

Executive dysfunction in drug-induced psychosis

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ABSTRACT

Executive dysfunction is a core feature of drug-induced psychosis. Executive function is an important cognitive domain crucial for an individual to achieve adaptive living. The present researchers undertook a neuropsychological assessment of executive functioning among Nigerian patients diagnosed with drug-induced psychosis (DIP). The assessment tools employed were mini-mental status examination (MMSE), trail making test parts A and B, fluency test and Stroop colour word test (SCWT), the executive function components assessed were working memory, inhibition, fluency and set shifting. Ninety-seven participants consisting of patients diagnosed with drug-induced psychosis (n=53, 4 females and 49 males) and a control group of 44 persons (21 females and 23 males) participated in the study. There were statistically significant differences between DIP cases and controls on all the executive function components assessed. Utilizing regression analysis; the most significant predictors of the trail making test (TMT) part B among cases were general cognitive functioning ($t = 4.47, p < 0.001$) and current age ($t = 3.30, P = 0.002$). Drug-induced psychosis cases, showed more executive functioning impairment than controls on the components assessed. Hence, drug-induced psychosis patients are more vulnerable to executive dysfunction than the general population.

Introduction

Executive functioning (EF) deficits have been known to occur in persons who have had severe brain injuries (Ratiu & Talos 2004; Goldstein et al., 2014) and drug-induced psychosis (DIP) (Mauri 2016; Ham et al., 2017; Jatau et al., 2021). Executive dysfunction renders individuals unable to cope with the performance of a series of goal-motivated behavior necessary to achieve adaptive existence in an ecologically and psychologically evolving world. Such include the ability to generate thought and think flexibly, to update and manipulate information mentally, to inhibit what is undesirable or irrelevant to current goals, to self-regulate, and to plan and adjust behaviour as appropriate to the current situation (Jurado & Rosselli, 2007). Executive functioning are cognitive control processes which facilitate decision making, planning and goal-driven behaviour (Wray et al., 2020; Miyake et al., 2020). Intact executive functioning is critical to human existence. Yet there are unresolved questions about executive function executive functioning which demand urgent answers. According to Rabinovici et al. (2015), specific questions which capture executive dysfunctions include inquiries regarding the patient's difficulty with planning or organization, problems with multitasking, poor judgment or decisions, impaired concentration/short attention span, difficulty with problem solving, mental rigidity/inflexibility, and impulsivity.

Cahn-Weiner et al. (2002), posit that executive function include inhibitory control, working memory and

cognitive flexibility. Intact executive functions are critical to the ability to adapt to an ever-changing world. Some researchers (Stuss & Benson, 1986; Aron et al., 2004) in their study of the frontal lobe, identified anticipation, goal selection, preplanning, monitoring, and use of feedback as executive skills and have posited that the anatomical site of these skills is the prefrontal cortex. They have also suggested that the ability to maintain or shift a mental set, to establish goals, and to plan are especially important elements of executive functioning noting that these components could be measured by various neuropsychological assessment tools. We define executive functioning in this study as an individual's ability to initiate, sustain/perpetuate and complete the series of goal-motivated behaviours required for adaptive living. We do hope that this definition minimizes the variations, mixed reports, and related issues of imprecise and conflicting definitions and operationalization executive functioning researchers have grappled with over the years (Diamond, 2012; Blair, 2016; Snyder et al., 2016).

Executive function components

Executive function can be split into four distinct components: working memory, inhibition, set shifting, and fluency (four factor model of executive function). These components may be differentially affected in individual patients and act together to guide higher-order cognitive constructs such as planning and organization. (Rabinovici et al., 2015; Ferguson et al., 2021). While dysexecutive syndromes were first described

in patients with frontal lesions, intact executive functioning relies on distributed neural networks that include not only the prefrontal cortex, but also the parietal cortex, basal ganglia, thalamus, and cerebellum (Siew et al., 2019). Executive dysfunction arises from injury to any of these regions, their white matter connections, or neurotransmitter systems (Ferguson et al., 2021). Hence, the present study focused on the neuropsychological assessment of the four components of executive functioning namely, working memory, inhibition or inhibitory control, set-shifting and fluency.

Working memory can be viewed as limited capacity system that permits us to temporarily process, store, and consciously manipulate information. An early model proposed by Baddeley and Hitch (1974) split working memory into a phonologic loop that maintains auditory and verbal information and a visuospatial sketchpad that maintains visual information (Rabinovici et al., 2015).

In advanced cases, patients exhibit utilization behaviour (picking up and using objects they observe for no clear purpose), echolalia (involuntarily repeating what is heard), or echopraxia (involuntarily imitating actions) (Rabinovici et al., 2015). Set shifting inherently relies on working memory and inhibition control. Persons with deficits in set shifting have problem with rigidity and multitasking (Rabinovici et al., 2015). Fluency refers to the ability to maximize the production of verbal or visual information within a specific period, without repeating responses. Deficits on these measures reflect lack of initiation or inertia, or disorganization. The three most common types of fluency tasks are category, letter, and design. For category fluency (also known as semantic fluency), subjects are asked to generate as many words as possible from a specified category (animals). For letter or phonemic fluency, subjects are asked to generate as many words as possible that start with a specified letter (G), excluding names of people and places or grammatical variants of previous responses. For design fluency, subjects are asked to generate as many unique designs as possible while applying a fixed set of rules (using four lines to connect the dots) within sixty seconds (Rabinovici et al., 2015). Notably, performance on this task is sensitive to variation in executive function and semantic memory (Kim et al., 2019).

Drug Use and Mental Disorders

Drug-induced psychosis refers to a medical condition resulting from use and abuse of certain psychoactive substances which interfere with brain connectivity and functionality (Mauri, 2016). One of the earliest reports about the effects of cannabis on mental health originated in India from the Indian Hemp Commission of 1893 (Kulhalli et al., 2007). Nevertheless, drug-induced psychosis resulting from use/abuse of Cannabis (Indian hemp/Igboo/Moroko), alcohol, cocaine and heroin has now assumed global proportions (Mauri 2016; Jatau et al., 2021). Fiorentini et al. found that the propensity to develop psychosis is influenced by the severity of use and dependence. This position is also supported by Ham et al. (2017) who claim that psychotic symptoms can be elicited in

healthy human adults when exposed to drugs. Jatau et al. (2021) noted that world drug report-2019 of the United Nations Office on Drugs and Crime (UNODC) estimated that 271 million (5.5%) of the global population (aged between 15 and 64 years), had used drugs in the previous year (UNODC, 2019). They found a prevalence of 20–40% (among students) and 20.9% (among youths) drug abuse in Nigeria. The Global Burden of disease Study 2017 reported that globally, in 2017, about 585,000 deaths were due to drug use (UNODC, 2019). The UNODC 2018 report found that one in seven (about 14.2%) persons (aged 15–64 years) had used a drug in the past year. It was also found that one in five (20%) individuals who had used drug in the past year is suffering from drug-related disorders (United Nations Office on Drugs and Crime 2018). Latest global estimates reveal that about 5.5 per cent of the population aged between 15 and 64 years have used drugs at least once in the past year, while 36.3 million people, or 13 per cent of the total number of persons who use drugs, suffer from drug use disorders; which implies that Nigeria, with 14.4% drug use prevalence is significantly above the global average (UNODC World Drug Report 2021).

Executive dysfunction in mental disorders especially cases of psychosis has become a global mental health concern requiring further investigation (Rabanca-Souza et al, 2016). Despite of these, there exists a paucity of research focusing on executive dysfunction in drug-induced psychosis among clinical populations in Nigeria and most countries of the Global South.

Blair (2016), in her review, found evidence of trainability of executive functioning among the children population. She opines that malleability during that stage of executive functioning development aided success in such training. Two approaches to executive functioning training were identified namely, Direct training method and Indirect training approach (Diamond & Lee, 2011; Melby-Lervag & Hulme, 2013). In the former, repetitive practices on a specific EF task, usually a working memory task, in which improvement in performance on that task is the goal, while. Indirect training involves repetitive practice on activities that exercise executive functioning, such as learning mathematics or martial arts, in which becoming better at math or achieving martial arts mastery is the goal (Klingberg, 2010).

For adult patient population, clinical experience suggests that diagnosis, psychopharmacological treatment results enable the patient achieve a level of insight whereby s/he can commence cognitive re-training, rehabilitation and eventual re-integration into the larger society. Research evidence suggests that not enough is being done to democratize access to screening and rehabilitation processes and programmes (Jatau et al., 2021). Countries of the Global South like Nigeria, predominantly rich in natural resources require the creative and ingenious endowment of her young adults in order to harness the said resources.

We hypothesized that: (1) Drug-induced psychosis patients (clinical subjects) will perform significantly worse than controls on tests of general cognitive functioning

(measured by MMSE). (2) Clinical subjects will perform significantly worse than controls on tasks assessing working memory. (3) Clinical cases will perform significantly worse than controls on tests measuring set shifting. (4) Clinical subjects will perform significantly worse than controls on tasks assessing inhibitory control and fluency.

Materials and Methods

Sample

A total of 97 participants (25 females and 72 males) were included in the study. This included a sample consisting of fifty-three Drug-induced Psychosis patients aged between 18 and 68 years selected after consent was obtained at the In-Patient and Out-Patient departments of Federal Neuropsychiatric Hospital, Benin City, Nigeria. There was a control group of forty-four volunteers aged between 18 and 68 years. The control group was drawn largely from religious communities with a demonstrable aversion to smoking, alcohol and drug use. Subjects in both cases and control groups had the mini mental status examination (MMSE), modified version of Stroop Colour Word Interference Test from subtests of the Delis-Kaplan Executive Function System (D-KEFS), the Trail Making Test (TMT) from the D-KEFS, and Fluency tasks, individually administered to them.

Instruments

Mini-mental State Examination (MMSE)

The Mini-Mental State Examination is a 30-point questionnaire used to detect cognitive impairment, assess its severity and also monitor variations in cognitive performance over time. It was developed by Folstein, Folstein and McHugh (1975, 1998). The MMSE takes 5-10 minutes to administer and is therefore practical to use repeatedly and routinely. The MMSE is effective as a screening tool for cognitive impairment with older, community dwelling, hospitalized and institutionalized adults. Assessment of an older adult's cognitive function is best achieved when it is done routinely, systematically and thoroughly. In scoring the MMSE, 25-30 suggests a normal scoring range, 18-24 suggests a mild to moderate impairment of cognitive functioning while scores under 17 suggest a severe cognitive impairment. The procedure is repeated for Trail Making Test Part B except that it is explained to individuals that they must alternate between numbers and letters sequentially. Results for both TMT A and B are reported as the number of seconds required to complete the task; therefore, higher scores reveal greater impairment.

Average Deficient Rule of Thumb

Trail A 29 seconds > 78 seconds Most in 90 seconds

Trail B 75 seconds > 273 seconds Most in 3 minutes

Examiner Qualification & Training: None required

Summary of strengths and weaknesses:

Fluency: Fluency represents the ability to maximize the production of verbal or visual information in a specific time period, while avoiding repeating responses. The three most common types of fluency tasks are category, letter, and design. Verbal fluency tasks are often included in neuropsychological assessment, in clinical practice, and in research. The popular use of the verbal fluency tasks most likely stems in part from their face validity as tests of both verbal ability and executive control (Shao et al., 2014). Subjects are required to retrieve words of their language, which undoubtedly requires them to access their mental lexicon. They need to focus on the task, select words meeting certain criteria, avoiding repetition, which certainly involves executive control processes (Fisk & Sharp, 2004). Serious deficits in either verbal ability or executive control should manifest themselves in poor performance in the fluency tasks.

The validity of the fluency tasks as a measure to assess verbal ability, specifically lexical access ability, has been confirmed in numerous studies comparing groups of participants that would be expected to differ in this ability. Salthouse (1991, 1996) found that participants with smaller vocabularies produced fewer words than did participants with larger vocabularies. Similarly, children with Specific Language Impairment or dyslexia, who often have word finding difficulties (e.g., Snowling et al., 1988; Seiger-Gardner, & Brooks, 2008; Bragrad et al., 2012), have been shown to have deficits in verbal fluency performance compared to typically developing children (Cohen et al., 1999; Weckerly et al., 2002). Therefore, the fluency tasks can be used as an efficient screening instrument of general verbal functioning (Rabinovici et al., 2015).

Stroop colour word test

The Stroop Color and Word Test (SCWT) is a neuropsychological test extensively used for both experimental and clinical purposes (Scarpina & Tagini, 2017). It assesses the ability to inhibit cognitive interference, which occurs when the processing of a stimulus feature affects the simultaneous processing of another attribute of the same stimulus (Stroop 1935). The purpose of the Stroop colour word test (SCWT) is to assess the ability of the individual to inhibit a habitual response for one that is less readily available. Multiple versions of the Stroop Test have been developed. Earlier versions such as the 5 × 20 grid version was chosen for standardization (Golden & Freshwater, 2002) because impaired individuals had difficulty reading across the rows, tending to lose their place. The Color-Word component consists of color words, but each one is printed in a color that differs from the written word (e.g., the word "red" will be printed in green or blue, but not in red).

Procedure

Cases were individuals diagnosed with drug-induced psychosis resulting from the use/abuse of cannabis, alcohol, cocaine or heroin recruited after ethical clearance from the Federal Neuropsychiatric Hospital, Benin City, Nigeria. Ethics Committee was received. Psychiatrists in the hospital were

contacted initially and generally, after preliminary information and verbal consent, they referred willing subjects to the researchers. All who met inclusion criteria were recruited, though about three opted out in the process of tests administration. Cases (53) and controls, (44) were personally administered the mini mental status examination (MMSE), TMT, SCWT and Fluency tasks by this researcher between the months of April and August, 2021. Time taken to complete all parts of the test and scores were recorded. Demographic details (gender, age, education etc) were also recorded for all participants.

The following instructions for Trail Making tests were adopted for modified version of Delis-Kaplan Executive Function System (D-KEFS) subtests: Part A Sample A: “There are numbers in circles on this page. Please take the pencil and draw a line from one number to the next, in order. Start at 1 [point to the number], then go to 2 [point], then go to 3 [point], and so on. Please try not to lift the pen as you move from one number to the next. Work as quickly and accurately as you can.” If there is an error: “You were at number 2. What is the next number?” Wait for the subject’s response and say, “please start here and continue.” Test A: If Sample A is completed correctly. Repeat the above instructions. Start timing as soon as the instruction is given to begin. Stop timing when the Trail is completed, or when maximum time is reached (150 seconds = 2.5 min). Part B Sample B: “There are numbers and letters in circles on this page. Please take the pen and draw a line, alternating in order between the numbers and letters. Start at number 1 [point], then go to the first letter, A [point], then go to the next number, 2 [point], and then the next letter, B [point], and so on. Please try not to lift the pen as you move from one number or letter to the next. Work as quickly and accurately as you can.” If there is an error: “You were at number 2. What is the next letter?” Wait for the subject’s response and say, “please start here and continue.” Test B: If Sample B is completed correctly. Repeat the above instructions. Start timing as soon as the instruction is given to begin. Stop timing when the Trail is completed, or when maximum time is reached (300 seconds = 5 minutes) For category fluency (also known as semantic fluency), subjects were asked to generate as many words as possible from a specified category (eg, animals or groceries). For letter fluency (also referred to as phonemic fluency), subjects were asked to generate as many words as possible that start with a specified letter (G), excluding names of people and places or grammatical variants of previous responses. In design fluency test, examinees were instructed to draw as many different designs as possible in one minute, while avoiding repeating previous designs.

Demographic characteristics:

The mean ages (mean, M), (standard deviations, SD) of the cases and controls were 33.17 (SD = 9.11) and 31.90 (SD = 14.46) years respectively. Mean ages of cases and controls were not different statistically (t=1.007, p= .319>0.05). Gender-wise distribution of the sample was 7.7% females, 92.38% males among cases and 47.7% females, 52.3% males

Table 1: Mean (M) and standard deviation (sd) for study variables with clinical group (n = 53) and group control (n = 44)

Variables	Clinical Group		Control Group	
	M	SD	M	SD
MMSE	20.88	4.52	25.11	4.5
TMT Part A	103.90	78.38	54.59	18.82
TMT Part B	197.80	89.02	98.95	40.45
SCWT	2.17	2.05	3.09	2.11
Fluency	24.32	7.94	30.38	10.94
Age	33.17	9.11	31.90	14.46
School Years	13.22	2.37	13.43	1.96
Duration of illness	1.65	5.37	Not Applicable	Not Applicable

among controls. There were greater number of males than females among drug-induced psychosis cases. MMSE scores of cases, and controls were 20.88 (SD = 4.52), 25.11 (SD = 4.45) respectively [Table 1]. There was significant difference between cases and controls on MMSE score. Controls had significantly higher MMSE scores than cases (t = 6.85, p<0.001).

The mean years of education (SD) were comparable: for cases 13.22 (SD=2.37) years, and controls 13.43 (SD=1.96) years. There were no significant differences between cases and controls on education

DIP cases versus controls:

There were significant differences between cases and controls on Part A of the TMT. DIP cases (102.90 (SD=78.38secs) took significantly more time than controls (54.59 (SD=18.82secs) (t= 4.55, p<0.001) [see Tables 1 and 3] On Part B of the TMT, cases (197.80 (SD=89.02 secs) took significantly more time than controls as well (98.95 (SD=40.45secs) (t =8.21, p <0.001) [Tables 1 and 4 refer]. In total fluency tasks (semantic fluency +polemic fluency +design fluency), cases performed significantly worse 24.32 (SD=7.94) than controls 30.38 (SD=10.94) (t= 5.60, p<0.001) [see Tables 1 and 6]. Similarly, the Stroop colour word test performance of cases 2.17 (SD=2.05) was significantly worse than controls 3.09 (SD=2.11) (t= 3.13, p = 0.003) [Tables 1 and 5 refer]. And there were significant differences between cases and controls on MMSE scores. Cases 20.88(SD=4.52) and controls 25.11(SD=4.45) (t=6.85, P<0.001).

Analyses among patients:

Regression analyses were performed to test for effects of different demographic variables on MMSE, TMT, SCWT, and Fluency among cases. Variables selected for analyses were age, duration of illness and school years. Analysis suggested that higher scores on Part B of the TMT scores were positively predicted by age and general cognitive functioning. (t=3.30, p=.002) (t=4.47, <.001) [Table 2] And for schizophrenics, age and general cognitive functioning are positive predictors of TMT B (t=2.54, p=.014) TMT Part B is negatively predicted by

Table 2: Regression analysis showing age and MMSE scores as predictors of DIP patients TMT Part B performance

Model	Unstandardized Coefficients		Standardized Coefficients	<i>t</i>	Sig.
	<i>B</i>	<i>SE</i>	Beta		
(Constant)	274.80	60.58		4.536	.000
1 TOTAL MMSE score of drug induced psychosis patients	-.9.82	2.19	-.49	-4.479	.000
Age of drug induced psychosis patients in years	3.94	1.19	.40	3.305	.002

school years and duration of illness ($t=1.32$, $p=.186>.05$) ($t=.140$, $p=.890>.05$). Fluency is negatively predicted by age ($t=1.92$, $p=.060>.50$), education ($t=1.34$, $p=.185>.05$) and duration of illness ($t=1.50$, $p=0.139$)

Discussion

The major finding of this study was that drug-induced psychosis cases performed worse than controls. To our knowledge, this is one of the first few reports of inhibitory control, working memory, set shifting and fluency components of executive functioning, among drug-induced psychosis patients in Nigeria. We found that Nigerian subjects diagnosed with drug-induced psychosis performed worse than controls on Parts A and B of the TMT, assessing inhibitory control, working memory and set shifting components of executive ability; SCWT assessing working memory and inhibitory control; fluency tasks assessing fluency and working memory components of executive functions; and MMSE assessing working memory and general cognitive functioning (Rabinovici et al., 2015). The deficits observed in the performances on these measures can be the direct consequence of comprehensive deficits in executive functions emanating from the disorder, or an indirect manifestation related to some underlying genetic disorders marked by executive dysfunction such as schizophrenia (Bhatia et al., 2009). Age has been found to adversely affect executive function, but the effect was pronounced among drug-induced psychosis cases more than controls (Arafat & Shoquirat 2019). The cases took more time to complete Part B of TMT than normal subjects, in agreement with other studies (Bhatia et al., 2009; Arafat & Shoquirat, 2019).

Age was an important predictor of TMT performance in our cases. Our results are consistent with those by Bhatia et al. (2009). Cognitive abilities were adversely affected by psychotic symptoms. (Bhatia et al., 2009). There should be vigorous campaign geared towards reduction of stigmatization of those diagnosed with drug-induced psychosis. If this is done, cases may be reported early enough to enable early detection, treatment and rehabilitation; Subjects with higher general cognitive functioning scores took less time on all parts of the TMT, most subjects were male. This could be attributed to low levels of substance use among females in general. Our findings indicate that drug-induced psychosis due to abuse features prominently in clinical practice (Fiorentini 2011) (Arafat & Shoquirat 2019).

There should be vigorous campaign geared towards reduction of stigmatization of those diagnosed with drug-induced psychosis. If this is done, cases may be reported early enough to enable early detection, treatment and rehabilitation; The government should democratize (make available to largest possible number of people) access to screening and rehabilitation processes and programmes. Such a measure could reverse the trend. In order to advance executive functioning research, future studies may consider adopting a three-stage approach that covers (a) initiation stage of goal-motivated behaviour (b) sustenance stage of goal-motivated behavior and (c) completion stage of goal-motivated behaviour which make up executive functioning. This may require modification of existing assessment tools or the invention of novel and relevant assessment tools

In conclusion, we report a fairly large Nigerian sample of Drug-induced psychosis patients performed worse than controls on MMSE tasks, Part A and Part B of the TMT, Fluency tasks, and SCWT. Hence drug-induced psychosis subjects recorded dysfunction in the four components of executive functions investigated. The cases performed worse than the controls, suggesting that drug-induced psychosis patient are more vulnerable to executive dysfunction than the general population. There are some limitations of this study. The neuropsychological measures used in our study were cross-sectional. Cases were older than controls and the medication status of subjects was not controlled for; and these factors could not be accounted for in cases/controls differences. (Bhatia et al 2009). Further research should be using a broader study sample diagnosed with drug-induced psychosis that is caused by substances studied here and others not included here. This may lead to more observations and a more accurate result. Absence of validation of executive function tests in the country may cast a shadow over generalizability of research findings.

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