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Impulse control behaviours in a Malaysian Parkinson's disease population

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Abstract

Background: Impulse control behaviours are repetitive and excessive activities that may be subsyndromal and not fulfil the criteria for impulse control disorder. These activities have potential to negatively impact on the daily lives of sufferers. We conducted a study to investigate the prevalence of impulse control behaviours and its associated features in Parkinson's disease in our population. *Methods:* We conducted a prospective cross-sectional study on consecutive patients attending neurology clinic. Inclusion criteria include idiopathic Parkinson's disease patients with Hoehn & Yahr stage I-IV. Eighty patients were enrolled and screened for impulse control behaviours using the Questionnaire for Impulsive-Compulsive Disorder for Parkinson's disease (QUIP). *Results:* Prevalence of impulse control behaviours among our cohort was 11.3%; the features significantly associated with it were higher level of education (p=0.02), advanced stage of disease (p=0.03) and higher levodopa dosage (p= 0.01). The commonest impulse control behaviour in our cohort was compulsive medication use (7.5%), followed by hobbyism (6.3%), hypersexuality (5%), compulsive buying (3.75%), punding (2.5%), walkabout (2.5%), compulsive eating (1.25%) and pathological gambling (1.3%).
Conclusions: There is an association between impulse control behaviour and higher levodopa dosage in a study on patients with Parkinson's disease in Malaysia. We also found a low prevalence of pathological gambling as compared to studies performed in the West.

INTRODUCTION

Impulse control disorder (ICDs) is a collective term to describe a group of disorder characterized by the failure to resist the impulse to carry out an action that may bring harm to oneself or others.[1] ICDs include pathological gambling, hypersexuality, compulsive buying and compulsive eating. The definition of ICDs is very strict. Repetitive, excessive and compulsive activities may exist in a continuum and these subsyndromal behaviors have been collectively labeled as impulse control behaviors (ICBs).[2,3] The effects of ICBs on patients can be equally disruptive. ICBs include punding, walkabout, compulsive medication use and hobbyism.

ICBs, if left undiagnosed and untreated, have great potential to negatively impact on the patients' life, i.e. financial ruin in patients with pathological gambling and breakdown of long-standing relationships in patients with hypersexuality and hobbyism.

The development of ICBs in Parkinson's disease have been shown to be influenced by the use of dopamine agonist.[4] Traditionally, the treatment of Parkinson's disease is initiated with dopamine agonist instead of levodopa. This is to delay the development of motor response complications such as dyskinesia due to prolonged levodopa therapy.[5]

The presence of ICBs is easily missed in day-to-day clinical practice and patients occasionally deny the presence of these symptoms upon direct

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questioning, thus compounding the problem further.[6] To this end, the Questionnaire for Impulsive-Compulsive Disorder for Parkinson's disease (QUIP) was developed. The utility of QUIP as a screening tool has been validated in previous studies, with a sensitivity rate of 96%, but not very specific and therefore may pick up sub-syndromal ICBs as well.[7]

The dosage of dopamine agonist in an Asian Parkinson's disease patient is typically much lower as compared to their western counterpart. Intuitively, it is expected that the corresponding prevalence of ICBs in Asian PD patient would also be low. However, a recent study on the Malaysian Parkinson's disease population using QUIP as a screening tool found the prevalence rate of ICBs of 24.6%, exceeding quoted rates in some studies performed in the western population.[8]

We embarked on a study to determine the prevalence rate of ICBs and its associated risk factors in our own population.

METHODS

We conducted a cross-sectional observational study at Universiti Kebangsaan Malaysia Medical Centre from June 2012 to December 2012. Consecutive PD patients attending neurology clinic were invited to participate in the study. Inclusion criteria were patients aged 18 and older, with Hoehn & Yahr stage I-IV and having been on stable dopaminergic medication for the last 3 months. Diagnosis of PD was made by a neurologist according to the UK PD Brain Bank Criteria. Exclusion criteria were cognitive impairment based on a Montreal Cognitive Assessment (MoCA) score of less than 26/30. The study complies with the Declaration of Helsinki and was approved by the institutional ethics committee.

Subjects who agreed to participate and gave informed consent were interviewed and examined clinically. We collected information pertaining to disease history and socio-demographic characteristics such as gender, age and ethnicity. Information pertaining to the level education of the subjects were also collected and categorized into primary, secondary and tertiary level education.

Study subjects were screened for the presence of ICBs using the Questionnaire for Impulsive-Compulsive Disorder in Parkinson's disease (QUIP). This is a validated self-administered questionnaire to screen for ICBs in PD patients. The questionnaire is divided into 3 sections; section 1 assesses 4 ICDs (hypersexuality, pathological gambling, compulsive eating and compulsive buying); section 2 assesses other compulsive behaviors (punding, hobbyism and walkabout) and section 3 assesses compulsive medication use. QUIP has a sensitivity rate of 96% for the detection ICDs and ICBs.[7] In our study, the questionnaire was administered to the subject, and on certain occasions aided by a trained interviewer for translation into Malay or Chinese. Subjects were deemed QUIP positive according to the standard published criteria.

For analytic purposes, the total daily levodopa equivalent unit (LEU, mg/day) was calculated based on previously established methods, where 100mg of levodopa= 130 mg of levodopa in controlled released form, 70 mg of levodopa if also using entacapone, 1 mg of pramipexole, 5 mg of ropinirole, 5 mg of rotigotine and 100 mg of piribedil.[9,10]

All data were analysed using SPSS20.0 statistical software package. Shapiro-Wilk test was used to test for normality. Results were expressed by mean+/- standard deviation (SD) or median with interquartile range (IQR). To compare means of two normally distributed data, Student t-test was used. For non-normally distributed data, Mann-Whitney U test was used to compare between groups. For comparison of proportions between two groups, Pearson chi-square test was used.

A p value of <0.05 was deemed as statistically significant.

RESULTS

Baseline demographic data

Out of 95 subjects screened, 80 fulfilled the inclusion and exclusion criteria and thus were enrolled into the study. The mean age was 63.4 years $\pm$ 8.3 and the mean duration of illness was 4 years (2-7.8).

Forty-seven (58.8%) subjects were Chinese, 28 (35%) were Malay, 3 (3.8%) were Indian and 2 (2.5%) were from other races listed. There were 49 (61.3%) male subjects in the study. (Table 1)

Almost half (47.5%) of the subjects recruited received secondary level education, with 28.8% receiving primary level education and the remaining 23.8% had tertiary level education. (Table 1)

In the cohort, 38 (47.5%) subjects were exclusively on levodopa, 14 (17.5%) were exclusively on dopamine agonist, and the remainder 28 (35%) of subjects were taking a combination of both levodopa and dopamine

Table 1: Baseline characteristics of study population

		n=80
Age, years ; mean (SD)		63.4(8.3)
Ethnicity	Malay	28 (35%)
	Chinese	47 (58.8%)
	Indian	3 (3.8%)
	Others	2 (2.5%)
Gender	Female	31 (38.8%)
	Male	49 (61.3%)
Education	Primary	23 (28.8%)
	Secondary	38 (47.5%)
	Tertiary	19 (23.8%)
Hoehn & Yahr	Stage 1	15 (18.8%)
	Stage 2	43 (53.8%)
	Stage 3	19 (23.8%)
	Stage 4	3 (3.8%)
Disease duration, years		4 (2-7.8)
MoCA; mean (SD)		28.8 (1.1)
Levodopa, mg/day		300 (150-723)
Dopamine agonist LEU, mg/day		50 (42-100)
Levodopa + dopamine agonist LEU, mg/day		334 (219-914)

Data is expressed as median (IQR) unless otherwise stated.
MoCA, Montreal Cognitive Assesment (range of score 0-30); LEU, Levodopa equivalence unit.

agonist. 42 subjects (51%) were taking dopamine agonist, either as a sole agent or in combination with levodopa. With regards to the specific dopamine agonist used, 10 subjects were on piribedil, 26 subjects were on pramipexole, 4 subjects were on ropinirole and 2 subjects were on rotigotine.

The median levodopa equivalency unit (LEU) for dopamine agonist therapy in our cohort was 50mg/day (42-100). The median LEU for levodopa therapy was 300mg/day (150-723). Finally, the median LEU for levodopa and dopamine agonist combined, was 334mg/day (219-914). (Table 1)

More than half (43 subjects, 53.8%) of our subjects were in *Hoehn & Yahr* (H&Y) stage 2, 19 (23.8%) subjects were in H&Y stage 3, 15 (18.8%) subjects were in H&Y stage 1 and 3 (3.8%) of subjects were in H&Y stage 4. (Table 1)

The Montreal Cognitive Assessment (MoCA) mean score for the cohort was 28.8 points $\pm$1.12.

Impulse control behaviour using QUIP

All the patients recruited were screened for ICBs using the QUIP assessment tool. Nine (11.3 %) subjects were found to be QUIP positive at screening (Table 2).

In our cohort, the commonest ICB was compulsive medication use (7.5%), followed by hobbyism (6.25%), hypersexuality (5%), compulsive buying (3.75%), punding (2.5%), walkabout (2.5%), compulsive eating (1.25%) and pathological gambling (1.25%). (Figure 1)

There was a statistically significant difference in the mean levodopa dose between the QUIP positive and negative groups($p = 0.01$).The mean dopamine agonist dose (in LEU) in the QUIP poitive group was almost double that of the QUIP negative group (97.5mg vs 50mg) but this was not statistically significant (p=0.39). (Table 2)

Subjects who were QUIP positive had a higher

Table 2: Presence of ICBs using QUIP

		QUIP positive N=9	QUIP negative N=71	*p value*
Age, years ; mean (SD)		64.7 (7.09)	63.2 (8.5)	0.63[a]
Ethnicity	Malay	4 (14.3%)	24 (85.7%)	
	Chinese	3 (6.4%)	44 (93.6%)	0.09[b]
	Indian	1 (33.3%)	2 (66.7%)	
	Others	1 (50.0%)	1 (50.0%)	
Gender	Female	2 (6.5%)	29 (93.5%)	0.47[b]
	Male	7 (14.3%)	42 (85.7%)	
Education	Primary	0 (0.0%)	23 (100%)	
	Secondary	4 (10.5%)	34 (89.4%)	0.02[b]
	Tertiary	5 (26.3%)	14 (73.7%)	
Hoehn & Yahr				
	Stage 1	2 (13.3%)	13 (86.7%)	
	Stage 2	1 (2.3%)	42 (97.7%)	0.03[b]
	Stage 3	5 (26.3%)	14 (73.7%)	
	Stage 4	1 (33.3%)	2 (66.7%)	
Disease duration, years; mean(SD)		7.0 (4.5)	5.1 (4.1)	0.13[b]
MoCA; mean (SD)		29.3 (1.12)	28.7 (1.1)	0.87[c]
Levodopa (mg/day)		973 (657-1031)	188 (150-400)	0.01[c]
Dopamine agonist LEU (mg/day)		97.5 (50.2-160)	50 (33-100)	0.39[c]
Levodopa + dopamine agonist LEU (mg/day)		1069(936-1277)	300 (163-450)	0.04[c]

Data is expressed as median (IQR) unless otherwise stated.
MoCA, Montreal Cognitive Assesment (range of score 0-30); LEU, Levodopa equivalence unit; QUIP, Questionnaire for impulsive compulsive disorders in Parkinson's disease.
a, independent t-test; b, Pearson chi-square test; c, Mann-Whitney u test

level of education as compared to subjects who screened negative, with all of the QUIP positive subjects having at least a secondary education. This was shown to be statistically significant (p=0.02). (Table 2)

There were no statistically significant differences in mean age, duration of disease, ethnicity and gender between the QUIP positive and negative groups (Table 2).

Five (6.3%) subjects screened positive in Section 1 (ICD) of QUIP. Of these, four had additional features of ICB, based on positive screening in Section 2 and Section 3. The remaining 4 subjects screened positive only in Section 2 and Section 3, but not in Section 1. (Table 3)

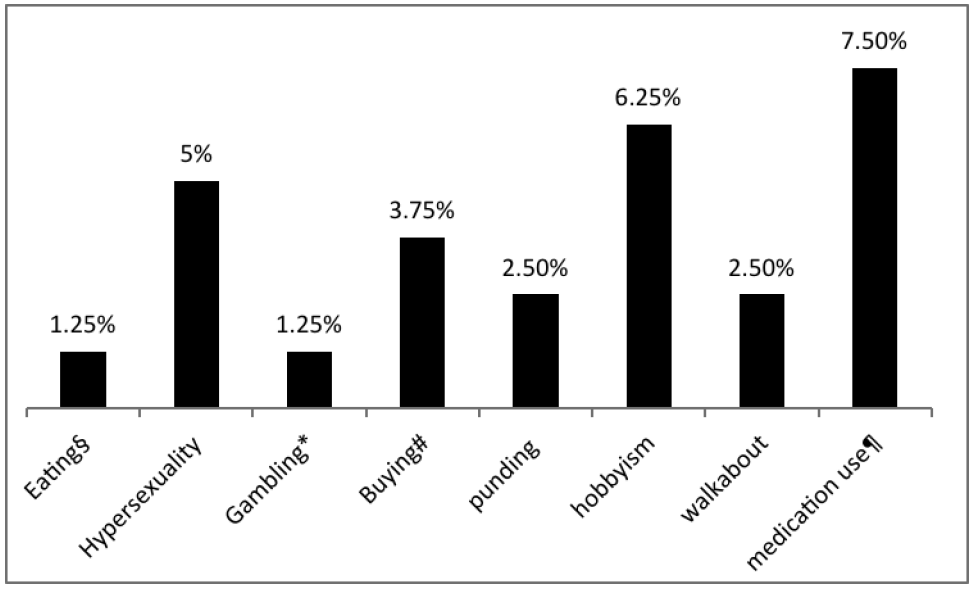
The type of anti-parkinson medication that the subjects were on in those that were QUIP positive were as follows; 4 were on pramipexole, 1 on piribedil, 1 on ropinirole and 1 on rotigotine, and 2 subjects were only on levodopa.

DISCUSSION

Our study showed that the prevalence of ICBs among patients with PD in our center using the QUIP questionnaire was 11.3%.

Lee *et al*, in a study conducted in a South Korean population, found the prevalence rate of ICBs to be 10.1%.[11] This appears on the surface to be at par with our finding but their study did not include compulsive medication use and therefore their prevalence rate for ICBs may in fact be higher than ours. Kim *et al*, in another study performed in a Korean population, using QUIP as the assessment tool, detected a point prevalence rate of 15.5% of ICBs in PD patients.[12]

It is difficult to make comparisons of the



§Compulsive eating
*Pathological gambling
#Pathological buying
¶ Compulsive medication use.

Figure 1. Frequency of ICBs spectrum in cohort

prevalence rate with other studies due to the differences in the assessment tools used. Nevertheless, earlier studies generally quote a prevalence rate of ICBs in PD ranging between 6% to 25%, and our results appears to be in keeping with this trend.[13-16]

Several studies have demonstrated the strong association between the development of ICBs and dopamine agonist; some advocating a dose-dependant relationship while others an 'all or nothing' relationship.[13,17-19] Although our study showed that subjects who were QUIP positive

Table 3: ICBs in QUIP positive subjects

Questionnaire for Impulsive-Compulsive for Parkinson's disease patients (QUIP)									
Patient	**Section 1**				**Section 2**			**Section 3**	
	Eating §	**Hypersexuality**	**Gambling ***	**Buying #**	**punding**	**hobbyism**	**walkabout**	**medication use¶**	
1	+	+		+		+	+	+	
2								+	
3					+	+			
4				+			+	+	
5						+		+	
6		+							
7		+	+	+	+	+			
8						+		+	
9		+						+	

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had almost double the dopamine agonist dose as compared to the subjects who were QUIP negative, the findings were not statistically significant. We feel this may be due to the small sample size of the study and we wonder whether a further study with a bigger sample would reveal a statistically significant result. It is important however to note that in our study, 7 of 9 subjects who were QUIP positive were on dopamine agonist.

Our study showed a clear dose-dependant relationship between total daily levodopa and ICBs. There was a statistically significant difference in the daily levodopa dose in QUIP positive and QUIP negative patients, with median levodopa dose of 973mg per day and 188 mg per day, respectively. Similarly, Weintraub *et al*. and Chiang *et al*. also showed an association between higher levodopa dosages and ICBs.[17,18] To our knowledge, ours is only the third study that has demonstrated this association.

We found that pramipexole was the most common dopamine agoinst associated with QUIP positive subjects, but we feel this is more a reflection of prescribing patterns at the centre where the study was performed rather than any inherent properties unique to pramipexole as compared to the other dopamine agonist.

In our study, we found that all of our subjects who were screened positive for ICBs had at least a secondary level education, and this trend was shown to be statistically significant. Our findings echoed the DOMINION study which also found that their patients with ICDs tended to have a more formal education.[17] A possible explanation for this finding would be subjects with a higher education level are more likely to be able to recognise subtle changes in their behaviour and report it accordingly.

Interestingly, we found a significantly higher risk of developing ICBs among those with more advanced disease. To our knowledge, this finding has never been reported in previous studies on ICBs in Parkinson's disease. This may be a reflection of our finding that higher levodopa dosage is associated with ICBs. Parkinson's disease patients at a more advanced stage of disease have a tendency to require higher total daily levodopa dose. The association between ICBs and more advanced disease needs to be clarified and investigated further in a larger study.

We found that compulsive medication use was the most commonly reported ICBs in our study. Studies by Lim *et al*. and Lee *et al*., performed in Malaysia and South Korea respectively, found punding to be the most common reported ICBs in their study.[8,11] Kim *et al.*, using QUIP and performed in another South Korean cohort however, found the most common ICBs in their cohort was hypersexuality.[12]

Pathological gambling and compulsive eating were found to be the least common ICBs in our cohort, with a prevalence rate of 1.8%, respectively. PD studies on pathological gambling in western populations quotes a much higher figure of between 2.3-9.3%. [4] The prevalence of pathological gambling in PD in Asian cohorts is much lower than in Western population, ranging between 0.32% to 2.6%.[18] The possible exception to this low trend is a study by Aeyung *et al*. which found the prevalence of pathological gambling in PD patients in Hong Kong to be 6.1 %.[19]

There are several possible explanations. Firstly, dopamine agonists have been shown to be an independent risk factor for pathological gambling.[20] Asian patients are typically treated with lower doses of dopamine agonist, due to a variety of reasons which includes perception of disease and treatments, as well as cost concerns.[8] Asian cohorts tends to have a considerably lower total LEU dopamine agonist as compared to western cohorts (our study dopamine agonist LEU 50mg/day; DOMINION dopamine agonist LEU 300mg/day).

Secondly, it is well known that cultural and environmental differences play an important role the development of ICBs. This is exemplified by the difference in the prevalence rate of pathological gambling between the United States of America and Canadian cohorts in the DOMINION study, which was attributed to the more easy availability of casino gambling in the United States.[17] Asian countries may be more restrictive with regards to gambling activities, either due to governmental policy or religious sensitivities.

In much the same way that compulsive sexual behaviour is more common in men and compulsive buying is more common in women, mirroring the patterns in the general population, the question whether other cultural difference imparts certain influence in the development on certain ICBs, e.g. religion, ethnic differences, social class, needs to be investigated further.[15,26-28] This is one possible explanation between the marked difference in the prevalence rate of our study and Lim *et al.*, which quoted a prevalence rate of 24.6% of ICBs in PD patients, as compared to 11.3% in ours.[8] This is despite the study being performed using the same assessment tool and in the same urban population but differing catchment area as ours. Our cohort was made up of approximately

35% Malays as opposed to only 10% in Lim *et al.*'s study. Malays are Muslim by religion and issues such as gambling and hypersexuality are considered sinful and taboo, consequently leading to the possibility of under-reporting of these symptoms during assessment.

Of late, the popularity of gambling is increasing due to the spread of legalised gambling and a significant proportion of this rise is in internet gambling.[21] Presently, restricted access is thought to play a role in keeping the prevalence rate of pathological gambling in Asian countries low. This may change in future as the internet becomes more widely available and we may see a significant rise in the prevalence of pathological gambling in Asia.

The main limitation in this study was the small sample size. Moreover, our cohort were recruited from patients living in an inner city area having treatment for Parkinson's disease at a well-established tertiary care centre specialising in movement disorders. The study therefore lacks the random distribution of prospective population-based study designs. A bigger multi-centre study, involving urban and rural populations should be conducted in future as a follow-up study.

In conclusion, we found the prevalence rate of ICBs in our study was 11.3%, in keeping with results from other studies worldwide. Our finding appears to suggest that there is an association between impulse control behaviour and higher levodopa dosage. We found that pathological gambling to be uncommon in our cohort, in contrast to findings in the western population.

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DISCLOSURE

Conflict of interest: None

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