INTERNATIONAL JOURNAL OF PSYCHOLOGY AND NEUROSCIENCE

Neuropsychological Assessment and Cannabis Use: A Systematic Review

Maria Clea Marinho Lima
Federal University of Pernambuco, Pernambuco, Brazil

Marcelo Moraes Valença
Federal University of Pernambuco, Pernambuco, Brazil
Correspondence: Maria Clea Marinho Lima
Email: clea.marinho@hotmail.com

Abstract

Background: Due to the wide spread of cannabis use in the world, the adverse effects of cannabis use on the neurocognitive functions has attracted the interest of researchers and the number of research on the topic has increase. Despite the high prevalence of drug use among young people, studies that focus on the chronic use are still incipient and their results are inconsistent. **Aim:** To undertake systematic literature review of studies that assess the neurocognitive effects of chronic cannabis use, comparing the findings among adults and adolescents. **Methods:** There were found 644 studies, of which only 9 complied with the acceptance criteria. **Results:** The studies were grouped the studies in adolescents (2 studies) and adults (7 studies) and analyze in categories that comprise the most common neurocognitive domains, displaying only the significant results. Seven areas have been assessed, six for studies with adults and five studies with adolescents. In general, the studies showed negative effects on the use of cannabis in all areas studied. **Conclusion:** The studies focused, in its entirety, the residual effects of the drug, consistently exploited, not occurring studies that assessed the effects of consumption in long term that would be more appropriate for the investigation of chronic use. The results show the need for further studies with adolescents and studies that assess the effects of chronic cannabis use during development.

Keywords: cannabis, neuropsychological tests, neuropsychology, review.

Introduction

Cannabis ranks as one of the most consumed illicit drug in the world (European Monitoring Centre for Drugs and Drug Addiction, 2014; United Nations Office on Drugs and Crime, 2014). Global estimates of cannabis use point between 125 and 227 million users worldwide (European Monitoring Centre for Drugs and Drug Addiction, 2014), only in Europe, 14.6 million young people (15-34 years) have used the drug (United Nations Office on Drugs and Crime, 2014). The prevalence of cannabis use is located around 2.7% to 3.8%, the highest recorded prevalence above the prevalence of opiates, cocaine and ecstasy. Among the dependence of capacity of other substances, it is estimated that cannabis presents a low disability (below five per million). Moreover, cannabis has a low risk for other health problems (United Nations Office on Drugs and Crime, 2014). Despite the high prevalence of cannabis use, not all of your users have problems. The reason the probability set for the development of schizophrenia at any time after consumption, is 6.7 to subjects who had consumed cannabis more than 50 times, observing the dose-dependent effect (Artamendi Fernandez-Fernandez-Hermida, Secades- Villa, & Garcia-Portilla, 2011). The substance of most psychotropic activity of cannabis, delta-9-tetrahydrocannabinol (THC), is involved in a number of changes and symptoms. intoxication are checked, sedation, changes in anxiety levels, neurocognitive and psychotic symptoms. The frequency of these changes depends on the frequency of use, age of onset and genetic characteristics of users (Bhattacharyya et al, 2009; Bhattacharyya et al.,2012; Bhattacharyya & Sendt, 2012; Cousijn, et al., 2012; Di Forti, et al, 2012.; Morrison, et al, 2011.; Moore, et al., 2007; Swendsen, et al., 2010; Yu et al., 2008). Changes in learning are closely associated with the modulation promoted by endocannabinoids receptors, which have a key activity for the synaptic regulation throughout the central nervous system as is the receptor for cannabinoid 1 (CB1) the most abundant receptor in the brain (Heifers & Castillo, 2009; Morrison, et al., 2011; Terry, et al., 2009).

A few decades ago, studies that address the neurocognitive effects of cannabis use have being done, when considered as a whole, show that evidences have been accumulated about the existence of harmful effects on memory, attentiveness, inhibitory control, the executive functions and making decisions. In general, these studies focus on the findings of the effects of acute intoxication, since studies on the long-term effects are inconsistent. Some factors that may contribute to inconsistency are differences in the demographic characteristics of the populations studied, methodological differences in the application of neurocognitive tests, variations in drug use patterns and possible comorbidities (Solowij & Pesa, 2010). The intensity of effects can be related to the early onset, pointing to the existence of an increased vulnerability time window during adolescence (Meier et al, 2012;. Pope, et al., 2003).

The studies on the adverse effects of cannabis have stated that long-term use can lead to dependence , which is characterized by impaired control over the use of cannabis and difficulties to cease use despite damage (Hall & Degenhardt , 2009; Volkow , Baler , Compton, & Weiss , 2014). Since adolescence comprises a period of increased vulnerability to brain development (Malone & Hill , 2010), and due to the scarcity of studies comparing the findings of adulthood to adolescence findings, this study aims to review critically studies evaluating changes in neurocognitive functioning of regular marijuana users, following a contemporary criteria of the studies, discussing the persistence of cognitive deficits and their possible implications, making a comparison of findings in adults and adolescents.

Methods

Research Strategy: scientific publications surveys were conducted through the electronic databases Medline and LILACS during the period 2009 to 2014. The following descriptors were used: cannabis, marijuana, marihuana, neuropsychol*, Cognit *, assessment, executive functioning, memory measures, learning, attention and impulsivity. A trilingual sample studies (Portuguese, Spanish and English) was adopted.

Selection criteria: All studies were included according to the PRISMA protocol. A total of 9 studies was obtained. They included studies that explicitly obeyed the following criteria: ***Inclusion criteria:*** Use of neuropsychological tests involving chronic cannabis users; Inclusion of a group of cannabis users individuals who were not users of other psychoactive substances in abstinence period (control group). ***Exclusion***

Criteria: Diagnostic existence of any disorder following the classification of DSM-IV (except for behavior disorder, disorder of alcohol and nicotine due to the fact the high level of comorbidity); Studies involving participants who had head trauma history, loss of consciousness for significant time and use of psychotropic drugs; Studies that tested the effects of acute cannabis intoxication or derivatives; Studies including neuroimaging techniques.

Data collection: The data collection process was conducted by two reviewers independently, meetings were held for exhibition, meeting the data collected separately and satisfaction evaluation of the selection criteria. Articles were extracted the author's name and year of publication, data subjects (sample size, gender and age group), data of cannabis use (frequency of use, age of onset and duration of abstinence), type of neuropsychological test performed and what the variables measured, exclusion criteria (comorbidities, neurological diseases and other diseases preclusion). They were collected statistically significant data for each measured variable, taking care to check if there was some correction for multiple comparisons in order to avoid bias.

Results

They found 644 studies that have gone through an evaluation primarely by analyzing their titles and abstracts. This selection discarded 635 studies, for non-compliance with the selection criteria. From these studies, 468 did not meet the inclusion criteria, 95 had some of the exclusion criteria and 72 were revisions. Of the publications found, 9 were classified by addressing neurocognitive functioning. These studies were divided according to the age of the participants in adult studies (7 studies) and adolescents (2 studies, considering individuals teenagers under 18 years). Within the above two groups, they were divided in cognitive domains. Data on the study can be seen in Tables 1 and 2.

TABLE 1. Studies evaluating the effects of chronic cannabis use in adults.

studies	Year	Samples	M/F	using standard	Abstinence	Neuropsychological tests	Results
Thames, Arbid, & Sayegh	2014	Sample 158 Users 109 Controls 49	56/102	No report	No report	Trail Making Test , Stroop Test, WAIS-IV, BVMT-R e HVLT-R	Recent users showed significantly worse performance than controls , crossing the cognitive domains of attention and processing speed , working memory and executive functioning . There were no statistically significant differences between old and new users about the neurocognitive performance.
Bosker, et al.	2013	Sample 49 Users 19 Controls 30	49/00	Mean 10.5 cigarettes per day 5 days per week	23 days	CTT e DAT	The performance of users in the CTT and the DAT was changed during the start day compared to the control group. Psychomotor performance in chronic users improved over the three weeks of abstinence, but there was no recovery equivalent to the performance of the control group .
Lisdahl & Price	2012	Sample 58 Users 23 Controls 35	29/29	Mean 1014 cigarettes in life	7 days	CVLT-II, Ruff 2 & 7 e D-KEFS	The increased use of cannabis is associated with psychomotor speed / slow skill sequence , sustained attention less efficiency and higher cognitive inhibition errors. Gender significantly moderated the effect of the use upon the psychomotor speed / skill sequence in which men have a more robust negative relationship .
Gonzalez, et al.	2012	Sample 130 Users 65 Controls 65	75/55	At least 1 last 30 days	24 hours	HVLT-R, IGT, Go-Stop e BART	There was a significant impoverishment of users compared to control in learning and memory . There was no significant difference in impulsive behavior measurements.
Gruber, Sagar, Dahlgren, Racine, & Lukas	2012	Sample 62 Users 34 Controls 28	48/14	At least 5 last 7 days	12 hours	WCST, Stroop Test, Trail Making Test, ROCF, WAIS-R, CVLT e COWAT	Users had poorer performance than the control in various measures of executive functions. These differences between groups were attributed to early onset (before age 16) .
Grant, Chamberlain, Schreiber, & Odlaug	2012	Sample 232 Users 16 Controls 216	163/69	1 or 2 times per week, last 12 months	No report	CANTAB	There was a significant difference in the quality of decisions and executive planning. Inhibition of response , spatial working memory and sustained attention were intact .
Fontes, et al.	2011	Sample 148 Users 104 Controls 44	100/48	Started before 15yo - 1.7 cigarettes per day Started after 15yo - 1.5 cigarettes per day	before 15yo - 4.1 days after 15yo - 3.8 days	WCST, FAB, Stroop Test e WAIS-R	group of individuals who started using cannabis before age 15 showed a significantly poorer performance compared with the controls and with the individuals in the group that began after 15 years in tasks that measure sustained attention , impulse control and executive function.

BART - Balloon Analogue Risk Task; BVMT-R - Brief Visual Memory Test-Revised; CANTAB - Cambridge Neuropsychological Test Automated Battery; COWAT - Controlled Oral Word Association Test; CTT - Critical Tracking Task ; CVLT - California Verbal Learning Task ; CVLT-II - The California Verbal Learning Test-Second Edition; DAT - Divided Attention Task; D-KEFS - Delis-Kaplan Executive Functioning Scale; FAB-Frontal Assessment Battery; GoStop - GoStop Impulsivity Paradigm; HVLT-R - Hopkins Verbal Learning Test – Revised; IGT - Iowa Gambling Task; ROCF - Rey-Osterrieth Complex Figure; WAIS-R - Wechsler Adult Intelligence Scale – Revised; WAIS-IV - Wechsler Adult Intelligence Scale-Fourth Edition; WCST - Wisconsin Card Sorting Test.

TABLE 2. Studies evaluating the effects of chronic cannabis use in adolescents.

studies	Year	Samples	M/F	using standard	Abstinence	Neuropsychological tests	Results
Dougherty et al.[29]	2013	Sample 93 Users 45 Controls 48	66/27	Mean 5.2 days per week	at least 18 hours	CANTAB, IMT, B-P, BSRT, ID/ED, IGT, GoStop, TCIP e SKIP	Of all the cognitive and behavioral domains tested , memory and learning , attention, impulsivity and decision-making had injury associated with the use of cannabis.
Hanson et al.[30]	2010	Sample 40 Users 19 Controls 21	33/7	More than 4 times of marijuana last month	3 weeks	HVLT-R, Ruff 2 & 7 e WAIS-III	Users have shown poor verbal learning, verbal working memory and accuracy of attention compared to the control . There were improvements in users to learning and memory after a week of abstinence, for working memory after 3 weeks. Already attention and processing speed remained impaired in 3 weeks .

B-P - Brown-Peterson Memory Test; BSRT - Buschke Selective Reminding Test; CANTAB - Cambridge Neuropsychological Test Automated Battery; GoStop - GoStop Impulsivity Paradigm; HVLT-R - Hopkins Verbal Learning Test - Revised ; ID/ED - Intradimensional/Extradimensional Shift; IGT - Iowa Gambling Task; IMT - Immediate Memory Task; SKIP - Single Key Impulsivity Paradigm; TCIP - Two Choice Impulsivity Paradigm e WAIS-III - Wechsler Adult Intelligence Scale-Third Edition.

Studies evaluating the effects of chronic cannabis use in adults

The results were subdivided according to the neurocognitive domains, namely: **Decision making**: Grant Chamberlain, Schreiber & Odlaug (2012) used the Cantab instrument, using the Cambridge Gamble Test sub-test (CGT), which assesses the decision and risk taking. It was found that users took less rational decisions than the controls. According to Gonzalez et al. (2012), the poor performance in the test Iowa Gamble Test (IGT) was significantly associated with alcohol use in past 24 months and with a greater number of cannabis dependence symptoms.

Learning and memory: Gonzales et al, (2012) using two of the sub-tests HVLT-R, the Total Recall Immediate and Delayed Recall, managed to find significant differences between the user and control groups. According to the authors, the use of nicotine in the past 24 months was significantly associated with a poor performance in HVLT-R Total Immediate Recall. Lisdahl & Price (2012) showed significant differences between users and controls for CVLT-II test, using the sub-tests iMediate Memory and Delayed Memory and Recognition Memory. The high alcohol consumption in the period of the last year, regardless of cannabis use, works as impoverishment predictor of CVLT II Delayed Memory.

Attention /speed of information processing: According Thames, Arbid, & Sayegh (2014), the controls had performances best users in WAISR Digit Symbol tests and Symbol Search, and impaired performance was associated with the amount of times was the use of cannabis, establishing a negative relationship. Lisdahl & Price (2012) used the Ruff 2 & 7 test to measure the speed components of attention and accuracy of attention, and users had worse performance than controls. Control of gender, IQ, depressive symptoms, body mass index, use of alcohol and other drugs in the last year, in addition to the high consumption of cannabis showed these factors as predictors for a poor rate of sustained attention. In a study by Bosker et al. (2013), the ability to divide attention between two tasks performed simultaneously was tested, the DAT. In this study, the test was undertaken on three occasions: on the first, on the eighth day, sometime in the interval between 14 and 16 and sometime in the interval between 21 and 23 withdrawal. The result for users was better gradually in the second, third and fourth moments from the first day, and the result of this group was lower than the independent control of withdrawal time.

Working memory: Thames, Arbid , & Sayegh (2014) used the Stroop Color Test - Word, letters following sub - test number and the WAIS -R for measuring the verbal working memory, and found significant differences between groups. According Thames, Arbid , & Sayegh (2014), recent users performed worse in tests compared with older users and controls , and demonstrated a negative association between the number of times that cannabis was used with neurocognitive performance.

Executive functioning: Gruber, Silveri, Dahlgren & Yurgelun-Todd (2011) applied the WCST, and the result showed that users committed more errors, set of losses and total losses than controls. Early onset users also showed more damage than the controls with respect to complete categories, perseverant errors, total errors, a set of losses and total losses. Fontes et al. (2011) applied the same test and got similar results among early-onset users and control for persevering errors and completed categories. Regarding the FAB test that evaluates factors similar to those evaluated by the WCST, Fontes et al. (2011) found that early onset group had significantly poor performance compared to the early and late groups control. Regarding the Stroop test, Gruber, Sagar, Dahlgren, Racine, & Lukas (2012) found a significant difference between early-onset and user control for read errors of commission of words, accuracy and errors of commission. Thames, Arbid, & Sayegh (2014) found through the Stroop test the user group, whether recent or old users, has performed worse than the control. Sources et al. (2011) also applied the Stroop test and obtained results similar to those obtained by Gruber et al. when compared early-onset users with controls.

Thames, Arbid, & Sayegh (2014) found that the old and new users had significantly worse performance than controls in relation to test scores Trail Making Part B. The amount of times that cannabis was used was negatively associated with all the measures of this cognitive domain. The sub-pattern Cantab instrument, One-Touch Stocking of Cambridge, was used by Grant, Chamberlain, Schreiber, & Odlaug (2012) and as a result, showed that users required a significantly greater number of attempts that controls to obtain correct answers. The COWAT test was undertaken by Gruber et al. in order to verify the ability to produce words under strict conditions. This test showed that early-onset users generated significantly fewer words than early users later. Lisdahl & Price (2012) used the subtests Trail Making Test Ruff 2&7 - Part B, Verbal Fluency, Fluency Design and Colour Word Interference Test D-KEFS for the measurement of executive functioning. In this study, users had worse performance than the control group for all sub-tests, showing a loss of executive functioning. With gender control, IQ, symptoms of depression, body mass index, use of alcohol and other drugs in the last year and the high consumption of cannabis, it was found that were predictors of poor performances sequencing ability, psychomotor speed and accuracy cognitive inhibition. The accuracy of Design Fluency was the only significant result to establish a relationship between abstinence and cognitive functioning.

Performance engine: In your study, Bosker et al. (2013) used the CTT test to measure the ability to control an error signal shown in a compensatory track test of the first order. In this test, users have played better after the eighth day after the interval between 14 and 16 and after the interval between 21 and 23 abstinence in relation to the start day. The results of users, compared to the control, were lower at all times.

Studies evaluating the effects of chronic cannabis use in adolescents

The results were subdivided according to the neurocognitive domains, namely:

Decision-making: In their study Dougherty et al. (2013) used two tests for the measurement of the decision and risk-taking, the ID / ED and IGT. Comparing the user and control groups, Dougherty et al. achieved a significantly higher decision making error rate than controls for both tests.

Learning and Memory: Dougherty et al. (2013) used the B-P tests (Total Recall) to assess short-term memory and BSRT test to assess learning and transfer to long-term memory. The results show that users had significantly poorer performance than controls. The number of cigarettes smoked in the last year and the number of alcoholic drinks consumed in the last year were significantly related to the performance of B-P Total Recall test.

Attention / Speed of Information Processing: Dougherty et al.

(2013) used to measure sustained attention two instruments, the Cantab and IMT. For both tests, the performance of users was significantly poorer than the controls. Hanson et al. (2010) undertook Ruff 2 & 7 test to verify the visual attention and information processing speed. In this test, users were significantly less accurate than the controls in the first and third sessions and in the second session there was a marginal result.

Working memory: The study of Hanson et al. (2010) applies the sequencing sub-test WAIS-III of the letter-number to measure verbal working memory in three sessions. In this study users performed worse than the controls in the first and second session, however, there was a significant difference only for the second session. Group relations were found with regard to the variables age and socioeconomic status with the WAIS -III test.

Impulsivity: Dougherty et al. (2013) undertook their study in four tests to measure impulsive behavior, they were : IMT, GoStop, TCIP and SKIP. In the four tests, the results showed a significant difference between groups, pointing to the group of users such as greater impulsivity compared to the control. The poor results of the ICC test were associated with the high number of cigarettes smoked in the last year and consumed alcoholic drinks in the last year.

Discussion

None of the studies included in this review aimed to assess the effects of chronic cannabis use after a major discontinuity of the drug, which prevented the possibility of addressing the issue excluding the residual effects of cannabis. A study with the aim of measuring the half-life of some toxic components of cannabis in the blood showed that THC concentrations measured remain in the bloodstream even after seven days of abstinence (Karschner, et al., 2009), while most of the studies included in this review reports much lower withdrawal periods this. Therefore, the absence of studies that address the long-term effects of cannabis use limited spectrum of damages that could be assessed.

Among the various neurocognitive domains are known residual effects of cannabis use for attention, decision-making, impulsivity, working memory, verbal fluency and executive functions. The term residual effects may extend for several days (for 20 days), but in most cases, these effects occur at an initial period in relation to discontinue the use and display of reduced intensity effects. These effects are generally more intense in users who have a pattern of heavy use and are consumers for a longer time (Crean, Crane, & Mason, 2011). However, the studies included in the review confirmed many neurocognitive changes attributed to residual effects in the areas already mentioned, contributing to increase the list of neurocognitive damage in the area of psychomotor performance (Bosker, et al., 2013).

In review, the problem of cannabis use by drivers was treated, and illustrated the need for more studies on the effects of cannabis use being illustrated the need for more studies on the effects of cannabis on psychomotor performance. This study comes to present as an alternative a period of rest prior to the direction between 3 and 4 hours after the use of cannabis to avoid the effects of acute drug intoxication (Armentano, 2013).

Confronting these arguments with the results obtained by Bosker et al. (2013), it is evident that the harmful effects of chronic cannabis use occur in a period that goes beyond the immediate hours after using the drug. The Bosker study et al. followed chronic cannabis users for a 23-day withdrawal period, with psychomotor losses throughout the study period, suggesting the harmful effects extend beyond the period of residual effect of the drug, but without evaluating the long-term effects.

For better control of confounding variables, studies should include tools for measuring symptoms of withdrawal, for example, the symptoms present in the second stage of addiction, called the withdrawal stage. The discontinuation of cannabis use is associated with the emergence of anxiety symptoms (Bonn-Miller & Moos, 2009) and depression (Graaf, et al., 2010) withdrawal phase characteristics. The occurrence of these changes is commonly associated with neurocognitive impairment, notably on memory and attention (Beblo, Sinnamon, & Baune, 2011). Of the included studies (9 studies), only 4 states included instruments for measuring depression (Gonzalez, et al., 2012; Gruber, Sagar, Dahlgren, Racine, & Lukas, 2012; Hanson, et al., 2010; Lisdahl & Price, 2012) and 3 states included instruments for measuring anxiety (Gonzalez, et al., 2012; Gruber, Sagar, Dahlgren, Racine, & Lukas, 2012; Hanson, et al., 2010). Knowledge about the neurocognitive effects of major depression disorder are not yet fully elucidated, requiring tightening to control these symptoms in neurocognitive studies (Mcclintock, Husain, Greer, & Cullum, 2010). On the other hand, are well-known effects of anxiety on cognitive domains such as attention, working memory and executive functions on the model of the Attentional Control Theory (Ansari & Deraskshan, 2011).

With respect to higher rates of mood changes in cannabis users, the literature shows a modest excess cases of major depression in cannabis users compared to nonusers. In relation to the fact that the age of onset of cannabis use have an effect on an increase in depressive phases, there was no statistical difference between early adopters (began use in adolescence) and late users (began use in adulthood) in with respect to their depressive phases can not be confirmed this hypothesis (Fairman & Anthony, 2012). On the other hand, several studies involving the use of cannabis and cannabis use disorder with anxiety (Kedzior & Laeber, 2014). The results related to inhibitory control may also suffer influence of withdrawal symptoms as drug addiction comprises impulsive and compulsive effects. Characteristically the third phase of addiction, called the concern stage /anticipation, involves changes in complex neuronal circuits, including the cingulate gyrus, cortex dorsolateral prefrontal cortex and frontal lower, regions related to disturbed inhibitory control (Koob & Volkow, 2010).

A study of changes in the microstructure of white matter showed that there was an association between the fraction anisotropy (FA), general diffusivity and trace the presence of impulsivity. These data were calculated for 6 locations including the front bilateral regions. The results of this study showed a positive correlation between impulsivity and left frontal FA values and an inverse correlation between impulsivity with the trait. According to this study, the early use may be related to reduced FA and high diffusivity that contribute to the difficulty of use and discontinued use of cannabis (Gruber, Silveri, Dahlgren, & Yurgelun-Todd, 2011). However, the measuring instrument used by that study is a self-report questionnaire of impulsivity (Barratt Impulsivity Scale - BIS) and, according to the literature, the result of this type of instrument may not correlate with the findings of neurocognitive tests. Different methodologies measured different dimensions of impulsivity (Wu, et al., 2009). In the studies included in this review, the use of self-report questionnaires to impulsiveness was not prevalent practice, only 3 studies showed the use of BIS (Dougherty, et al., 2013; Gonzalez, et al., 2012; Gruber, Sagar, Dahlgren, Racine, & Lukas, 2012). As expected there were no correlations between BIS and neurocognitive results for impulsiveness.

The results found in the studies included in this review corroborate studies on white matter of the brain of adolescents. In one study it was observed changes in the white matter of adolescents with high FA in the right occipital regions, the internal capsule and the upper longitudinal fasciculus. With the average diffusivity, the increase was more evident in the right occipital lobe, while the left inferior longitudinal fasciculus showed low average diffusivity (Bava, Jacobus, Mahmood, Yang, & Tapert, 2009). In another study on quality of white matter in adolescents, it was found that FA in the temporal areas are related to depletion of attention, working memory and processing speed. There was also a positive association between FA in the occipital region, working memory and visuomotor sequencing complex, on the other hand, there was a negative association between FA in previous regions and verbal memory performance (Bava, Jacobus, Mahmood, Yang, & Tapert, 2010). Both studies are early and do not have proper control for variable alcohol consumption, but provide benefits to show a loss in fronto-parietal circuit and suggest neuroadaptive mechanism complicated by the use of substances.

Neurocognitive damage caused by chronic cannabis use in adults have been widely studied in recent decades, however, knowledge about such damage in adolescents is still incipient. Other insights into the harmful effects of cannabis in adults have been fomented in these studies, the subjects of the studies are grouped according to the time of onset of drug use, namely in early onset period (before age 17) and period late start. These studies have helped to determine the existence of a time window of greater vulnerability of the brain to the effects of cannabis throughout its development. Among the changes commonly seen in adolescents, are changes in attention, verbal learning and memory, sequencing capacity, psychomotor speed, executive functions and working memory (Jacobus, Bava, Cohen-Zion, Mahmood, & Taperta, 2009). Our analysis has confirmed the greatest number of studies involving adults (7 items) compared to studies involving adolescents (2 studies). It was also verified grouping subjects according to the start time of the drug in early-onset and late-onset groups groups (2 studies). In these studies, it was found that early onset users performed worse than the control and late-onset users in the domain executive functioning, which can be justified by a higher risk for neurocognitive damage caused by cannabis in the early periods of brain development (Fontes, et al., 2011; Gruber, Sagar, Dahlgren, Racine, & Lukas, 2012). Overall, changes could be seen in all of the above neurocognitive domains for adults, while for teenagers changes were observed in 5 of the above areas, there is no data to psychomotor performance in adolescents.

A new agenda for research on the effects of cannabis has been proposed. In this new approach, based on observation of dose-related cognitive impairments in attention, working memory, verbal learning and memory functions, the goal is to check factors that begin to interfere with adherence to treatment (Sofuoglu, Sugarman, & Carroll, 2010). The longitudinal studies aimed at monitoring of possible cognitive impairment in users that predispose them to discontinue use of cannabis seems a promising avenue for future studies with chronic users.

In conclusion, this review has assembled a set of studies that have been effective in measuring only the changes resulting from the residual effects of cannabis use, as well explored, while the long-term effects that characterize the cumulative damage of the drug in the body were not achieved. A large number of confounding variables still occurs in these studies and if necessary make a standardization effort to avoid biases and the establishment of more stringent criteria for the allocation of the sample. The studies showed changes in several cognitive domains correlated with several demographic variables and can be checked more severe damage due to the early onset of drug use. The authors emphasize the need for further studies to investigate the effects of chronic cannabis use in adolescents and future systematization advance in order to determine the effects of cannabis on the neurocognitive functioning throughout development.

References

Ansari, T., & Deraskshan, N. (2011). The neural correlates of impaired inhibitory control in anxiety. Neuropsychologia: An

International Journal in Behavioral and Cognitive Neuroscience, 49, 1146-53. doi: 10.1016/j.neuropsychologia.2011.01.019. Epub 2011 jan15.

Armentano, P. (2013). Cannabis and psychomotor performance: a rational review of the evidence and implications for public policy. Drug Testing and Analysis, 5, 52-6. doi: 10.1002/dta.1404.

Bava, S., Frank, L. R., Mcqueeny, T., Schweinsburg, B., Schweinsburg, A. D., & Tapert, S. F. (2009). Altered white matter microstructure in adolescent substance users. Psychiatry Research: Neuroimaging, 173(3), 228-47. doi: 10.1016/j.pscychresns.2009.04.005. Epub 2009 Aug 20.

Bava, S., Jacobus, J., Mahmood, O., Yang, T. T., & Tapert, S. F. (2009). Functional consequence of marijuana use in adolescents. Pharmacology. Biochemistry and Behavior, 92(4), 559-65. doi: 10.1016/j.pbb.2009.04.001.

Bava, S., Jacobus, J., Mahmood, O., Yang, T., & Tapert, S. (2010). Neurocognitive correlates of white matter quality in adolescent substance user. Brain and Cognition, 72(3), 347-54. doi: 10.1016/j.bandc.2009.10.012. Epub 2009 Nov 22.

Beblo, T., Sinnamon, G., & Baune, B. (2011). Specifying the neuropsychology of affective disorders: clinical, demographic and neurobiological factors. Neuropsychology Review, 1-23. doi: 1007/s11065-011-9171-0. Epub 2011 Jun 10.

Bhattacharyya, S., & Sendt, K. (2012). Neuroimaging evidence for cannabinoid modulation of cognition adn affect in man. Frontiers in Behavioral Neuroscience, 6(22), 1-4. doi: 10.3389/fnbeh.2012.00022.

Bhattacharyya, S., Crippa, J., Allen, P., Martin-Santos, R., Borgwardt, S., & al, F.-P. e. (2012). Induction of psychosis by 9-tetrahydrocannabinol reflects modulation of prefrontal and striatal function during attentional salience processing. Archives of General Psychiatry, 69(1), 27-36. doi: 10.1001/archgenpsychiatry.2011.161.

Bhattacharyya, S., Fusar-Poli, P., Borgwardt, S., Martin-Santos, R., Nosarti, C., & Carrol, C. e. (2009). Modulation of mediotemporal and ventrostriatal function in humans by delta-9-tetrahydrocannabinol. Archives of General Psychiatry, 66(4), 442-51. doi: 10.1001/archgenpsychiatry.2009.17.

Bhattacharyya, S., Wiers, R., Ridderinkhof, K., Brink, W., Valtman, D., & Goudriaan, A. (2012). Grey matter alterations associated with cannabis use: results of a VBM study cannabis users and healthy controls. NeuroImage, 59, 3845-51. doi: 10.1016/j.neuroimage.2011.09.046. Epub 2011 Sep 29.

Bonn-Miller, M., & Moos, R. (2009). Marijuana discontinuation, anxiety symptoms, and relapse to marijuana. Addictive Behaviors, 34, 782-85. doi: 10.1016/j.addbeh.2009.04.009.

Bosker, W., Karschner, E., Lee, D., Goodwin, R., Hirvonen, J., & Innis, R. e. (2013). Psychomotor function in chronic daily cannbis smokers during sustained abstinence. Plos One: A Peer-Reviewed, Open Access Journal, 8(1), 1-7. doi: http://dx.doi.org/10.1371/journal.pone.0053127.

Cousijn, J., Wiers, R. W., Ridderinkhof, K., Brink, W., Veltman, D., & Goudriaan, A. (2012). Grey matter alterations associated with cannabis use: results of a VBM study in heavy cannabis users healthy controls. NeuroImage, 59, 3845-51. doi: 10.1016/j.neuroimage.2011.09.046. Epub 2011 Sep 29.

Crean, R., Crane, N., & Mason, B. (2011). An evidence based review of acute and long-term effcets of cannabis use on executive cognitive functions. Journal of Addiction Medicine, 5(1), 1-8. doi: 10.1097/ADM.0b013e31820c23fa.

Di Forti, M., Ivegbe, C., Sallis, H., Kolliakou, A., Falcone, M., & Paparelli, A. e. (2012). Confirmation that the aktl (rs2494732) genotype influences the risk of psychosis in cannabis users. Biological Psychiatry, 72, 811-16. doi: 10.1016/j.biopsych.2012.06.020. Epub 2012 Jul 24.

Dougherty, D., Mathias, C., Dawes, M., Furr, R., Charles, N., & Liguori, A. e. (2013). Impulsivity, atttention, memory, and decision-making among adolescent marijuana users. Psychopharmacology, 226(2), 307-19. doi: 10.1007/s00213-012-2908-5.

Fairman, B., & Anthony, J. (2012). Are early-onset cannabis smokers at an increased risk of depression spells? Journal of Affective Disorders, 138(1-2), 54-62. doi: 10.1016/j.jad.2011.12.031.

Fernandez-Artamendi, S., Fernandez-Hermida, J., Secades-Villa, R., & Garcia-Portilla, P. (2011). Cannabis y salud mental. Actas Españolas de Psiquiatria, 39(3), 180-190. Taken from: http://www.unioviedo.es/psiquiatria/publicaciones/documentos/2011/2011_Fernandez-Artamendi_Cannabis-SPA.pdf.

Fontes, M., Bolla, K., Cunha, P., Almeida, P., Jungerman, F., & al, L. R. (2011). Cannabis use before age 15 and subsequent executive functioning. The British Journal of Psychiatry: The Journal of Mental Science, 198, 442-47. doi: 10.1192/bjp.bp.110.077479.

Gonzalez, R., Schuster, R., Mermelstein, R., Vassileva, J., Martin, E., & Diviak, K. (2012). Performance of young adult cannabis users on neurocognitive mesaures of uimpulsive behavior and their rekationship to symptoms of cannabis use disorders. Journal of Clinical and Experimental Neuropsychology, 34(9), 962-76. doi: 10.1080/13803395.2012.703642. Epub 2012 Aug 10.

Graaf, R., Radovanovic, M., Laar, M., Fairman, B., Degenhardt, L., & Aguilar-Gaxiola, S. e. (2010). Early cannabis use and estimated risk of later onset of depression spells: epidemiologic evidence from the population-based world health organization world mental health survey initiative. American Journal of Epidemiology, 172(2), 149-59. doi: 10.1093/aje/kwq096. Epub 2010 Jun 9.

Grant, J., Chamberlain, S., Schreiber, L., & Odlaug, B. (2012). Neuropsychological deficits associated with cannabis use in young adults. Drug and Alcohol Dependence, 121((1-2)), 159-62. doi: 10.1016/j.drugalcdep.2011.08.015.

Gruber, S., Sagar, K., Dahlgren, M., Racine, M., & Lukas, S. (2012). Age of onset marijuana use and executive function. Psychology of Addictive Behaviors: journal of the Society of Psychologists in Addictive Behaviors, 26(3), 496-506. doi: 10.1037/a0026269.

Gruber, S., Silveri, M. M., Dahlgren, M. K., & Yurgelun-Todd, D. (2011). Why so impulsive? White matter alterations are associated with impulsivity in chronic marijuana smokers. Experimental and Clinical Psychopharmacology, 19(3), 231-42. doi: 10.1037/a0023034.

Hall, W., & Degenhardt, L. (2009). Adverse health effects of non-medical cannabis use. The Lancet, 374, 1383-91. doi: 10.1016/S0140-6736(09)61037-0.

Hanson, A., Winward, J., Schweinsburg, A., Medina, K., Bown, S., & Tapert, S. (2010). Longitudinal study of cognition among adolescent marijuana users overthree weeks of abstinence. Addictive Behaviors, 35(11), 970-76. doi: 10.1016/j. addbeh.2010.06.012.

Heifers, B., & Castillo, P. (2009). Endocannabionoid signaling and long-term synaptic plasticity. Annual Review of Physiology, 71, 283-306. doi: 10.1146/annurev.physiol.010908.163149.

Jacobus, J., Bava, S., Cohen-Zion, M., Mahmood, O., & Taperta, S. F. (2009). Functional consequences of marijuana use in adolescents. Pharmacology Biochemistry and Behavior, 92(4), 559-65. doi: 10.1016/j.pbb.2009.04.001. Epub 2009 Apr 5.

Karschner, E., Schwilke, E., Lowe, R., Darwin, W., Herning, R., & Cadet, J. e. (2009). Implications of plasma 59-tetrahydrocannabinol, 11-hydroxy-thc, and 11-nor-9-carboxy-thc concentrations in chronic cannabis smokers. Journal of Analytical Toxicology, 33(8), 469-77. Taken from: http://jat.oxfordjournals.org/content/33/8/469.long.

Kedzior, K., & Laeber, L. (2014). A positive association between anxiety disorders and cannabis use or cannabis use disorders in the general population - a meta-analysis of 31 studies. BMC Psychiatry, 14(136), 01-22. doi: 10.1186/1471-244X-14-136.

Koob, G., & Volkow, N. (2010). Neurocircuitry of addiction. Neuropsychopharmacology, 35, 217-38. doi: 10.1038/npp.2009.110.

Lisdahl, K., & Price, J. (2012). Increased marijuana and gender predict poorer cognitive functioning in adolescents and emerging adults. Journal of the International Neuropsychological Society: JINS, 18(4), 678-88. doi: 10.1017/S1355617712000276.

Malone, D., & Hill, M. R. (2010). Adolescent cannabis use and psychosis: epidemiology and neurodevelopmental models. British Journal of Pharmacology, 160, 511-22. doi: 10.1111/j.1476-5381.2010.00721.x.

Mcclintock, S., Husain, M., Greer, T., & Cullum, C. (2010). Associations between depression severity and neurocognitive function in major depressive disorder: a review and synthesis. Neuropsychology, 24(1), 9-34. doi: 10.1037/a0017336.

Meier, M., Caspi, A., Ambler, A., Harrington, H., Houts, R., & Keefe, R. e. (2012). Persistent cannabis users show neuropsychological decline from childhood to midlife. Proceedings of the National Academy of Sciences of the United States of America, 27, E2657-E2664. doi: 10.1073/pnas.1206820109. Epub 2012 Aug 27.

Moore, T., Zammit, S., Lingford-Hughes, A., Barnes, T., Jones, P., & Burke, M. e. (2007). Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. The Lancet, 319-328. doi: http://dx.doi.org/10.1016/S0140-6736(07)61162-3.

Morrison, P., & Murray, R. (2009). From real-world events to psychosis: the emerging neuropharmacology of delusions. Schizophrenia Bulletin, 35(4), 668-74. doi: 10.1093/schbul/sbp049.

Morrison, P., Nottage, J., Stone, J., Bhattacharyya, S., Tunstall, N., & Brenneisen, R. e. (2011). Disruption of frontal theta coherence by d9-tetrahydrocannabinol is associated with positive psycothic symptoms. Neuropsychopharmacology, 827-836. doi: 10.1038/npp.2010.222.

EMCDDA - European Monitoring Centre for Drugs and Drug Addiction . (2014) . European Drug Report . Luxembourg: the EU Publications Office. doi: 10.2810/3792.

Pope, H., Gruber, A., Hudson, J., Cohane, G., Huestis, M., & Yurgelun-Todd, D. (2003). Early-onset cannabis use and cognitive deficits:whats is the nature of the association? Drug and Alcohol Dependence, 69, 303-10. doi: 10.1016/S0376-8716(02)00334-4.

Sofuoglu, M., Sugarman, D. E., & Carroll, K. M. (2010). Congnitive function as an emerging treatment target for marijuana addiction. Experimental and Clinical Psychopharmacology, 18(2), 109. doi: 10.1037/a0019295.

Solowij, N., & Pesa, N. (2010). Cognitive abnormalities in cannabis use . Journal of Psychiatry, 32, 31-40. doi: http://dx.doi.org/10.1590/S1516-44462010000500006.

Swendsen, J., Conway, K., Degenhardt, L., Glantz, M., Jin, R., & Merikangas, K. (2010). Mental disorders as risk factors for substance use, abuse and dependence: results form the 10-year follow-up of the national comorbidity survey. Addiction, 105(6), 1117-28. doi: 10.1111/j.1360-0443.2010.02902.x.

Terry, G., Liow, J., Zoghbi, S., Hirvonen, J., Farris, A., & Lerner, A. e. (2009). Quantitation of cannabinoid CB1 receptors in healty human brain using positron emission tomography and an inverse agonist radioligand. NeuroImage, 48(2), 362-70. doi: 10.1016/j.neuroimage.2009.06.059. Epub 2009 Jun 30.

Thames, A., Arbid, N., & Sayegh, P. (2014). Cannabis use and neurocognitive functioning ing a non-clinical sample of users. Addictive Behaviors, 39(5), 994-99. doi: 10.1016/j.addbeh.2014.01.019.

UNODC - United Nations Office on Drugs and Crime. (2014). World Drug Report 2014. Viena. Taken from: https://www.unodc.org/documents/wdr2014/World_Drug_Report_2014_web.pd.

Volkow, N., Baler, R., Compton, W., & Weiss, S. A. (2014). Adverse health effects of marijuana use. The New England Journal of Medicine, 370(23), 2219-227. doi: 10.1056/NEJMc1407928.

Wu, C., Liao, S., Lin, K., Tseng, M., Wu, E., & S.K, L. (2009). Multidimensional assessments of impulsivity in subjects with history of suicidal attempts. Comprehensive Psychiatry, 50(4), 315-21. doi: 10.1016/j.comppsych.2008.09.006. Epub 2008 Nov 21.

Yu, M., Solowij, N., Respondek, C., Whittle, S., Fornito, A., Pantelis, C., & Lubman, D. (2008). Regional brain abnormalities associated with long-term heavy cannabis use. Archives of General Psychiatry, 65(6), 1-8. doi: 10.1001/archpsyc.65.6.694.

How to cite this Article: Lima, M.C.M. & Marcelo Moraes Valença, M.M. (2015). Neuropsychological Assessment and Cannabis Use: A Systematic Review**.** *International Journal of Psychology and Neuroscience*, *2* (2), 133-152.
Received: 04/06/2016; **Revised**: 10/07/2016; **Accepted:** 20/08/2016; **Published online:** 31/08/2016**;** **ISBN 2183-5829**