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Short communication

Neuropsychological deficits associated with cannabis use in young adults[☆]

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ABSTRACT

Background: Cannabis is the most widely used illicit substance and has been associated with cognitive impairment. It is unclear whether such impairment can occur in the absence of potential confounding influences of co-morbid axis-I disorders and use of other illicit substances.
Method: Young adult volunteers (18–29 years) were recruited from the general community on the basis of having no axis-I disorders or history of illicit substance use other than cannabis use. Subjects were then grouped according to presence or absence of cannabis use (>1 time/week over past 12 months). Cognition was compared between groups using selected paradigms from the CANTAB.
Results: Cannabis users (N = 16) and controls (N = 214) did not differ significantly on salient demographic characteristics. Compared to controls, cannabis users showed significant impairments on quality of decision-making (Cambridge Gamble task), and executive planning (One Touch Stockings of Cambridge task). Response inhibition, spatial working memory, and sustained attention were intact.
Conclusions: This study identified cognitive deficits in cannabis users even in the absence of axis-I disorders and a history of using other illicit drugs. Future work should use longitudinal designs to track whether these deficits predate cannabis use or are due to its consumption.

1. Introduction

Cannabis is the most widely used illicit substance (Substance Abuse and Mental Health Services Administration, 2010), and has been associated with poor academic achievement, unemployment, legal problems, and heightened risk of developing a psychotic disorder (Hall and Degenhardt, 2009). Despite considerable research, there are conflicting opinions regarding cannabis use and its association with cognitive dysfunction (Iversen, 2003; Hart et al., 2010).

There is broad consensus that cannabis intoxication often results in short-term dysfunction across a range of cognitive domains in healthy volunteers (Makela et al., 2006; Almeida et al., 2008; Hunault et al., 2009), though not all studies have been consistent in this regard (Heishman et al., 1997; Almeida et al., 2008; Hart et al., 2010). The extent to which chronic cannabis use is also associated with cognitive impairments remains less clear. Early cross-sectional studies reported associations between heavy chronic cannabis use and impaired verbal fluency and word recognition memory; some studies reported that these deficits persisted for just a few days following cessation of cannabis intake (Pope et al., 2001), while others suggested that these deficits persisted for a month or longer (Bolla et al., 2002; Pope et al., 2003). Research using various neuropsychological tests has confirmed that chronic cannabis use can be associated with dysfunction across a range of functions including aspects of memory, attention, inhibitory control, and executive planning (Almeida et al., 2008; Solowij and Pesa, 2010).

Limitations afflicting this extant literature, which may have contributed to the findings, include: use of different cognitive paradigms, some of which were not well-validated; recruitment of cannabis users with potentially confounding axis-I disorders; and the recruitment of cannabis users with a history of using other illicit drugs (Hart et al., 2010; Solowij and Pesa, 2010).

We recruited a cohort of young adults without potential confounders and investigated cognitive function in cannabis users using a range of well-validated translational paradigms (Owen et al., 1990; Coull et al., 1995; Rogers et al., 1999; Aron et al., 2003). Potential advantages of these paradigms include their validation in animal and human studies involving focal lesions and neuroimaging (Chamberlain and Sahakian, 2007; Robbins and Arnsten, 2009; Clark, 2010; Chamberlain et al., 2011). We hypothesized that cannabis users would exhibit deficits across a range of cognitive domains, consistent with the notion that cannabis use in young people is associated with deleterious effects on cortico-sub-cortical circuitry.

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Table 1
Comparison of demographic and clinical characteristics between cannabis users and controls.

Variables	Cannabis users (N = 16)	Controls (N = 214)	F/chi-s	p
Age (years), mean ± SD	21.75 ± 2.91	21.19 ± 3.21	0.453	0.501
Gender, male, N (%)	10 (62.5%)	153 (72.2%)	0.583	0.445
Annual income, USD, mean ± SD	17,206 ± 19,623	15,351 ± 16,319	0.187	0.666
Educational achievement, N (%)				
High School or below	4 (25.0%)	19 (9%)	2.514[a]	0.285
College	11 (68.8%)	170 (80.2%)		
Beyond College	1 (6.3%)	23 (10.8%)		
Nicotine users, N (%)	5 (31.3%)	36 (17%)	1.245[a]	0.265
Current alcohol use, N (%)	14 (87.5%)	141 (66.9%)	2.257[a]	0.133
Substance use disorder in first-degree family member, N (%)	5 (31.3%)	50 (23.4%)	0.168[a]	0.682

Subjects with current axis I disorders, including substance use disorders (other than cannabis use) were excluded from the study.
[a] Yates' corrected.

2. Method

2.1. Subjects

Participants comprised non-treatment-seeking adults aged 18–29 years who were recruited via media advertisements for a study examining impulsivity. Exclusion criteria included presence of axis-I disorders (besides cannabis dependence/abuse), history of any non-cannabis illicit drug use, and inability to understand/undertake the procedures and provide written consent.

The study procedures were carried out in accordance with the Declaration of Helsinki. The Institutional Review Board of the University of Minnesota approved the study and the consent. After all procedures were explained, subjects provided voluntary written informed consent.

2.2. Assessments

Raters assessed each subject using the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998) and a semi-structured instrument examining a range of behaviors (e.g., nicotine, alcohol and illicit substance use). Subjects were asked about frequency of cannabis use during the last 12 months (average frequency of use per typical week), and about any lifetime use of cannabis (yes/no).

Cognitive functions were assessed using well-validated computerized paradigms from the Cambridge Neuropsychological Test Automated Battery (CANTAB). We did not ask cannabis users to abstain from smoking or change their habits prior to participation, as we wished to evaluate cognition under normal circumstances in day-to-day life. Domains of interest were selected on the basis of their dissociable nature and the existing literature on effects of cannabis on cognition in healthy volunteers (tests comprised: Cambridge Gamble, One Touch Stockings of Cambridge, Stop-Signal, Spatial Working Memory, and Rapid Visual Information Processing tasks) (www.camcog.com provides citations to full task descriptions and previous validations).

2.3. Data analysis

All subjects meeting inclusion criteria were grouped based on whether they used cannabis one or more times per week during the last 12 months ("cannabis users") or had no use over the past 12 months ("controls"). The two groups were recruited from the same background population, using identical recruitment and screening, in order to avoid differential recruitment bias and to minimize confounds.

Group demographic and clinical characteristics, along with singular-type cognitive outcome variables where compared using t-tests and chi-squared tests. For the Cambridge Gamble and One-Touch Stockings of Cambridge tasks, results were analyzed using analysis of variance (ANOVA) using task-appropriate within-subject factors and between-subject factor of group. This being an exploratory study using selected tests tapping orthogonal domains, significance was defined as $p < 0.05$ uncorrected.

3. Results

The group sizes were $N = 16$ cannabis users and $N = 214$ controls. None of the controls reported any lifetime cannabis use. Groups did not differ significantly on demographic characteristics (Table 1).

For those reporting cannabis use within the past 12 months, the mean frequency of use was 3.1 ± 2.2 times per week (range 1–7). Three users met criteria for cannabis dependence and two for cannabis abuse. None of the cannabis users and controls reported past substance use disorder otherwise.

On the Cambridge Gamble task (Fig. 1), there was a main effect of group on the proportion of rational decisions made ($F = 6.139$, $p = 0.014$), due to cannabis users making significantly fewer rational decisions overall. There was no significant group by level interaction ($F = 0.409$, $p = 0.747$) or group by condition interaction ($F = 2.314$, $p = 0.130$). There was a significant main effect of level on the proportion of rational decisions ($F = 9.659$, $p < 0.001$), and of condition (ascend/descend, $F = 17.616$, $p < 0.001$), but there was no significant interaction ($F = 1.623$, $p = 0.183$). There was no significant effect of group on the proportion of points gambled ($F = 0.839$, $p = 0.361$), a significant group by level interaction ($F = 1.495$, $p = 0.215$), or group by condition interaction ($F = 0.142$, $p = 0.706$). There was a significant effect of level ($F = 145.45$, $p < 0.001$) and a significant effect of condition ($F = 105.78$, $p < 0.001$), but no significant interaction between the two ($F = 1.807$, $p = 0.145$).

On the One-Touch Stockings of Cambridge task (Fig. 1), there was a main effect of group on choices to correct solution ($F = 6.711$, $p = 0.010$) and a significant group by difficulty interaction ($F = 3.332$, $p = 0.005$). This finding was attributable to cannabis users requiring more attempts to obtain correct solutions, especially at the harder levels of difficulty (3–6). There was a significant effect of difficulty overall ($F = 62.092$, $p < 0.001$). There was no main effect of group on latency to correct solution ($F = 0.782$, $p = 0.378$) or a significant group by difficulty interaction ($F = 0.915$, $p = 0.470$). There was a main effect of difficulty ($F = 78.355$, $p < 0.001$).

Groups did not differ significantly on Stop-Signal Reaction Time (SSRT) (171.25 ± 66.92, 170.39 ± 43.45 ms; $t = 0.074$, $p = 0.941$), on SSRT reaction times for go trials (407.16 ± 91.39, 439.10 ± 124.25 ms; $t = 1.007$, $p = 0.315$), in terms of total errors (19.75 ± 18.95, 14.07 ± 13.32; $t = 1.591$, $p = 0.113$), or strategy scores on the Spatial Working Memory task (31.00 ± 6.49, 28.54 ± 6.09; $t = 1.550$, $p = 0.123$), or on target detection or false alarms on the Rapid Visual Information Processing task (0.743 ± 0.169, 0.743 ± 0.173; $t = 0.002$, $p = 0.998$; 0.011 ± 0.022, 0.007 ± 0.015; $t = 0.872$, $p = 0.384$, respectively).

4. Discussion

This is the first study to explore associations between cannabis use and CANTAB cognitive performance in a sample of young people free from axis-I disorders (besides cannabis dependence/abuse) and free from a history of other illicit substance use. Though cannabis use has been associated with deficits across an array of domains in the literature, some of these findings may have been attributable to these confounds. The key finding was that cannabis use was associated with elevated risky decision-making on the

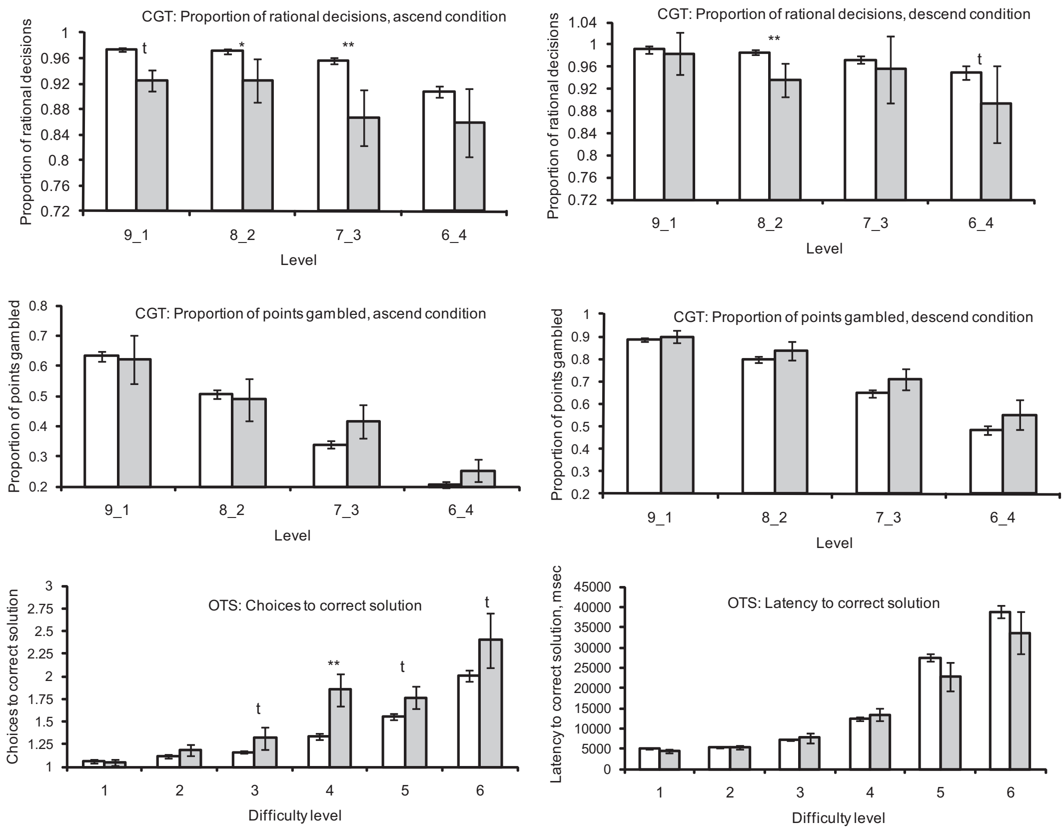

Fig. 1. Performance on the Cambridge Gamble task (CGT) and One-Touch Stockings of Cambridge Task (OTS). Shown in white bars, mean ± SD controls; in grey, mean ± SD cannabis users. Group differences: *t* = trend ($0.05 < p < 0.10$), *$p < 0.05$, **$p < 0.01$.

Cambridge Gamble task and impaired executive planning on the Stockings of Cambridge task. These significant deficits occurred alongside relative sparing on measures of general motor performance, sustained attention, spatial working memory, and response inhibition. While this study highlights selective dysfunction in a relatively pure sample of cannabis users, it should be noted that many cannabis users have co-morbidities and use other substances, and that these users would be expected to manifest a broader range of executive dysfunction than found herein. Discrepancies between the current cognitive findings and those reported previously could also reflect other factors including differences in the nature of the samples (we studied young people and a relatively small proportion of cannabis users met criteria for dependence/abuse).

Cannabis users showed less rational decision-making on the Cambridge Gamble task than controls; they were more likely to make 'risky' judgments and to select statistically unlikely, i.e., irrational, outcomes, despite resulting in punishment (negative feedback/loss of points). This impairment occurred across risk ratios, in the absence of more generalized problems with response speed or decisions regarding what proportion of points to gamble. We are unaware of any previous studies examining effects of cannabis or THC on this specific paradigm. Using the Iowa Gambling task, which bears parallels to the CGT, decision-making deficits have previously been reported in association with cannabis use (Whitlow et al., 2004; Hermann et al., 2009). These findings suggest that cannabis users are relatively insensitive to negative punishment. Interestingly, imaging research has demonstrated under-responsiveness of various neural regions (e.g., anterior cingulate, medial prefrontal, and superior parietal cortices) during decision-making in cannabis users (Wesley et al., 2011).

The ability to plan ahead is typically assessed in the laboratory using executive planning paradigms, such as the One-Touch Stockings of Cambridge task. Executive planning is dependent upon distributed neural circuitry including the dorsolateral prefrontal cortices (Owen et al., 1990; Williams-Gray et al., 2007). We found that cannabis users were less able to plan successfully, particularly at more challenging levels. These findings draw parallels with those of previous research conducted in adolescent cannabis users, which reported significant impairment on the Delis–Kaplan Executive Function System planning test (Medina et al., 2007).

These findings may explain the association between cannabis use in adolescents and young adults and a range of problematic behaviors. Cannabis use has been associated with driving under the influence (Alvarez et al., 2007), high-risk sexual behavior (Hendershot et al., 2010), and poor school performance and school drop-out (Cox et al., 2007). It is likely that risky decision-making and impaired ability to plan, mediated by underlying dysregulation of fronto-striatal circuitry, may mediate such deleterious behaviors.

Several limitations of the current study should be noted. This was a cross-sectional study with the inherent limitations thereof; the cognitive findings may have been driven by unmeasured factors associated with cannabis use rather than by cannabis use itself. We did not ask cannabis users time since last intake and this clearly would have been useful in retrospect, as would more information about quantity of use. This study cannot clarify whether cognitive problems predate cannabis use, or are due to it, nor potential differential effects of intoxication, acute withdrawal, protracted withdrawal or residual effects as opposed to chronic use. Lifetime use estimates were also not recorded. In a post hoc secondary analysis, however, we found no significant correlations between cognitive performance on deficient measures in the cannabis users and average weekly cannabis intake (all $p > 0.10$, Spearman's r). The study was likely underpowered to detect such correlations.

The selective nature of the cognitive deficits that were identified suggests that results are not simply attributable to more general problems, e.g., relating to IQ. The group sizes were unmatched with a relatively small sample size in the cannabis group, and this may have reduced statistical power, though the study was sufficiently powered to identify core deficits versus controls. The sample size differences were an inevitable consequence of our strategy to recruit all people from the same underlying population using identical screening criteria, to avoid introducing differential recruitment bias. Other non-significant tasks on the CANTAB, however, may be less sensitive than the Cambridge Gamble task and Stockings of Cambridge task, and significant differences could possibly be obtained with larger sample sizes.

In summary, our results suggest that young adults who use cannabis demonstrate selective cognitive dysfunction in terms of decision-making and executive planning. The question remains whether such dysfunction predates the use of cannabis or rather may be due to it.

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Contributors

Dr. Grant, Dr. Chamberlain, Ms. Schreiber, and Mr. Odlaug contributed to the initial draft of the manuscript, data analysis, and revisions. Each author has studied the manuscript in its current form, agrees to the order of authorship, and approves it for submission.

Conflict of interest

Ms. Schreiber reports no biomedical financial interests or potential conflicts of interest.

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References

Aron, A.R., Fletcher, P.C., Bullmore, E.T., Sahakian, B.J., Robbins, T.W., 2003. Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. Nat. Neurosci. 6, 115–116.

Almeida, P.P., Novaes, M.A., Bressan, R.A., Lacerda, A.L., 2008. Review: executive functioning and cannabis use. Rev. Bras. Psiquiatr. 30, 69–76.

Alvarez, F.J., Fierro, I., Del Rio, M.C., 2007. Cannabis and driving: results from a general population survey. Forensic Sci. Int. 170, 111–116.

Bolla, K.I., Brown, K., Eldreth, D., Tate, K., Cadet, J.L., 2002. Dose-related neurocognitive effects of marijuana use. Neurology 59, 1337–1343.

Chamberlain, S.R., Sahakian, B.J., 2007. The neuropsychiatry of impulsivity. Curr. Opin. Psychiatry 20, 255–261.

Chamberlain, S.R., Robbins, T.W., Winder-Rhodes, S., Müller, U., Sahakian, B.J., Blackwell, A.D., Barnett, J.H., 2011. Translational approaches to frontostriatal dysfunction in attention-deficit/hyperactivity disorder using a computerized neuropsychological battery. Biol. Psychiatry 69, 1192–1203.

Clark, L., 2010. Decision-making during gambling: an integration of cognitive and psychobiological approaches. Philos. Trans. R. Soc. Lond. B Biol. Sci. 365, 319–330.

Coull, J.T., Middleton, H.C., Robbins, T.W., Sahakian, B.J., 1995. Clonidine and diazepam have differential effects on tests of attention and learning. Psychopharmacology (Berl.) 120, 322–332.

Cox, R.G., Zhang, L., Johnson, W.D., Bender, D.R., 2007. Academic performance and substance use: findings from a state survey of public high school students. J. Sch. Health 77, 109–115.

Hall, W., Degenhardt, L., 2009. Adverse health effects of non-medical cannabis use. Lancet 374, 1383–1391.

Hart, C.L., Ilan, A.B., Gevins, A., Gunderson, E.W., Role, K., Colley, J., Foltin, R.W., 2010. Neurophysiological and cognitive effects of smoked marijuana in frequent users. Pharmacol. Biochem. Behav. 96, 333–341.

Heishman, S.J., Arasteh, K., Stitzer, M.L., 1997. Comparative effects of alcohol and marijuana on mood, memory, and performance. Pharmacol. Biochem. Behav. 58, 93–101.

Hendershot, C.S., Magnan, R.E., Bryan, A.D., 2010. Associations of marijuana use and sex-related marijuana expectancies with HIV/STD risk behavior in high-risk adolescents. Psychol. Addict. Behav. 24, 404–414.

Hermann, D., Lemenager, T., Gelbke, J., Welzel, H., Skopp, G., Mann, K., 2009. Decision making of heavy cannabis users on the Iowa Gambling Task: stronger association with THC of hair analysis than with personality traits of the Tridimensional Personality Questionnaire. Eur. Addict. Res. 15, 94–98.

Hunault, C.C., Mensinga, T.T., Bocker, K.B., Schipper, C.M., Kruidenier, M., Leenders, M.E., de Vries, I., Meulenbelt, J., 2009. Cognitive and psychomotor effects in males after smoking a combination of tobacco and cannabis containing up to 69 mg delta-9-tetrahydrocannabinol (THC). Psychopharmacology (Berl.) 204, 85–94.

Iversen, L., 2003. Cannabis and the brain. Brain 126, 1252–1270.

Makela, P., Wakeley, J., Gijsman, H., Robson, P.J., Bhagwagar, Z., Rogers, R.D., 2006. Low doses of delta-9 tetrahydrocannabinol (THC) have divergent effects on short-term spatial memory in young, healthy adults. Neuropsychopharmacology 31, 462–470.

Medina, K.L., Hanson, K.L., Schweinsburg, A.D., Cohen-Zion, M., Nagel, B.J., Tapert, S.F., 2007. Neuropsychological functioning in adolescent marijuana users: subtle deficits detectable after a month of abstinence. J. Int. Neuropsychol. Soc. 13, 807–820.

Owen, A.M., Downes, J.J., Sahakian, B.J., Polkey, C.E., Robbins, T.W., 1990. Planning and spatial working memory following frontal lobe lesions in man. Neuropsychologia 28, 1021–1034.

Pope Jr., H.G., Gruber, A.J., Hudson, J.I., Cohane, G., Huestis, M.A., Yurgelun-Todd, D., 2003. Early-onset cannabis use and cognitive deficits: what is the nature of the association? Drug Alcohol Depend. 69, 303–310.

Pope Jr., H.G., Gruber, A.J., Hudson, J.I., Huestis, M.A., Yurgelun-Todd, D., 2001. Neuropsychological performance in long-term cannabis users. Arch. Gen. Psychiatry 58, 909–915.

Robbins, T.W., Arnsten, A.F., 2009. The neuropsychopharmacology of fronto-executive function: monoaminergic modulation. Annu. Rev. Neurosci. 32, 267–287.

Rogers, R.D., Everitt, B.J., Baldacchino, A., Blackshaw, A.J., Swainson, R., Wynne, K., Baker, N.B., Hunter, J., Carthy, T., Booker, E., London, M., Deakin, J.F., Sahakian, B.J., Robbins, T.W., 1999. Dissociable deficits in the decision-making cognition of chronic amphetamine abusers, opiate abusers, patients with focal damage to prefrontal cortex, and tryptophan-depleted normal volunteers: evidence for monoaminergic mechanisms. Neuropsychopharmacology 20, 322–339.

Substance Abuse and Mental Health Services Administration, 2010. Results from the 2009 National Survey on Drug Use and Health: Volume I. Summary of National Findings. Office of Applied Studies, NSDUH Series H-38A, HHS Publication No. SMA 10-4586. Rockville, MD.

Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J. Clin. Psychiatry 59, 22–33, quiz 34-57.

Solowij, N., Pesa, N., 2010. Cognitive abnormalities and cannabis use. Rev. Bras. Psiquiatr. 32 (Suppl. 1), S31–S40.

Wesley, M.J., Hanlon, C.A., Porrino, L.J., 2011. Poor decision-making by chronic marijuana users is associated with decreased functional responsiveness to negative consequences. Psychiatry Res. 191, 51–59.

Whitlow, C.T., Liguori, A., Livengood, L.B., Hart, S.L., Mussat-Whitlow, B.J., Lamborn, C.M., Laurienti, P.J., Porrino, L.J., 2004. Long-term heavy marijuana users make costly decisions on a gambling task. Drug Alcohol Depend. 76, 107–111.

Williams-Gray, C.H., Hampshire, A., Robbins, T.W., Owen, A.M., Barker, R.A., 2007. Catechol O-methyltransferase Val158Met genotype influences frontoparietal activity during planning in patients with Parkinson's disease. J. Neurosci. 27, 4832–4838.