

# Do Neurodegenerative Diseases Affect Creativity? Divergent Thinking in Frontotemporal Dementia and Parkinson's Disease

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Creativity is considered to be one of the most important characteristics that humans possess. It emerges from fundamental cognitive operations and the activation of specific brain regions. In several neurological disorders, such as frontotemporal dementia (FTD) and Parkinson's disease (PD), creativity plays an important role in diagnosis and rehabilitation strategies. This study examined the link between creativity and pathology in a sample of neurological patients (idiopathic PD,  $n = 17$ ; FTD,  $n = 11$  with behavioural or semantic variants), and 15 healthy subjects (Mini Mental State Examination score  $\geq 20$ ; age range, 45 to 85 years) using the Divergent Thinking Test. The FTD group exhibited lower scores than the PD and control groups. Furthermore, PD patients performed significantly better on the single DTT factor, *originality*, than controls.

These results are discussed in relation to neurological mechanisms that may influence creative strategies in dementia. Finally, it has been proposed creativity therapy as a cognitive rehabilitation approach, which may help patients enhance and maintain cognitive functions, reduce the severity of emotional disorders, and promote social interactions.

The neuroanatomical correlates of the creative process and the ability to produce artwork are not easy to describe. Through philosophical speculation, several studies over the past decade have attempted to define what makes an individual an artist. Creativity is defined as “the ability to understand, develop and express in a systematic fashion, novel orderly relationships” (Heilman, Nadeau, & Beversdorf, 2003), and has been considered to be one of the most important characteristics that humans possess.

From a neuroscience perspective, several brain areas are activated during creative processes. In fact, neuroimaging studies have demonstrated the engagement of the bilateral inferior temporal gyri, left insula, left parietal lobule, right angular gyrus, and regions in the prefrontal cortex (PFC; Dietrich & Kanso, 2010).

Park, Kirk, and Waldie (2015) identified a specific brain network during the performance of tasks requiring creativity comprising the medial prefrontal cortex, the inferior frontal gyrus, left insula, left parietal lobule, and the right angular gyrus.

Based on previous meta-analyses of functional magnetic resonance imaging (fMRI) studies investigating creativity, it has been reported that, in addition to overlapping regions of the bilateral PFC and occipitotemporal cortex contributing to creativity across multiple domains, there is also a domain-specific, neural contribution to these types of creativity.

A recent review (Pidgeon et al., 2016) examined fMRI activity among studies investigating visual creativity. Given existing technologies, generating visual solutions may require greater involvement of several processes, such as manipulation of visual imagery, inhibition of irrelevant ideas, planning, and evaluation, compared with tasks in which solutions are not required to be functional or realistic (Cross, 2001).

Thus, similar to other higher mental functions, it is assumed that creativity emerges from fundamental cognitive operations characterized by cognitive processes, including working memory, sustained attention, planning, cognitive flexibility, mentalizing, and abstraction (de Souza et al., 2014).

Progressive neurodegenerative disease that disrupts the interactions between the frontal and temporal, parietal and occipital lobes, or between the dominant and non-dominant hemispheres, has been shown to affect the creativity process, as noted by artistic changes in patients with frontotemporal dementia (FTD) (Mell, Howard, & Miller, 2003), Alzheimer's disease (Gretton & Ffytche, 2014) and Parkinson's disease (PD; Inzelberg, 2013). Nevertheless, there are inconclusive results that suggest a link between executive functions and creativity. Different studies have demonstrated that all dimensions of the creative process are impaired in patients with the FTD behavioral variant, whereas patients with semantic dementia exhibited an enhancement in artistic creativity (de Souza et al., 2010). Moreover, Miller, Ponton, Benson, Cummings, and Mena (1996) showed that patients with semantic variants of frontotemporal lobar degeneration (FTLD) with severe degeneration of the striatal, temporal, and left inferior frontal-insular regions, were able to create works of art.

In contrast, significant deterioration of creative ability was observed in those with frontal variants of FTLD (de Souza et al., 2014).

Dopaminergic drugs appear to be able to enhance verbal and visual creative thinking in PD patients (Faust-Socher, Kenett, Cohen, Hassin-Baer, & Inzelberg, 2014). This evidence suggests that creativity cognition—which is affected by mesolimbic dopamine—may be influenced or triggered by the use of psychotropic agents.

The art produced by neurological patients reveals that when brain damage is localized or diffuse, or when neurodegenerative brain disease is present, artistic depictions of the imagination linked to creative brain processes are still possible.

In this study, our aim was to examine creative cognition in neurological patients with PD and FTD, measured by means of the Divergent Thinking Test (DTT), a test comprising 12 frames that require verbal and figurative skills aimed at estimating the level of creativity according to dimensions or cognitive functions. Several cognitive tests

of divergent thinking have been used to assess levels of creative cognition; however, these picture-based exercises provide opportunities to evaluate—using the appropriate tools—creative brain processes.

## METHODS

### Participants

Seventeen patients with idiopathic PD, 11 with FTD (8 with the behavioral variant, 3 with the semantic variant), and 15 healthy subjects (HS) participated in this study (Table 1). The demographic characteristics of the groups are summarized in Table 1. All patients were recruited from the Fondazione IRCCS Ca' Granda, Policlinico Hospital of Milan, Italy, and from the III Neurological Clinic of the San Paolo Hospital of Milan according to criteria from either Rascovsky et al. (2011) and Gorno-Tempini et al. (2011) for FTD or the United Kingdom PD Brain Bank criteria (Hughes, Daniel, Kilford, & Lees, 1992) for PD.

The patients' motor disturbances were evaluated using Hoehn and Yahr staging (Hoehn & Yahr, 1967) and the Unified Parkinson's Disease Rating Scale (Martinez-Martin et al., 1994) for patients with PD. Scores were rated while patients were on medication. The inclusion criteria were as follows: age between 45 and 85 years; age at onset > 40 years; a Mini Mental State Examination (MMSE) score  $\geq 20$ ; and Hoehn and Yahr stage 1 to 3 for patients with PD. Individuals with concurrent psychiatric illnesses, such as schizophrenia or manic depression, a documented or suspected history of drug abuse or alcoholism, diabetes mellitus, or cerebral infarction or tumour, were excluded. All patients with PD were taking levodopa or dopamine agonists, or both, whereas patients with FTD were taking disease-related drugs (citalopram hydrochloride, quetiapine, rivastigmine, promazine hydrochloride, haloperidol, hydroxyzine, dihydrochloride, lorazepam, escitalopram oxalate, paroxetine, and hydrochloride).

Similarly, among HS, those with major problems, such as traumatic brain injury, epilepsy, neurosyphilis, HIV infection, or medical illness other than diabetes, were excluded.

TABLE 1  
Clinical and demographic characteristic of the sample.

	PD	HS	FTD
Subject	17	15	11
Gender	4 F; 13 M	6 F; 9 M	6 F; 7 M
Age	61.47 $\pm$ 9.6	61.87 $\pm$ 8.55	70 $\pm$ 4.83
Education	12.24 $\pm$ 4	11.33 $\pm$ 2.71	12.27 $\pm$ 3.97
MMSE	27.64 $\pm$ 2.6	28.2 $\pm$ 1.27	24.81 $\pm$ 3.1
LED	1456.735 $\pm$ 2277.8	-	-

PD = Parkinson's disease; HS = healthy subjects; FTD = Frontotemporal dementia; MMSE = Mini Mental State Examination; LED = Levodopa equivalent dose.

All subjects provided informed consent, and the protocol and procedures were approved by the institutional review board, and were conducted in accordance with the Declaration of Helsinki.

### DTT

The DTT task proposed by Williams and colleagues (Ruggiero, Lavazza, Vergari, Priori, & Ferrucci, 2018; Williams, 1994) was used (Figure 1). The DDT task consists of 12 frames consisting of a graphic line that acts as a stimulus to produce its own design. Subjects are asked to start from this graph to generate a drawing that will produce artwork that is as original as possible. The design evaluation provides five-factor scores of divergent thinking derived from Guilford analytical research on the factors of human intelligence: fluidity (FL), flexibility (FS), originality (O), and processing (E). Additionally, verbal skills are evaluated through the allocation of a title (T) to each frame—an ability that requires divergent semantic transformation. Total creativity score (ToT) was measured according to the sum of the raw scores of FL, FS, O, E, and T of each frame.

## RESULTS

To compare the three groups (i.e., FTD, PD, and HS), a one-way analysis of variance (ANOVA) with a between-factor of *group* was performed for demographic variables (age, years, education, and MMSE score) DTT total score (i.e., ToT), and for each of the single factors (i.e., FL, FS, O, E, and T). Tukey's post-hoc analysis was used to assess differences between the variables measured. No significant differences were found between the three groups (FTD, PD, and HS) for education ( $p = 0.7$ ); the FTD group was older than the PD ( $p = .03$ ) and HS groups ( $p = .05$ ), and had a lower MMSE score (FTD vs. PD,  $p = .009$ ; PD vs. HS,  $p = .002$ ).

PD patients exhibited the highest creativity DDT ToT score, whereas FTD patients exhibited the lowest (post hoc: PD vs. FTD,  $p = .0001$ ; FTD vs. HS,  $p = .0001$ ; PD vs. HS,  $p = .015$ ; Figure 2). The same pattern was observed for the sub-score O (post hoc: PD vs. FTD,  $p = .0001$ ; FTD vs. HS,  $p = .039$ ; PD vs. HS,  $p = .019$ ) and T (post hoc: PD vs. FTD,  $p = .0001$ ; FTD vs. HS,  $p = .0083$ ; PD vs. HS,  $p = .085$ ). FTD patients had lower subscores in FL (FTD vs. PD,  $p = .0001$ ; FTD vs. HS,  $p = .0001$ ) and FS (FTD vs. PD,  $p = .0001$ ; FTD vs. HS,  $p = .0001$ ) compared with the HS and PD groups; however, no differences were observed between the PD and HS groups (Table 2, Figure 3). No differences were found among the three groups for the E factor ( $p = .063$ ).

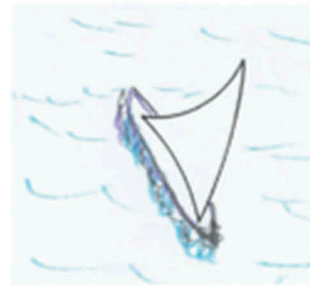
Example



A



B



C



FIGURE 1 Example of Divergent Thinking Test frame performed by (A) healthy subjects, (B) patients with Parkinson's disease, and (C) patients with frontotemporal dementia.

Pearson's correlation coefficients were calculated to verify the correlation between continuous variables (disease duration, levodopa equivalent dose [LED], patient age, and education level) and creative performance on the DTT. Correlations between the scores and the single continuous variables were analyzed. Multivariate correlations were then performed only selecting the factors that were significantly correlated with the variable under analysis.

There was a significant correlation between DTT ToT score and education ( $p = .018$ ) and age, ( $p = .001$ ) but not for MMSE ( $p = .17$ ); however, this was not confirmed by multifactor analysis.

There were no significant correlations between DDT subscores (FS, FL, E, O, T) and clinical and demographic characteristics (age, education, MMSE). In the PD group, only LED was correlated with the T factor ( $p = .01$ ).

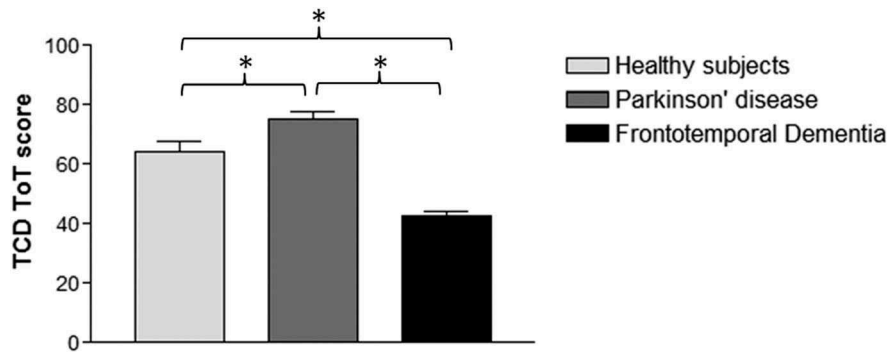


FIGURE 2 Divergent Thinking Test (DTT) total score (ToT) in healthy subjects (HS; white bar), Parkinson's disease (PD) patients (grey bar) and frontotemporal dementia (FTD) patients (black bar). Error bars are SEM.

Note that the DDT ToT score was significantly higher for patients with PD than for those with FTD and HS,  $p = .001$ . Conversely, the DDT ToT score was lower for FTD patients than HS,  $p = .001$ .

TABLE 2  
Scores of the of the Divergent Thinking test (DTT).

(mean ± SEM)	PD	HS	FTD
FL	11.53 ± 0.19	11.60 ± 0.23	8.6 ± 0.49
FS	9.11 ± 0.26	9.33 ± 0.31	5 ± 0.38
O	24.82 ± 1.18	19.47 ± 1.7	14.09 ± 0.93
E	10.06 ± 1.18	8 ± 2.45	3.9 ± 0.79
T	19.94 ± 1.23	15.73 ± 0.52	11 ± 0.92
TOT	75.47 ± 2.4	64.13 ± 3.74	42.64 ± 1.55

PD = Parkinson's disease; HS = healthy subjects; FTD = Frontotemporal dementia; FL = Fluidity; FS = Flexibility; O = Originality; E = Elaboration; T = Titles.

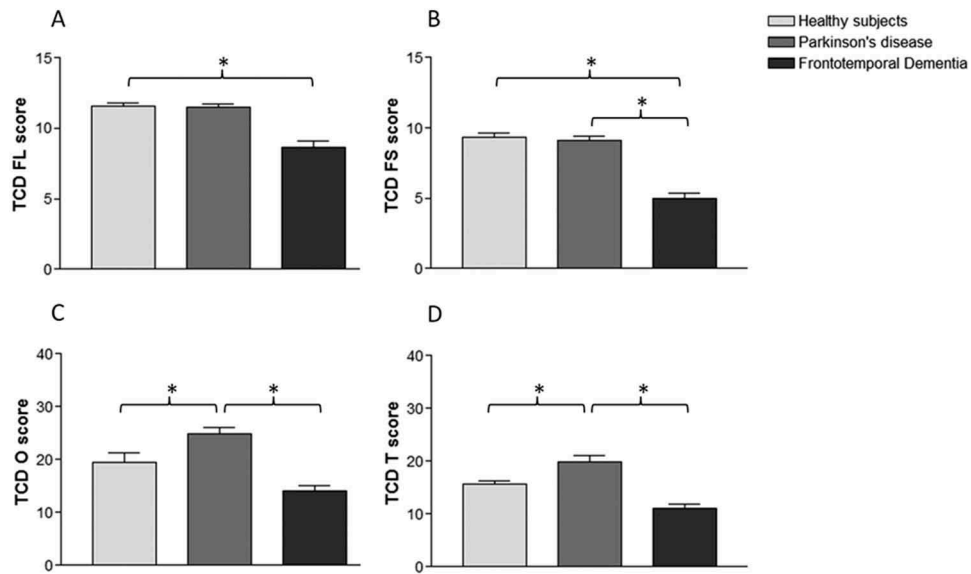


FIGURE 3 Divergent Thinking Test (DTT) single factor scores in healthy subjects (HS; white bar), Parkinson's disease (PD) patients (grey bar) and frontotemporal dementia (FTD) patients (black bar). (A) Fluidity score (FL); (B) Flexibility score (FS); (C) Originality score (O); (D) Title score (T). Error bars are SEM.

Note that patients with PD were more creative than HS and FTD patients in originality and title production. Conversely, FTD patients were less creative than PD patients and HS in fluidity, flexibility, originality and title production.

All data were analyzed using STATISTICA version 5.5 (Statistica, StatSoft, Inc., Italy). Unless otherwise indicated, all values are expressed as mean  $\pm$  SEM.

### Differences in DTT between behavior-FTD group and other groups

The same analysis was conducted in the FTD group, excluding patients with the semantic variant; a significant difference among the three groups for ToT score was found ( $p < .001$ ; post hoc: PD vs. FTD:  $p = .0001$ ; PD vs. HS:  $p = .019$ ; FTD vs. HS,  $p = .0003$ ).

A Tukey post-hoc analysis for each factor revealed that patients with PD were more creative than those in the HS and FTD groups in the O ( $p = .00013$ ; post hoc: PD vs. FTD:  $p = .00022$ ; PD vs. HS,  $p = .0025$ ), FS ( $p < .001$ ; post hoc: PD vs. FTD:  $p = .00012$ ; FTD vs. HS,  $p = .0012$ ), and FL ( $p = .000002$ ; post hoc: PD vs. FTD:  $p = .00012$ ; FTD vs. HS,  $p = .0012$ ) factors and T production ( $p = .000054$ ; post hoc: PD vs. FTD:  $p = .00016$ ; FTD vs. HS,  $p = .001$ ). No differences were found among the three groups for the E factor ( $p = .061$ ).

## DISCUSSION

This study aimed to examine the link between creativity and pathology in a sample of neurological patients. To our knowledge, this was the first clinical investigation to use the DTT, a validated and standardized measure of creative thinking. The DTT explores various dimensions of creativity in visual and verbal domains using quantitative (FL, FS, O, T) markers of creative production. The first result in a neurological sample was that FTD patients had the lowest DDT ToT score compared with the PD and control groups; the PD group had the highest total score.

Several studies have approached creativity from a neuroscience perspective with in-depth explorations of the cognitive and neural bases of the creative mind (Shamay-Tsoory, Adler, Aharon-Peretz, Perry, & Mayseless, 2011). Similar to other mental functions, it is believed that creativity emerges from fundamental cognitive operations related to specific brain organization, and characterized by cognitive processes such as working memory, sustained attention, planning, cognitive flexibility, mentalizing, and abstraction.

In this study, cognitive abilities measured by means of the DTT were significantly lower in FTD patients than in the other study groups. The worst performance in terms of DDT ToT and subcomponents found in FTD patients suggests that frontal function is implicated in creative processes.

Consistent with de Souza et al. (2010), who demonstrated that patients with the frontal variant of FTLTD were strongly impaired in all dimensions of the creative process, these results confirm that a disruption in the creativity

network—encompassing the frontal, parietal and temporal lobes—due to brain atrophy is associated with impairments in creative tasks. Although some studies have concluded that patients with semantic dementia demonstrate a focal degeneration in the left anterior temporal lobe, with impairment of language abilities and enhancement of artistic creativity (Miller et al., 1998, 1996), this study demonstrated that patients with FTD were less creative. An explanation for this result could be that only four patients had semantic dementia while the other eight had the behavioral variant; moreover, these results were also confirmed by more specific analysis.

The relationship between artistic output and brain disease is particularly complex, and brain disorders may lead to impairment of artistic production in multiple domains, especially the frontal area. Neurological conditions may also occasionally modify artistic style and lead to surprisingly innovative features in individuals who experience an initial loss of creativity (Piechowski-Jozwiak & Bogousslavsky, 2012). Conversely, PD patients performed significantly better on the DTT for the single factor O, compared with FTD patients and the control group. As discussed previously, creative output involves multiple cognitive processes of neuronal activity in a large network involving multiple cerebral areas.

The neurotransmitter dopamine plays a key role in these complex interactions; however, in PD depletion of the substantia nigra and the ventral tegmental area causes low dopamine concentrations in the brain. As reported by Faust-Socher et al. (2014), dopamine levels in the nucleus accumbens and its afferent connections could represent the neuroanatomical mechanism underlying latent inhibition. Latent inhibition is the ability to filter irrelevant stimuli, and this reduction may enhance divergent thinking, possibly by widening or loosening the associative network, as suggested by these results.

Another correlation between dopamine and creativity can be derived from the tendency toward novelty-seeking behavior. This tendency has been linked to the ventral striatum, substantia nigra, ventral tegmental area of the midbrain, and hippocampal areas that contain dopaminergic neurons (Jauk, Neubauer, Dunst, Fink, & Benedek, 2015). Because there was no correlation between LED and DTT ToT score in this study, the increased creativity in the PD group did not appear to be related to dopaminergic treatment. Despite the premorbid personality of PD patients, characterized by inflexibility and lack of novelty-seeking, they paradoxically exhibit increased creativity unrelated to dopaminergic treatment. However, results showed that L-dopa equivalent dose correlated with the T factor. Given that the T subscore is the ability to produce relevant titles for production, and scoring is based on the complexity of the vocabulary used, this evidence seems to be linked to linguistic



competence and vocabulary size, as well as verbal procedures, rather than a product of dopaminergic therapy.

Dopamine replacement therapy is the goal of treatment for PD. However, some patients develop compulsive abuse of dopaminergic drugs to ameliorate motor symptoms with addictive behavior, such as pathological gambling, hypersexuality, paranoia, and delusions or punding (Warren, O’Gorman, Lehn, & Siskind, 1060-1064). In this study, two PD participants drew female body parts; however, they did not exhibit dopamine dysregulation syndrome, which may explain the presence of the sexual theme.

The sexual theme has been reported by Witt and colleagues (Witt, Krack, & Deuschl, 2006), who described a patient who exhibited sexual context in his artistic work 3 months after deep brain stimulation; 2 years after the operation, there was a change in the hedonistic set-point.

Long-term habituation after chronic stimulation and reduction in medication likely explains the disappearance of the dopamine dysregulation syndrome, behavioral addictions, and dopaminergic medication abuse (Lhommée et al., 2012).

Nevertheless, owing to the small number of patients included in this study, it cannot entirely exclude any influence of dopaminergic treatment on divergent thinking.

A comparison between the groups revealed that patients with PD performed significantly better than the neurological group in the DTT. This result could be used to argue that poor creativity was an effect of general reduction in cognitive functioning in FTD patients who had a lower score on the MMSE, a measurement of global cognitive functioning. The neural model supports the role of the frontal lobe, the main connection between the temporal and parietal lobes, where knowledge and concepts are stored (Binder & Desai, 2011).

The observation that FTD patients exhibited decreased creativity points to the increased creativity in PD patients being specific, despite the progression of the disease. Given these considerations, creativity may play an important role in dementia patients in terms of evaluation and rehabilitation strategies. In fact, the DTT test is a simple, alternative tool to assess several cognitive domains, including cognitive flexibility both in patients and in healthy subjects. It can be easily administered and analyzed, providing an indirect measure linked to autonomy in activities of daily living.

Considering that dementia may affect semantic memory and frontal functions, as well as language and visuospatial domains, a training program on divergent thinking based on conceptual flexibility and strategic processes needed for generating creative solutions in a social setting, and navigating the complexities of social interactions, may encourage a more active cognitive and behavioral style, which could be reflected in improved cognitive symptoms.

The investigation of divergent thinking in dementia patients may help to understand the patient’s reserve regarding an intact semantic memory store and frontal-executive functions. Moreover, creative therapies may help dementia patients cope with their symptoms and benefit from expressing their emotions, with subsequent improvements in interaction skills. Thus, creativity therapy cannot only activate and stimulate several functions related to cognition and emotion, but can also be used to stimulate play and pleasure, important factors for achieving the goals of rehabilitation programs. Supporting this view, a cognitive approach using creativity may help patients enhance and maintain cognitive functions, reduce emotional disorders and promote personal independence.

Although the results are interesting, this study had some limitations. First, the sample size for each group was relatively small and not fully representative of the patient populations. Second, a complete neuropsychological assessment was not performed. Thus, it was not possible to quantify the overall level of cognitive decline and which functions were most compromised, as well as fatigue and attentional problems, during the tests. Third, emotional aspects of the creativity process were not assessed. Further studies are needed to investigate—using a specific tool—the emotional aspect of the creative process and how it affects its outcome.

Finally, although the use of clinical criteria improved the probability of correct diagnoses for patients with FTD, we are not able to define a certain diagnosis because this can only be achieved by pathological examination of postmortem tissue.

## DISCLOSURE STATEMENT

No potential conflict of interest was reported by the authors.

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