one or more processors causes performance of the following:

processing records of actuation of an actuator by an individual, the individual having been instructed to actuate the actuator as an acknowledgement of when the individual has completed a reward task;

producing an automated diagnosis of ICD, wherein a greater degree of actuation of the actuator by the individual is taken to indicate a greater likelihood that the individual has impulse control disorder; and

outputting the automated diagnosis of whether the individual has impulse control disorder.

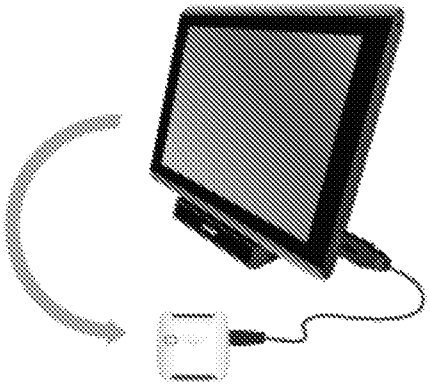

Figure 1

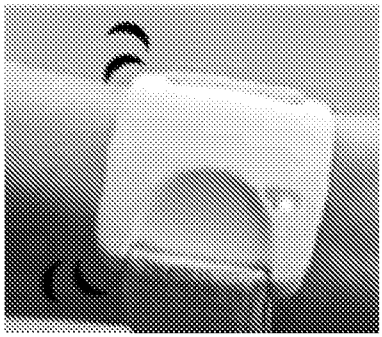

Figure 2

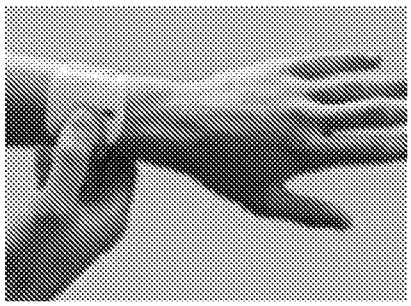

Figure 3

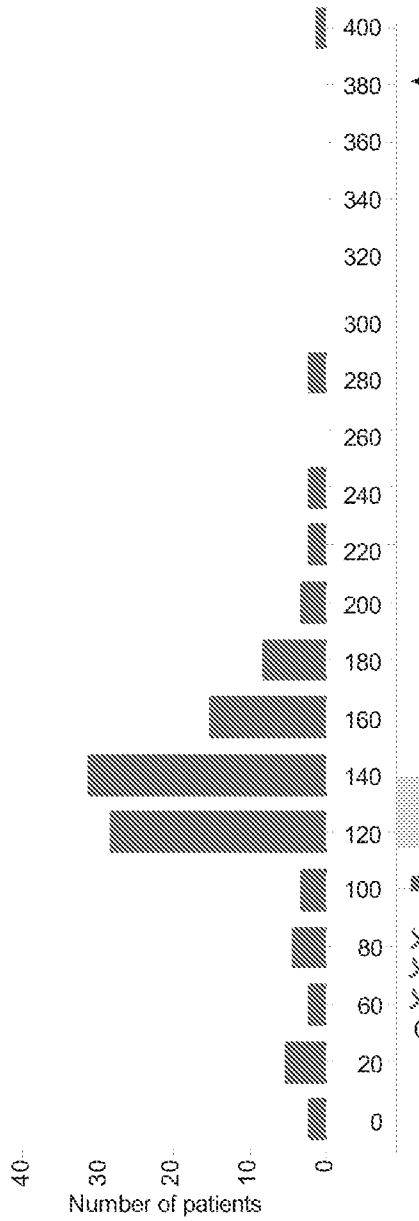

Figure 4a

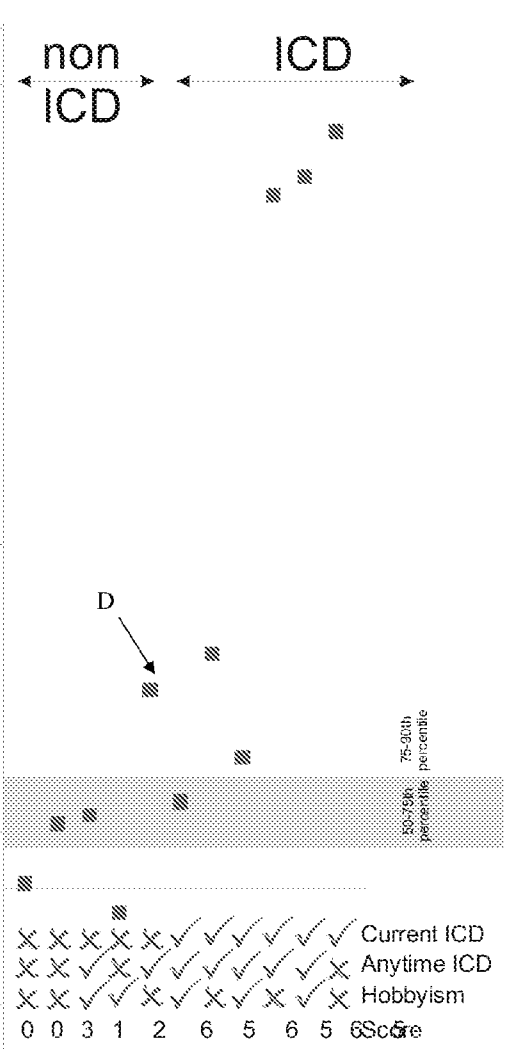

Figure 4b

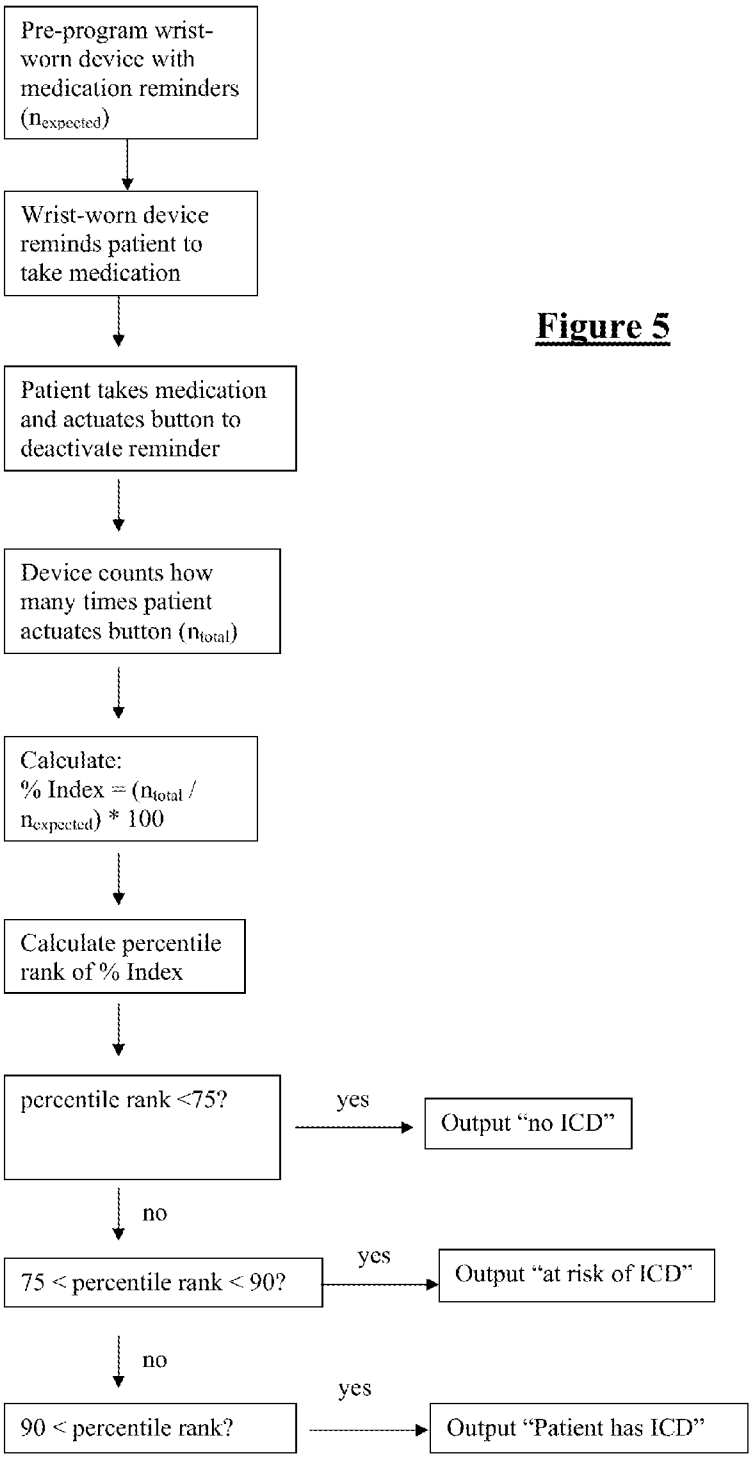
Pre-program wrist-worn device with medication reminders ($n_{expected}$)
Wrist-worn device reminds patient to take medication
Patient takes medication and actuates button to deactivate reminder
Device counts how many times patient actuates button (n_{total})
Calculate: % Index = (n_{total} / $n_{expected}$) * 100
Calculate percentile rank of % Index
percentile rank <75?
yes
Output "no ICD"
no
75 < percentile rank < 90?
yes
Output "at risk of ICD"
no
90 < percentile rank?
yes
Output "Patient has ICD"

Figure 5

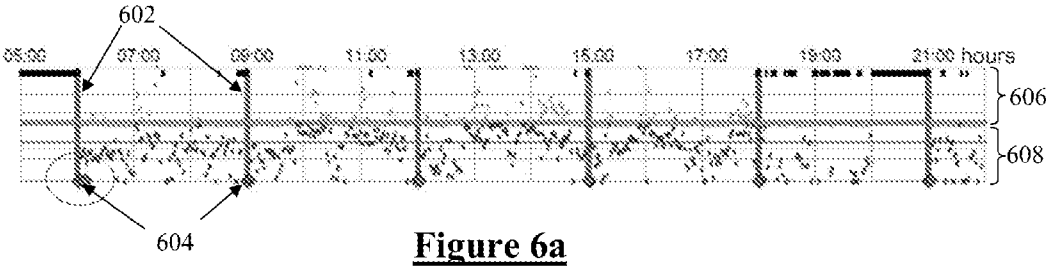

Figure 6a

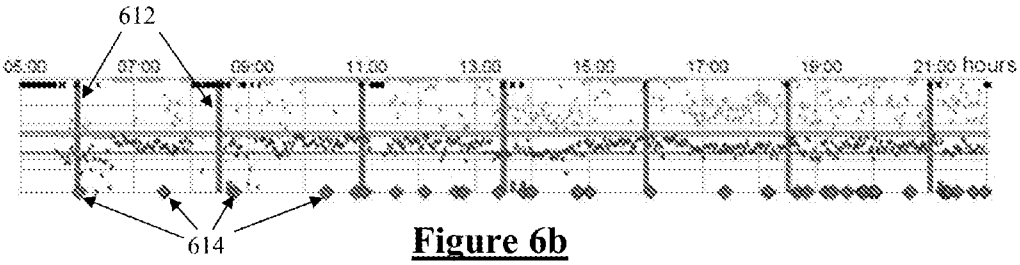

Figure 6b

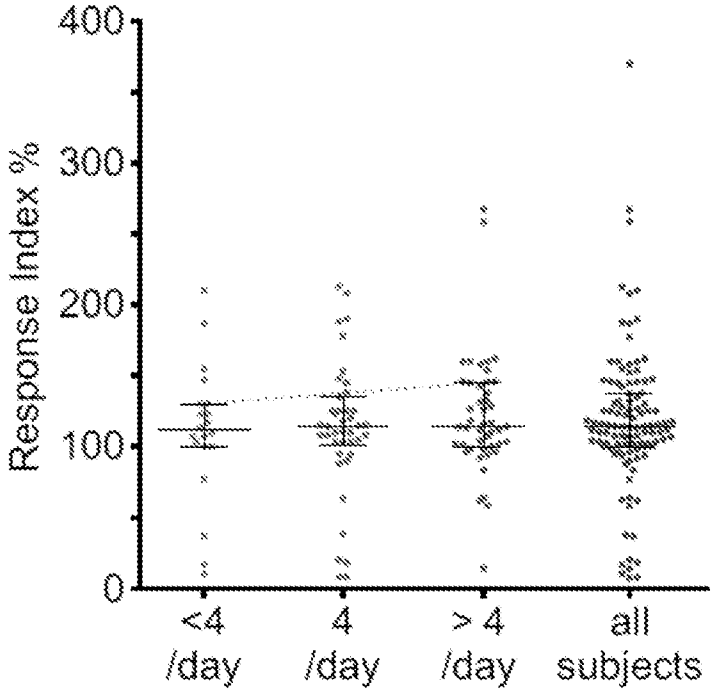

Figure 6c

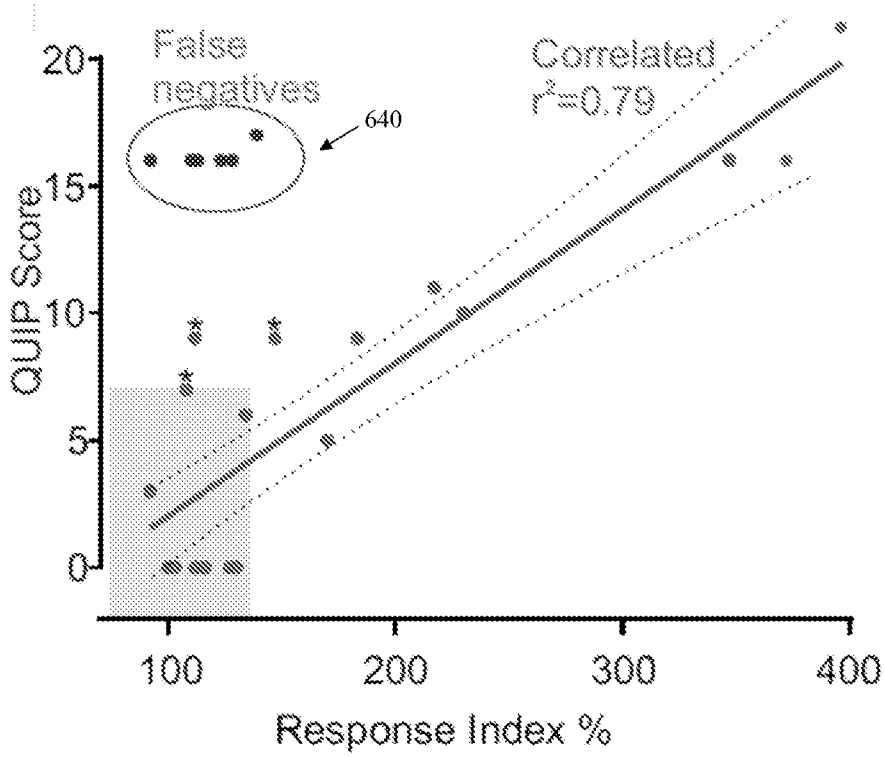

Figure 6d

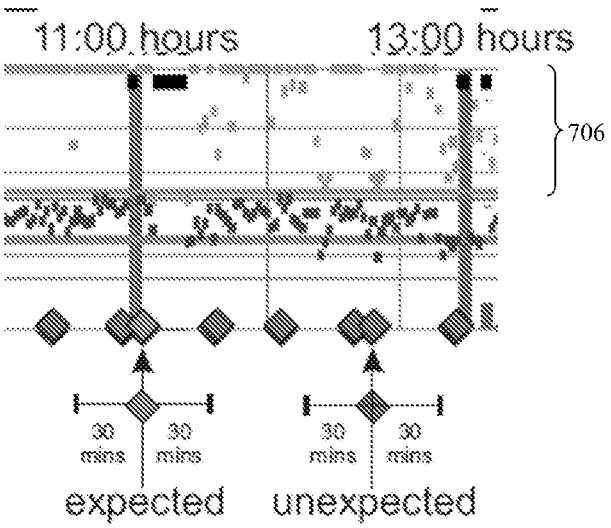

Figure 7a

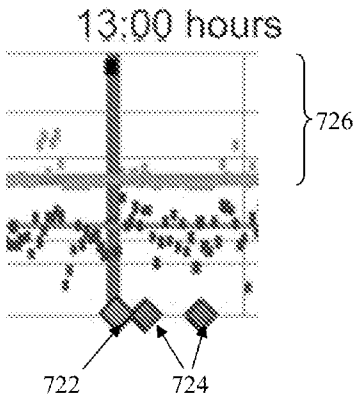

Figure 7b

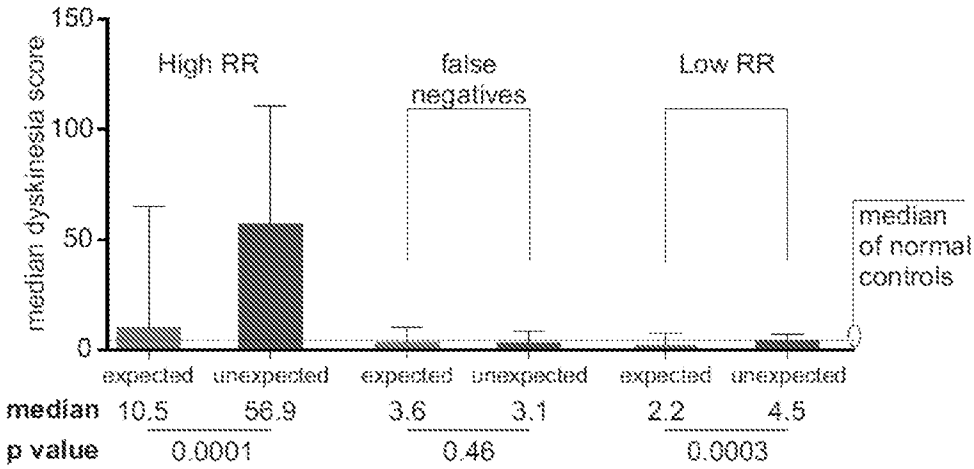

Figure 7c

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2014/000191

A. CLASSIFICATION OF SUBJECT MATTER

A61B 5/16 (2006.01) G09B 7/00 (2006.01) G09B 3/00 (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPODOC, WPI: CPC & IPC- A61B5/16/-; Keywords- impulse control disorder, addiction, diagnose, button, question, portable, remind, and like terms.

ESPACENET: CPC & IPC- A61B5/16; Keywords- impulse control disorder, addiction, diagnose, button, and like terms.

GOOGLE PATENTS & GOOGLE SCHOLAR search engines: Keywords- impulse control disorder, addiction, diagnose, button, question, portable, remind, and like terms.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Documents are listed in the continuation of Box C	

[X] Further documents are listed in the continuation of Box C [X] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 March 2014	27 March 2014
Name and mailing address of the ISA/AU	**Authorised officer**
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA Email address: pct@ipaustralia.gov.au Facsimile No.: +61 2 6283 7999	Marie Vozzo AUSTRALIAN PATENT OFFICE (ISO 9001 Quality Certified Service) Telephone No. 0262832384

INTERNATIONAL SEARCH REPORT		International application No.
C (Continuation).	DOCUMENTS CONSIDERED TO BE RELEVANT	**PCT/AU2014/000191**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2012/129636 A1 (MURRAY et al.) 04 October 2012 Pg. 9, l. 15-17; pg. 12, l. 22 to pg. 14, l. 6; pg. 16, l. 18 to pg. 17, l. 26; claims 12-14, 17-18	1-10
X	WO 1999/052038 A1 (HAZENBOS) 14 October 1999 Pg. 3, l. 19-33; pg. 6, l. 1-8; pg. 7, l. 15-22; pg. 8, l. 4-8; pg. 9, l. 5-16; pg. 10, l. 5-18	1-10
A	US 5913310 A (BROWN) 22 June 1999 Whole document	1-10
A	WO 2003/053245 A2 (JANSSEN PHARMACEUTICA N.V.) 03 July 2003 Whole document	1-10
A	US 4730253 A (GORDON) 08 March 1988 Whole document	1-10
A	US 6053866 A (MCLEOD) 25 April 2000 Whole document	1-10
P,X	EP 2660745 A2 (ALMOSNI et al.) 06 November 2013 Paras. [0017]-[0020], [0025]-[0030], [0046]-[0052]; tables I-III	1-3, 5, 9-10

INTERNATIONAL SEARCH REPORT Information on patent family members	International application No. **PCT/AU2014/000191**

This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document/s Cited in Search Report		**Patent Family Member/s**	
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Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

INTERNATIONAL SEARCH REPORT Information on patent family members	International application No. **PCT/AU2014/000191**

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INTERNATIONAL SEARCH REPORT Information on patent family members	International application No. **PCT/AU2014/000191**

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INTERNATIONAL SEARCH REPORT Information on patent family members	International application No. **PCT/AU2014/000191**

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Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

INTERNATIONAL SEARCH REPORT Information on patent family members	International application No. **PCT/AU2014/000191**

This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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