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# Оценка когнитивной неоднородности среди клинических подтипов шизофрении у постели больного с помощью теста рисования часов — предварительное исследование

R. Ransing<sup>1</sup> ✉, G. Sh. Sakekar<sup>2</sup>, O. Grigo<sup>2</sup>, P. Khairkar<sup>3</sup><sup>1</sup> BKL Walawalkar Rural Medical College, Ratnagiri, Maharashtra, India;<sup>2</sup> Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wadha, Maharashtra, India;<sup>3</sup> Kamineni Institute of Medical Sciences, Narketpally, India

## АННОТАЦИЯ

**Введение.** Когнитивный дефицит — это устойчивая и стойко сохраняющаяся основная черта шизофрении, связанная с повышенным риском психосоциальной инвалидизации. Когнитивный дефицит широко распространен и варьируется в зависимости от типа шизофрении и течения заболевания. Клиницисты часто упускают это из виду из-за сложности оценки. Тест на рисование часов (ТРЧ) — это краткий, простой и широко используемый инструмент когнитивного скрининга.

**Цель.** Сравнить уровень когнитивных нарушений среди подтипов шизофрении с помощью ТРЧ.

**Материалы и методы.** Показатели ТРЧ у пациентов, находящихся в стационаре с шизофренией трех клинических подтипов: параноидной ( $n = 45$ ), недифференцированной ( $n = 45$ ) и дезорганизованной ( $n = 45$ ), — были сопоставлены с показателями контрольной группы ( $n = 45$ ), сопоставимой по возрасту и полу. Тяжесть симптомов в каждой группе оценивалась с помощью ТРЧ, шкалы положительных и отрицательных симптомов (англ.: *Positive and Negative Symptoms Scale*, PANSS) и краткой шкалы психиатрической оценки (англ.: *Brief Psychiatric Rating Scale*, BPRS) на момент поступления. Для сравнения этих групп были использованы критерий  $\chi^2$  и односторонний ANOVA-тест с множественным сравнением Бонферрони. Были рассчитаны коэффициенты корреляции Пирсона для определения двунаправленной взаимосвязи между непрерывными переменными, включая оценку по шкалам PANSS, BPRS, ТРЧ и оценку мини-теста на психическое состояние (англ.: *Mini-Mental Status Examination*, MMSE), среди различных групп сравнения.

**Результаты.** Пациенты из группы дезорганизованного типа показали более низкие результаты ( $3,06 \pm 2,27$ ), чем пациенты группы параноидального типа ( $6,06 \pm 1,86$ ), группы недифференцированного типа ( $4,60 \pm 2,71$ ) и группы сравнения ( $8,68 \pm 1,22$ ),  $p < 0,004$ . Показатели ТРЧ отрицательно коррелировали с показателями PANSS ( $r = -0,47$ ,  $p < 0,001$ ) и BPRS ( $r = -0,47$ ,  $p < 0,001$ ) в трех подтипах. MMSE в большей степени коррелировало с оценкой ТРЧ в группе дезорганизованного типа ( $r = 0,65$ ,  $p < 0,001$ ), чем в группе параноидного типа ( $r = 0,43$ ,  $p < 0,05$ ).

**Заключение.** Полученные результаты свидетельствуют о том, что тест ТРЧ можно использовать у постели больного, чтобы различать дезорганизованный и параноидальный типы шизофрении. Различия в эффективности ТРЧ могут быть связаны с различным вовлечением нейронных коррелятов в разных подтипах шизофрении. Кроме того, эффективность ТРЧ может быть полезна клиницистам в повседневной клинической практике при выборе соответствующих фармакологических и психосоциальных вмешательств.

**Ключевые слова:** тест на рисование часов; шизофрения; когнитивный дефицит

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# Bedside Assessment of Cognitive Heterogeneity with Clock Drawing Performance among Clinical Subtypes of Schizophrenia — Preliminary Study

Ramdas Ransing<sup>1</sup> ✉, Gajanan Sh. Sakekar<sup>2</sup>, Omityah Grigo<sup>2</sup>, Praveen Khairkar<sup>3</sup><sup>1</sup> BKL Walawalkar Rural Medical College, Ratnagiri, Maharashtra, India;<sup>2</sup> Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wadha, Maharashtra, India;<sup>3</sup> Kamineni Institute of Medical Sciences, Narketpally, India

## ABSTRACT

**INTRODUCTION:** Cognitive deficit is the enduring, persistent, and core feature of schizophrenia associated with increased risk of psychosocial disability. The cognitive deficit is highly prevalent, and variable according to the type of schizophrenia and course of illness. It is often overlooked by clinicians because of the complexity of assessment. The clock drawing test (CDT) is a brief, simple, and widely used cognitive screening instrument.

**AIM:** To compare the level of cognitive impairment among subtypes of schizophrenia using CDT.

**MATERIALS AND METHODS:** The CDT performance of institutionalized patients with schizophrenia of three clinical subtypes, Paranoid ( $n = 45$ ), undifferentiated ( $n = 45$ ), and disorganized ( $n = 45$ ) was compared with age and sex-matched controls ( $n = 45$ ). The severity of symptoms in each group was assessed using Free drawn CDT, Positive and Negative Symptoms Scale (PANSS), and a Brief Psychiatric Rating Scale (BPRS) at the time of admission. The  $\chi^2$  test and One-way ANOVA test with Bonferroni multiple comparison test were used to compare these groups. Pearson correlation coefficients were calculated to determine the bi-variate relationship among continuous variables including PANSS score, BPRS score, CDT Score, and Mini-Mental Status Examination (MMSE) Score among various comparison groups.

**RESULTS:** The patients in the disorganized group ( $3.06 \pm 2.27$ ) performed more poorly than the paranoid group ( $6.06 \pm 1.86$ ), undifferentiated ( $4.60 \pm 2.71$ ), and the comparison group ( $8.68 \pm 1.22$ ),  $p < 0.004$ . The CDT performance was negatively correlated with the PANSS score ( $r = -0.47$ ,  $p < 0.001$ ) and BPRS score ( $r = -0.47$ ,  $p < 0.001$ ) among three subtypes. The MMSE was highly correlated with CDT score among the disorganized group ( $r = 0.65$ ,  $p < 0.001$ ) than the paranoid group ( $r = 0.43$ ,  $p < 0.05$ ).

**CONCLUSION:** Our findings suggest that the CDT test can be used at the bedside to distinguish between disorganized and paranoid types of schizophrenia. The disparity in CDT performance may be due to the different involvement of neural correlates among schizophrenia subtypes. Furthermore, CDT performance may be useful to clinicians in routine clinical practice in selecting appropriate pharmacological and psychosocial interventions.

**Keywords:** clock drawing test; schizophrenia; cognitive deficit

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## LIST OF ABBREVIATIONS

BPRS — Brief Psychiatric Rating Scale

CDT — Clock Drawing Test

CI — confidence interval

DSM-IV-TR — Diagnostic and Statistical Manual of Mental Disorders,  
IV edition, text revision

MMSE — Mini Mental Status Examination

NA — not available

PANSS — Positive and Negative Syndrome Scale

## INTRODUCTION

The term *Dementia Praecox* was coined by Emil Kraepelin to describe schizophrenia, a complex disease characterized by early onset, cognitive deficit, and a deteriorating course with hallucination and delusion [1]. The symptoms of schizophrenia are grouped into domains of dysfunction, which include positive symptoms, negative symptoms, affective symptoms, and cognitive impairment. These symptoms vary in severity, frequency, course of illness, and outcome across patients. Though the classification of schizophrenia is not beneficial, the researchers attempted to solve schizophrenia heterogeneity by clustering symptoms in different domains [2].

The DSM-IV-TR (Diagnostic and Statistical Manual of Mental Disorders, IV edition, text revision) classifies schizophrenia into subtypes, which include:

1) *paranoid*: associated with one or more systematized delusions and hallucinations;

2) *disorganized*: associated with disorganization in speech and behaviour;

3) *catatonic*: marked psychomotor disturbance;

4) *other subtypes* including undifferentiated type, residual type [3–4].

During the course of illness, clinical subtypes remain unstable [5], nonspecific to explain the etiology and pathophysiology, treatment, and prognosis of schizophrenia [6–8].

Cognitive deficit is a persistent, highly variable, enduring, and core feature of schizophrenia. Cognitive deficits vary across schizophrenia subtypes and are further classified as neurocognitive and social-cognitive deficits. The neurocognitive deficit affects specific brain areas and neural circuits, whereas the social cognitive deficit affects the process of interacting with the social world [9]. The neurocognitive deficits affect the speed of information processing, attention/vigilance [10], working memory [11], visual memory, reasoning, and problem-solving [12]. Cognitive deficit is one of the strong predictors of poor social and occupational outcomes among patients with schizophrenia [13]. The deficit in executive function and working memory is known to produce maximum cognitive

impairment. The early detection and intervention of cognitive impairment are required for disability limitation and better prognosis in schizophrenia [14].

Various approaches are used to assess the cognitive deficit in schizophrenia including experimental, ecological, psychometric, and neuropsychological approaches [15]. These approaches are complex, time-consuming, and limited to researchers only. Despite being aware of the potential implication of cognitive deficit in a patient with schizophrenia, clinician mostly fails to prioritize the assessment of cognitive deficit among subtypes. Thus, the need of the hour is that the cognitive test should be simple, easy to administer and interpret.

Clock drawing test (CDT) has been considered as reliable screening test to measure mild cognitive impairment in delirium and dementia along with Mini-Mental Status Examination (MMSE), besides, it is simple, easy to administer, and interpret [16, 17]. Though MSE and CDT are moderately correlated with each other, they measure different aspects of cognitive impairment. MMSE is considered a nonspecific measure of global cognitive function while CDT is a specific indicator of executive function [18]. The present study was aimed to compare the level of cognitive impairment among subtypes of schizophrenia using CDT.

## MATERIALS AND METHODS

The cross-sectional study was carried out at the Tertiary Care Rural Hospital of Central India and after obtaining permission from Institute Ethics Committee. After explaining the nature of the study, the written consent was obtained from all participants.

**The Inclusion criteria** for cases were:

1) age between 18 to 65 years;

2) minimum 10 years of education;

3) right-handed;

4) that fulfils the DSM-IV — TR for Schizophrenia.

**The Exclusion criteria** were the presence of delirium or dementia, organic diseases of brain, past history of head injury and epilepsy, learning disability, poor eyesight,

and hearing. Age and sex-matched controls were selected from the community fulfilling exclusion criteria and never visited psychiatry OPD in their lifetime. The patients who fulfilled the inclusion and exclusion criteria were assessed with Folstein MMSE [19], CDT (free drawn), Positive and Negative Syndrome Scale (PANSS) scale, and Brief Psychiatric Rating Scale (BPRS) on the day of admission. The CDT performance was assessed with Sunderland Scoring System [20]. The patient with schizophrenia was grouped later into three categories based on their clinical features as per DSM-IV-TR Diagnostic criteria.

**Socio-demographic characteristic.** A total of 135 patients of schizophrenia consisting of Paranoid ( $n = 45$ ), undifferentiated ( $n = 45$ ), and disorganized ( $n = 45$ ) groups were included. The age and sex-matched controls ( $n = 45$ ) were included in the study. The socio-demographic profile of the four groups is presented in Table 1. All four groups are age and sex-matched with male predominance

among paranoid subtype of schizophrenia. (66.7%, male vs 33.3%, female) followed by disorganised schizophrenia (62.2%, male vs 37.8%, female). A significant difference was observed in their years of education among patients with schizophrenia ( $11.11 \pm 2.31$ ) and the healthy group ( $13.56 \pm 1.71$ ,  $p < 0.001$ ). However, the educational status of a subgroup of schizophrenia was comparable to each other. Most of the patients with schizophrenia were unemployed, unmarried / divorced, and living alone. There were more unemployed patients in the disorganised group than in the paranoid group (71.11% vs 54.54%). The number of unemployed patients was almost equal (68.88%) in the undifferentiated and in the disorganized group ( $\chi^2 = 9.10$ ,  $df = 3$ ,  $p = 0.02$ ).

**Clinical Characteristics.** Clinical characteristics of study group are shown in Table 2, and results of Bonferroni post-hoc multiple comparison tests are shown in Table 3, Figure 1.

**Table 1.** Comparison of Socio-demographic Profile

Variables	Paranoid	Undifferentiated	Disorganised	Control	ANOVA Test
n	45	45	45	45	–
Age, years	26.45 ± 9.27	30.00 ± 7.13	27.00 ± 9.49	29.24 ± 7.47	p = 0.4271
Sex					
Male, n (%)	30 (66.66)	22 (48.88)	28 (62.20)	21 (45.45)	$\chi^2 = 5.30$ , df = 3, p = 0.15
Female, n (%)	15 (33.33)	23 (51.11)	17 (37.80)	24 (54.54)	
Years of education, n (%)	11.11 ± 2.31	11.10 ± 1.66	11.11 ± 2.31	13.56 ± 1.71	p < 0.001
Marital status					
Married, n (%)	22 (48.88)	14 (31.11)	10 (22.22)	22 (48.88)	$\chi^2 = 10.32$ , df = 3, p = 0.016
Unmarried / divorce, n (%)	23 (51.11)	31 (68.88)	35 (77.77)	23 (51.11)	
Occupation					
Employed, n (%)	21 (45.45)	14 (31.11)	13 (28.88)	25 (55.55)	$\chi^2 = 9.10$ , df = 3, p = 0.02
Unemployed, n (%)	24 (54.54)	31 (68.88)	32 (71.11)	20 (44.44)	

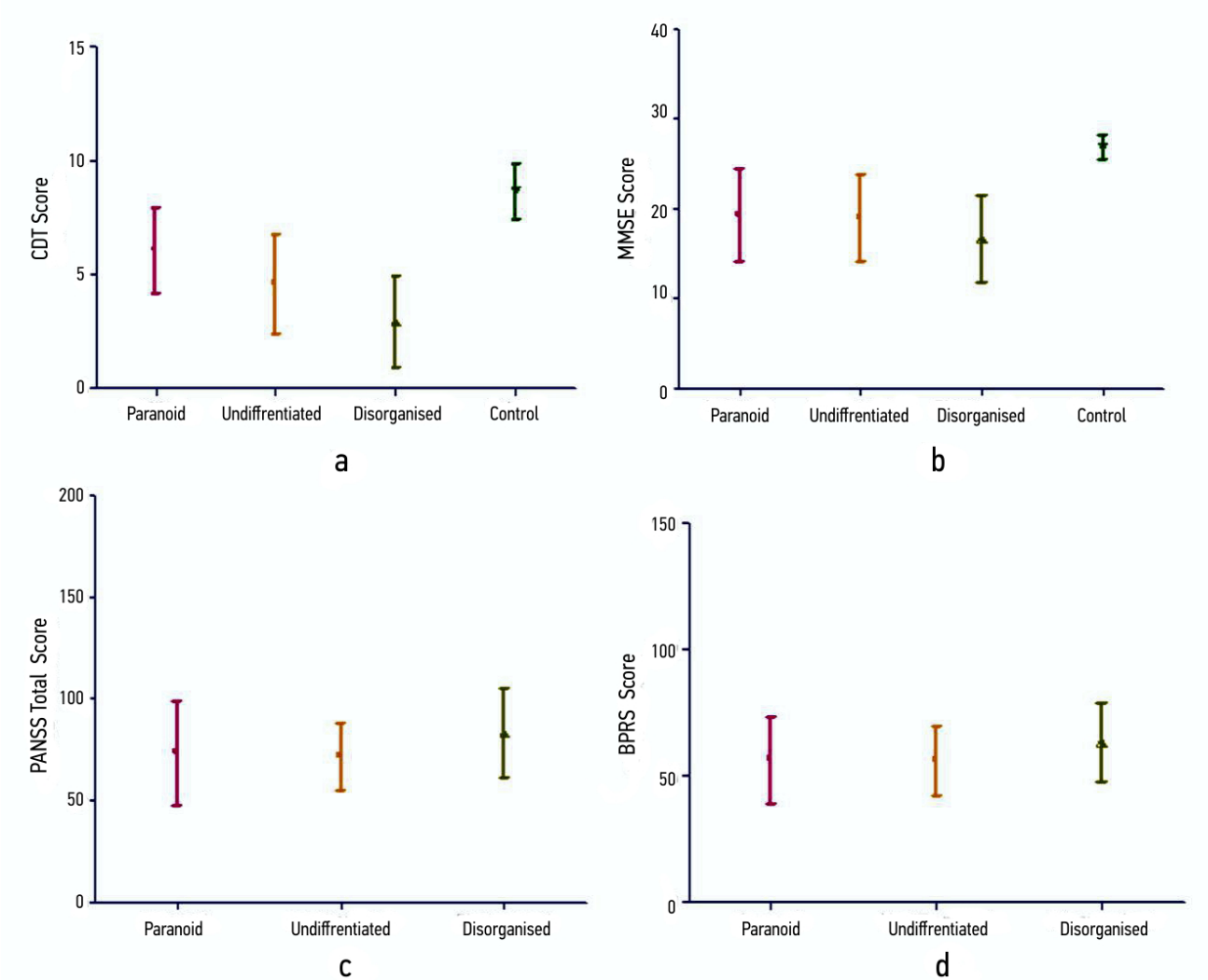
**Table 2.** Comparison among Subtypes of Schizophrenia

Variables	Paranoid	Undifferentiated	Disorganised	Control	ANOVA Test
n	45	45	45	45	–
CDT score (1–10)	$6.06 \pm 1.86$	$4.60 \pm 2.71$	$3.06 \pm 2.27$	$8.68 \pm 1.22$	$p = 0.004$
PANSS Total score	$73.43 \pm 25.69$	$71.80 \pm 16.42$	$83.36 \pm 22.14$	–	$p = 0.09$
PANSS-P score	$19.34 \pm 7.82$	$17.00 \pm 8.75$	$21.38 \pm 9.20$	–	$p = 0.27$
PANSS-N score	$17.41 \pm 8.68$	$16.60 \pm 5.93$	$19.29 \pm 9.20$	–	$p = 0.49$
PANSS-G score	$36.68 \pm 13.57$	$38.20 \pm 5.51$	$42.69 \pm 9.90$	–	$p = 0.04$
BPRS score	$56.23 \pm 17.03$	$55.90 \pm 13.91$	$63.44 \pm 15.49$	–	$p = 0.08$
MMSE score (0–30)	$19.30 \pm 5.15$	$19.00 \pm 4.80$	$16.69 \pm 4.86$	$26.88 \pm 1.38$	$p < 0.001$

**Table 3.** Bonferroni Post-Hoc Multiple Comparison among Subtypes of Schizophrenia

Variables	Comparison Group	Bonferroni's Post Hoc Comparison (95 % CI)					
	F, p	Paranoid & Undifferentiated	Paranoid & Disorganised	Paranoid & Control	Undifferentiated & Disorganised	Undifferentiated & Control	Disorganised & Control
CDT score (1–10)	87.38, p < 0.001	-0.17 to 3.10	2.14 to 4.13***	-3.57 to -1.64***	0.032 to 3.30*	-5.69 to -2.46***	-6.70 to -4.78***
PANSS Total	2.37, p < 0.09	-18.31 to 21.57	-21.99 to 2.14	NA	-31.45 to 8.34	NA	NA
PANSS-P	1.32, p < 0.27	-4.97 to 9.65	-6.46 to 2.39	NA	-11.68 to 2.922	NA	NA
PANSS-N	0.70, p < 0.49	-6.62 to 8.24	-6.38 to 2.62	NA	-10.11 to 4.73	NA	NA
PANSS-G	3.16, p < 0.047*	-11.26 to 8.22	-11.90 to -0.11*	NA	-14.21 to 5.235	NA	NA
BPRS	2.52, p < 0.085	-13.38 to 14.04	-15.52 to 1.08	NA	-21.23 to 6.14	NA	NA
MMSE	53.26, p < 0.001	-3.58 to 4.17	0.26 to 4.95*	-9.87 to -5.29***	-1.56 to 6.18	-11.71 to -4.04***	-12.46 to -7.91***

Notes: \* — p < 0.05, \*\* — p < 0.01, \*\*\* — p < 0.001; BPRS — Brief Psychiatric Rating Scale, CDT — Clock Drawing Test, CI — Confidence Interval, MMSE — Mini Mental Status Examination, NA — not available, PANSS — Positive and Negative Syndrome Scale



**Fig. 1.** Comparison between three clinical subtypes of schizophrenia with control group: on CDT (a, p = 0.004), MMSE (b, p < 0.001), PANSS score (c, p = 0.9), BPRS score (d, p = 0.08).  
Notes: BPRS — Brief Psychiatric Rating Scale, CDT — Clock drawing test, MMSE — Mini-Mental Status Examination, PANSS — Positive and Negative Syndrome Scale.



All patients with schizophrenia irrespective of their subtype performed worse on CDT than healthy controls ( $p = 0.004$ ). The CDT performance differed significantly across all four groups as reflected by highly significant group interaction ( $F = 87.38$ ,  $df = 3,145$ ,  $p < 0.001$ ). Among the patients with schizophrenia, disorganized group performed worse on CDT ( $3.06 \pm 2.27$ ) than the paranoid group ( $6.06 \pm 1.86$ ) and the undifferentiated group ( $4.60 \pm 2.71$ ). The patients in the undifferentiated group performed worse than in the paranoid group ( $p < 0.004$ ). On multiple comparison tests, the difference was more significant between paranoid and disorganised group (95% confidence interval (CI) 2.14–4.13,  $p < 0.001$ ) than between the undifferentiated and disorganised group (95% CI 0.03–3.30,  $p < 0.05$ ).

There was no significant difference among four groups on PANSS Total ( $p = 0.09$ ), PANSS — positive ( $p = 0.27$ ), PANSS — negative ( $p = 0.49$ ) and BPRS scale ( $p = 0.08$ ). The significant difference was observed on PANSS — G subscale ( $p = 0.04$ ). Bonferroni's Post-hoc multiple comparison tests were performed for comparisons between groups. A significant difference is observed between paranoid and disorganized groups (95% CI -11.90 – -0.11,  $p < 0.05$ , Bonferroni adjusted).

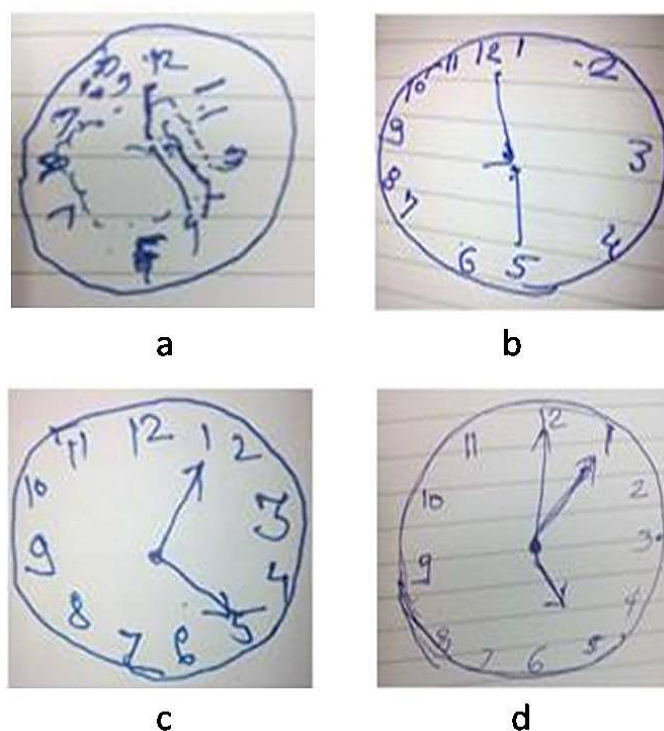
We observed significant differences between patients with schizophrenia and the control group ( $p < 0.001$ ). On

Multiple comparison significant difference was observed between paranoid and disorganized group (95% CI 0.26–4.95,  $p < 0.05$ , Bonferroni adjusted) than paranoid and undifferentiated (95% CI -3.58–4.17,  $p > 0.05$ , Bonferroni adjusted), undifferentiated and disorganised group (95% CI -1.56–6.18,  $p > 0.05$ , Bonferroni adjusted). The difference was highly significant between subtypes of schizophrenia and healthy control ( $p < 0.001$ ).

All analyses were performed using SPSS software version 20.0 (SPSS, Cary, N.C., USA). Descriptive statistics in terms of percentages was used for categorical variables such as sociodemographic characteristics and clinical characteristics. The Chi-Square test and Fisher's exact test were used for the analysis of categorical data. Student-independent t-tests were performed to analyze continuous data between two groups. One-way ANOVA was used to compare the continuous data for three or more groups. Pearson correlation coefficients were calculated to determine the bi-variate relationship among continuous variables including PANSS score, BPRS score, CDT Score, and MMSE Score among various comparison groups.

## RESULTS

The representative example of CDT task is depicted in Figure 2 according to subtypes of schizophrenia.



**Fig. 2.** Representative Examples of CDT by Patients with Schizophrenia: (a) patients with disorganised schizophrenia, Sunderland's Score — 3; (b) patients with Paranoid schizophrenia, Sunderland's Score — 5; (c) patients with undifferentiated schizophrenia, Sunderland's Score — 9; (d) patients with undifferentiated schizophrenia, Sunderland's Score — 10.

**Correlates of CDT Performance and Socio-Demographic and Clinical Variables.** The correlations between neurocognitive function measured on CDT, MMSE, and clinical variables were assessed with Pearson correlation coefficient. No significant correlation was observed between age, education, and CDT performance. The poorer performance on CDT positively correlated with poorer scores on MMSE among disorganised and paranoid subtypes of schizophrenia.

A high level of positive correlation is observed between CDT and MMSE among disorganised subtype of

schizophrenia (Pearson correlation coefficient  $r = 0.65$ ,  $p < 0.001$ ) than paranoid group ( $r = 0.43$ ,  $p < 0.01$ ). The MMSE score highly correlated with BPRS score ( $r = -0.47$ ,  $p < 0.001$ ), PANSS total ( $r = -0.47$ ,  $p < 0.001$ ), PANSS-negative ( $r = -0.45$ ,  $p < 0.05$ ), PANSS general ( $r = -0.45$ ,  $p < 0.001$ ) among paranoid group than disorganized group. Among disorganised groups, correlation between MMSE with BPRS score ( $r = -0.33$ ,  $p < 0.05$ ), PANSS total score ( $r = -0.40$ ,  $p < 0.01$ ) and PANSS negative ( $r = -0.32$ ,  $p < 0.05$ ) was observed. No significant correlations were observed between other clinical variables (Table 4).

**Table 4.** Pearson correlations ( $r$  value) of CDT Score with MMSE score, PANSS Score, BPRS Score among subtypes of schizophrenia

Variables	Paranoid (n = 45)		Undifferentiated (n = 45)		Disorganised (n = 45)		Control (n = 45)	
	MMSE score	CDT score	MMSE score	CDT score	MMSE score	CDT score	MMSE score	CDT score
Age	-0.041	-0.23	0.44	-0.021	0.069	0.11	0.12	0.059
Education	-0.029	-0.46	-0.11	-0.38	0.14	0.016	-0.10	0.19
MMSE	NA	0.43**	NA	0.11	NA	0.65***	NA	-0.02
BPRS	-0.47***	-0.16	-0.49	0.17	-0.33*	-0.19	NA	NA
PANSS Total	-0.47***	-0.20	-0.60	-0.14	-0.40**	-0.32**	NA	NA
PANSS Positive Scale	-0.24	-0.20	-0.46	0.15	-0.28	-0.16	NA	NA
PANSS Negative Scale	-0.47**	-0.19	-0.56	-0.39	-0.36*	-0.32*	NA	NA
PANSS General psychopathology scale	-0.45***	-0.13	-0.45	-0.22	-0.30*	-0.28	NA	NA

Notes: \* —  $p < 0.05$ , \*\* —  $p < 0.01$ , \*\*\* —  $p < 0.001$ ; BPRS — Brief Psychiatric Rating Scale, CDT — Clock Drawing Test, CI — Confidence Interval, MMSE — Mini-Mental Status Examination, NA — not available, PANSS — Positive and Negative Syndrome Scale

## DISCUSSION

To the best of our knowledge, no study seems to have compared neurocognitive functioning with clock drawing performance among subtypes of schizophrenia. However, few researchers in past attempted to assess clock drawing performance among schizophrenia patients without stratification in subtypes and elderly subjects [21, 22]. The age and disease process has a significant impact on clock drawing performance in schizophrenia [23]. We attempted to overcome this major limitation with inclusion of younger subjects and stratification in subtypes of schizophrenia.

As expected, we found that patients with schizophrenia have low scholastic performance compared to healthy

comparison. The cognitive decline in schizophrenia has been studied extensively and found to be associated with number of relapses, hospitalizations, premorbid IQ, length of illness, and depression [24–26]. In the present study, we tried to minimize the influence of education on clock drawing performance with a purposeful selection of subjects that are matriculated.

The index study confirms previous research finding that patients with a higher score on PANSS were performed worse on both MMSE and CDT score. Poorer performance score on CDT correlated with higher performance score on PANSS positive symptoms sub-scale [21]. These finding may be suggestive of potential impact of positive, negative and affective domains of schizophrenia on cognitive domains. P. Brazo, et al. (2002) in their

study found that patients with positive symptoms have better cognitive skills than disorganized subtype [27].

The patients with paranoid schizophrenia performed better on CDT and had higher MMSE score than other subtypes. They were mostly employed, married than another subtype. The CDT was studied as a specific indicator of executive function, and Mini mental status is considered as indicator of global cognitive function [18]. The intact executive function, working memory, sustained attention is required for occupational and social functioning [20, 28]. It may be suggestive of the patients with schizophrenia being cognitively superior to other subtypes. The most of the authors previously reported that the paranoid and undifferentiated group of schizophrenia are cognitively heterogeneous with near normal or normal cognitive function termed as '*Neuropsychologically normal schizophrenia*' [29–31].

The representatives of disorganized group were more unemployed, divorced or living single and had worst MMSE score and poor performance on clock drawing test. The employment requires the ability to plan, prioritize and solve the problems along with planning for future and setting goals. The wide range of neurocognitive functions is required for better occupational and social functioning, which includes attention, memory, executive function and learning. These all are affected in schizophrenia, which leads to increased unemployment among patients with schizophrenia. The index study suggests the unemployment is higher in disorganized group, which is secondary to impaired cognitive function and appears subtype specific. It can be assessed with clock drawing test at early stage to better plan management in clinical practice.

The poor performance of disorganized group on clock drawing test compared to paranoid and disorganized group may be suggestive of different underlying neurobiological mechanism contributing to same. The most of the previously conducted functional neuroimaging studies suggests that hypoactivity of mesocortical dopaminergic pathway to dorsolateral prefrontal cortex mediates cognitive and negative symptoms of schizophrenia, and hyperactivity of mesolimbic dopamine pathway to *nucleus accumbens* is being involved in positive symptoms of schizophrenia [32–34]. The one of the recently conducted studies suggests the correlation between severity of negative symptoms with grey matter volume reduction in ventrolateral prefrontal cortex, and severity of positive symptoms with grey matter reduction in temporal and medio-frontal cortex. Most of these symptoms were found to be associated with slowing down of processing speed and impairment in working memory [35].

The Nenadicetal achieved 98.5 % accuracy in classification of schizophrenia into three groups on the basis of Voxel Based Morphometry. They reported

association of stronger deficit in medial temporal and cerebellar region with disorganised subsyndrome, the paranoid/hallucinatory subsyndrome with superior temporal cortex, and negative subsyndrome with stronger deficit in thalamus [36]. Interestingly, in our study we found highly significant difference on clock drawing performance among disorganised and paranoid group which is almost comparable to their neuroimaging studies and may indicate the potential of CDT to delineate heterogeneous schizophrenia into their subtypes. However, it requires further exploration with both qualitative and quantitative analysis of CDT.

The various neurotransmitter systems have previously been postulated, which modulate the cognitive symptoms in schizophrenia along with positive, negative and affective symptoms. The antipsychotics use has been reported with improvement in cognitive function. Atypical antipsychotics such as quetiapine and olanzapine have been proven more efficacious in cognitive outcomes in patients with schizophrenia than *risperidone*, *ziprasidone*, and *haloperidol* [37]. The patient with better cognitive performance is able to maintain regular drug compliance and to monitor their symptoms. They are considered as suitable candidates for cognitive behaviour therapy. Thus, bedside assessment of cognitive heterogeneity may appear useful for clinicians to select appropriate pharmacotherapy and psychosocial therapy. The clinician may set different vocational and educational goals from those set for other patients and may allow higher degree of independent living.

**Limitations.** Our study has few limitations. Firstly, we included only inpatients who are obvious with higher severity of symptoms than outpatients. Therefore, further study with matched case control is warranted to generalize these finding in clinical practice. Secondly, it is expected that simple screening tests are usually insufficient to discriminate subjects with subtle cognitive impairment from cognitively healthy subjects. Thirdly, in index study, cognitive performance was not compared with any standardised neuropsychological test.

## CONCLUSION

The clock drawing test has potential to differentiate subtypes of schizophrenia from each other and healthy control. Being a brief, relatively time-efficient screening test, it is easy to administer, well accepted by patient and easy to document in clinical settings. It may help to measure improvement or deterioration in cognitive deficit, negative symptoms among patients with schizophrenia. It may guide the selection of psychotropics and a better understanding of underlying functional impairment of neural circuits in patient with schizophrenia.



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## ОБ АВТОРАХ

**\* Ransing Ramdas;**ORCID: <https://orcid.org/0000-0002-5040-5570>;e-mail: [ramdas\\_ransing123@yahoo.co.in](mailto:ramdas_ransing123@yahoo.co.in)**Sakekar Gajanan Shripad;**ORCID: <https://orcid.org/0009-0000-9700-008X>;e-mail: [gsakekar@gmail.com](mailto:gsakekar@gmail.com)**Grigo Omityah**, Assistant Professor;ORCID: <https://orcid.org/0000-0003-3384-1386>;e-mail: [dromityah@gmail.com](mailto:dromityah@gmail.com)**Khairkar Praveen**, д.м.н., профессор;ORCID: <https://orcid.org/0000-0003-3166-3547>;e-mail: [praveen.khairkar280@gmail.com](mailto:praveen.khairkar280@gmail.com)

## AUTHORS' INFO

**\* Ramdas Ransing**, MD;ORCID: <https://orcid.org/0000-0002-5040-5570>;e-mail: [ramdas\\_ransing123@yahoo.co.in](mailto:ramdas_ransing123@yahoo.co.in)**Gajanan Sh. Sakekar;**ORCID: <https://orcid.org/0009-0000-9700-008X>;e-mail: [gsakekar@gmail.com](mailto:gsakekar@gmail.com)**Omityah Grigo**, Assistant Professor;ORCID: <https://orcid.org/0000-0003-3384-1386>;e-mail: [dromityah@gmail.com](mailto:dromityah@gmail.com)**Praveen Khairkar**, MD, Dr. Sci. (Med.), Professor;ORCID: <https://orcid.org/0000-0003-3166-3547>;e-mail: [praveen.khairkar280@gmail.com](mailto:praveen.khairkar280@gmail.com)

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\* Автор, ответственный за переписку / Corresponding author