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TOOL USE DISORDERS IN NEURODEGENERATIVE DISEASES: ROLES OF SEMANTIC MEMORY AND TECHNICAL REASONING

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ABSTRACT

In the field of apraxia, it has been suggested that the ability to use tools and objects in daily life depends not only on semantic knowledge about tool function and context of use but also on technical reasoning about mechanical properties of tools and objects. The aim of the present work was to assess tool use abilities regarding these hypotheses in patients with neurodegenerative diseases and reduced autonomy. Performance of patients with Alzheimer's disease (n = 31), semantic dementia (n = 16) and corticobasal syndrome (n = 7) was compared to that of healthy control participants (n = 31) in familiar tool use tasks, functional/contextual associations and mechanical problem solving. A conversion method was applied to data in order to avoid ceiling effects. Tool use disorders were found in all patient groups but the underlying reasons were different. Patients with semantic dementia had difficulties in imagining and selecting familiar tools due to the semantic loss but they performed in normal range in mechanical problem solving tasks. Interestingly, they performed better with only one tool and its corresponding object, which is interpreted as a partial compensation of semantic loss by spared technical reasoning. Patients with corticobasal syndrome exhibited the reverse pattern, that is, mechanical problem solving deficits without semantic loss. However, additional qualitative research is needed to disentangle the relative contributions of motor and technical reasoning deficits to this pattern. Both of these profiles were found in patients with Alzheimer's disease. For all that, these patients did not commit the same errors as stroke patients with left brain-damage documented in previous works. Several hypotheses are proposed to account for the specificity of tool use disorders in neurodegenerative diseases, and recommendations are provided to caregivers.

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47 # KEYWORDS

48 *Keywords: Alzheimer's disease, semantic dementia, corticobasal degeneration, mechanical*

49 *problem-solving, apraxia.*

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ABBREVIATIONS

- AD: Alzheimer's disease (as a group).
- BEC: "Batterie d'Evaluation Cognitive" (a French neuropsychological battery)
- CBS: Corticobasal syndrome
- FAB: Frontal Assessment Battery
- FCA: Functional and Contextual Associations
- HC: Healthy controls (as a group)
- MMSE: Mini Mental State Examination
- MPS.C: Mechanical Problem Solving (choice condition)
- MPS.NC: Mechanical Problem Solving (no choice condition)
- RTU.C: Real Tool Use (choice condition)
- RTU.NC: Real Tool Use (no choice condition)
- SD: Semantic dementia (as a group)
- STU: Single Tool Use

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I. INTRODUCTION

1. 1. AIMS OF THE PRESENT STUDY

It is known that difficulties in using everyday tools and objects are a core manifestation of apraxia (Baumard, Osiurak, Lesourd, & Le Gall, 2014; Bieńkiewicz, Brandi, Goldenberg, Hughes, & Hermsdörfer, 2014; Goldenberg, 2009; Heilman, Maher, Greenwald, & Rothi, 1997). It is also well-known that patients with dementia have difficulties in performing usual activities as well as in solving complex or novel problems (McKhann et al., 2011). Nevertheless, only very few studies have investigated tool use abilities in neurodegenerative diseases (see for example Lesourd et al., 2013), perhaps because the cognitive processes underlying tool use are still under debate (Buxbaum, Shapiro, & Coslett, 2015; Osiurak & Badets, 2016; Osiurak, Jarry, & Le Gall, 2010, 2011; Osiurak & Le Gall, 2014). In view of recent models of apraxia, normal tool use may depend on two complementary mechanisms, that is, semantic knowledge about tool function and context of use (Osiurak, 2014; Rothi, Ochipa, & Heilman, 1991, 1997; Roy, 1996; Roy & Square, 1985), and technical reasoning about physical properties of tools and objects (Osiurak et al., 2010, 2011; Reynaud, Lesourd, Navarro, & Osiurak, 2016; for a similar view, see Goldenberg & Hagmann, 1998). In light of these hypotheses, the aim of the present study was to describe tool use disorders in dementia through a differential approach, in Alzheimer's disease, semantic dementia and corticobasal syndrome.

1. 2. THEORETICAL BACKGROUND

1.2.1. DEMENTIA SUBTYPES

Dementia is defined as a progressive decline of memory, reasoning, judgment, visuospatial skills, language and/or social behavior, interfering with usual activities and hence reducing autonomy (McKhann et al., 2011). Logically, tool use disorders should be observed

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in all-cause dementia but the underlying cognitive impairments are likely to be etiology-specific since the pattern of brain atrophy and the expected neuropsychological profile vary according to diagnosis. Semantic dementia is associated with circumscribed atrophy of the ventral temporal lobes. It is characterized by a loss of knowledge observed in language (i.e., fluent but empty speech, loss of word meaning, semantic paraphasias) and/or perception (i.e., prosopagnosia, impaired recognition of objects identity or function) contrasting with normal language processing (i.e., repetition, reading) and perception (i.e., perceptual matching, picture reproduction; Gorno-Tempini et al., 2011; Neary et al., 1998). Corticobasal degeneration is characterized by brain atrophy in the basal ganglia and in frontal and parietal brain regions. It is associated with asymmetric limb rigidity, akinesia, dystonia and/or myoclonus, as well as with orobuccal or limb apraxia (i.e., ideomotor and/or limb-kinetic apraxia), cortical sensory deficit and/or alien limb phenomenon, but additional cognitive impairments are exclusion criteria (Armstrong et al., 2013; Litvan et al., 1997). The clinical diagnosis of Alzheimer's disease requires either episodic memory disorders (i.e., amnestic presentation) or language, visuospatial or executive dysfunction (i.e., non-amnestic presentation; McKhann et al., 2011). Lesions are typically observed in the hippocampal region but they may also extend to frontal and parietal lobes.

According to Felician, Ceccaldi, Didic, Thinus-Blanc and Poncet (2003), cortical neurodegenerative diseases are well-suited models for testing cognitive-based hypotheses, for three reasons. First, lesions are relatively circumscribed at early stages of the disease. Second, in most cases the progression of cognitive impairments is stereotyped and sequential. Third, slowly progressive diseases may result in more stable functional reorganization than non-progressive lesions. Thus, it is appropriate to search for dissociations between semantic loss and problem solving deficits in neurodegenerative diseases.

1.2.2. THE SEMANTIC MEMORY HYPOTHESIS

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117 According to cognitive models of apraxia (Rothi et al., 1991, 1997; Roy, 1996; Roy &
118 Square, 1985), tool use depends on explicit semantic knowledge about tool-object usual
119 relationships (e.g., a hammer goes with a nail) and tool function (e.g., a hammer and a mallet
120 share the same purpose). Notice that we shall use the terms "tool" and "object" to refer to the
121 implement performing the action (e.g., screwdriver) and the recipient of the action (e.g.,
122 screw), respectively. Likewise, semantic memory may inform individuals about where to find
123 tools if not present in the visual field (e.g., knowing that a hammer can be found in a
124 workshop; see Osiurak, 2014; Osiurak et al., 2010). Loss of this type of knowledge causes
125 conceptual apraxia, which prevents patients from either selecting relevant tools among
126 distractors in multiple object tasks (Ochipa, Rothi, & Heilman, 1992), choosing among
127 several pictures the one that shares common features with a target picture (i.e., functional
128 association) or performing tool-related gestures in the absence of objects, as in single tool use
129 (to be described in section 2.Materials and methods). Semantic knowledge about tool function
130 and context of use is commonly associated to the ventral, temporal lobes (Goldenberg &
131 Spatt, 2009), a brain region that is early impaired in the course of Alzheimer's disease (Braak
132 & Braak, 1995, 1997) and semantic dementia (Galton et al., 2001). In comparison, temporal
133 lobe lesions are not typical of corticobasal degeneration (see for example Boeve, Lang, &
134 Litvan, 2003), even though there is a high heterogeneity as regards the distribution of cerebral
135 cortical lesions in this disease (Armstrong, Cairns, & Lantos, 1999; Tsuchiya, Ikeda,
136 Uchihara, Oda, & Shimada, 1997).

137 As a matter of fact, conceptual apraxia has been found in patients with Alzheimer's
138 disease (Crutch, Rossor, & Warrington, 2007; Derouesné, Lagha-Pierucci, Thibault, Baudoin-
139 Madec, & Lacomblez, 2000; Ochipa et al., 1992; Okazaki, Kasai, Meguro, Yamaguchi, &
140 Ishii, 2009; Rapcsak, Crosswell, & Rubens, 1989) and semantic dementia (Hodges, Bozeat,
141 Lambon-Ralph, Patterson, & Spatt, 2000; Hodges, Spatt, & Patterson, 1999; Moreaud,

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Charnallet, & Pellat, 1998). Interestingly, some patients may perform better with only one tool and its corresponding object (Bozeat, Lambon-Ralph, Patterson, & Hodges, 2002; Dumont, Ska, & Joanette, 2000; Ochipa *et al.*, 1992) even though there is no consensus on it (Derouesné *et al.*, 2000). In corticobasal degeneration, both single tool use and intransitive communicative gestures have been found to be impaired (Buxbaum, Kyle, Grossman, & Coslett, 2007). This may be accounted for by elementary motor, sensitive and proprioceptive disorders (Graham, Zeman, Young, Patterson, & Hodges, 1999) rather than by loss of conceptual knowledge since the latter is not part of the expected neuropsychological profile (Armstrong et al., 2013; Pillon et al., 1995).

For all that, a growing amount of evidence suggests that tool-related knowledge is neither necessary nor sufficient to support tool use (Buxbaum and Saffran, 2002; Buxbaum, Schwartz, & Carew, 1997; Hodges et al., 2000; Osiurak et al., 2008), which implies that non-semantic factors may compensate for semantic loss (Silveri & Ciccarelli, 2009).

1.2.3. THE TECHNICAL REASONING HYPOTHESIS

According to the technical reasoning hypothesis (Gagnepain, 1990; Le Gall, 1998; Osiurak et al., 2010, 2011; for a similar view, see Goldenberg, 2009; Goldenberg & Hagmann, 1998; Goldenberg & Spatt, 2009; Hartmann, Daumüller, Goldenberg, & Hermsdörfer, 2005), the use of both familiar and novel tools is made possible by reasoning on the relative, mechanical properties of tools and objects (e.g., copper is “resistant” when applied to sandstone but “breakable” when compared to diamond). This cognitive mechanism is likely to rely on the activity of the left inferior parietal lobe (Goldenberg, 2009; Orban & Caruana, 2014; Reynaud et al., 2016) and can be impaired independently from the presence of dysexecutive syndrome (Goldenberg, Hartmann-Schmid, Sürer, Daumüller, & Hermsdörfer, 2007). Parietal lobes are generally spared in semantic dementia (Mummery et al., 2000) but

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atrophied in Alzheimer's disease (Braak & Braak, 1991; Foundas, Leonard, Mahoney, Agee, & Heilman, 1997) and corticobasal degeneration (Litvan et al., 1997).

In a clinical setting, technical reasoning is thought to be involved in real tool use but can be more specifically assessed through mechanical problem solving tasks involving reasoning on the physical properties of novel tools and objects (Goldenberg & Hagmann, 1998; Heilman et al., 1997; Jarry et al., 2013). This ability has been rarely investigated in corticobasal degeneration. Spatt, Bak, Bozeat, Patterson and Hodges (2002) described five patients who met difficulties in novel tool selection and use. Likewise, patients with Alzheimer's disease seem to have deficits in unconventional tool use (Derouesné et al., 2000) and mechanical problem solving (Ochipa et al., 1992). Conversely, patients with semantic dementia may exhibit dissociation between impaired familiar tool use and spared mechanical problem solving skills (Hodges et al., 1999, 2000). Therefore, spared technical reasoning might compensate to some extant for semantic memory loss (as previously proposed by Hodges et al., 1999, 2002) but there is no extensive differential study on this topic and, unfortunately, existing data cannot be reinterpreted in that way due to frequent ceiling effects. In order to prevent this bias, we normalized data by combining raw efficiency scores and completion time (see section 2.4. General scoring system).

1.2.4. PREDICTIONS

The semantic memory hypothesis predicts that defective semantic knowledge about tool use (as demonstrated by deficits in Functional and Contextual Associations; see Section 2.2.3. Experimental protocol) should prevent patients from demonstrating the use of tools presented in isolation (i.e., Single Tool Use) because they should not be able to imagine neither the object which is usually associated with the tool, nor the typical action to be performed with it. Likewise, selection of a tool among distractors (i.e., Real Tool Use, Choice condition) is expected to be impaired seeing that different tools may offer similar technical potentials. For

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example, scissors, a knife and a screwdriver are all relevant to perform the action [driving a screw into a wooden board] but everyone is used to select the screwdriver because it is more frequent in our culture. In case of semantic loss, non-canonical (but technically relevant) tools might be selected. Said differently, there is no reason to select the screwdriver since the two other tools are also technically relevant, meaning that all of the three tools have an equal chance to be selected. In contrast, it can be predicted that using a tool with the corresponding object (i.e., Real Tool Use, No-Choice condition) is easier because in that case, technical reasoning alone might compensate the lack of knowledge about the tool and the object. Furthermore, according to the semantic memory hypothesis, positive correlations are expected between Functional/Contextual Associations, Single Tool Use and Real Tool Use.

According to the technical reasoning hypothesis, impaired technical reasoning (as demonstrated by deficits in mechanical problem-solving tasks; see Section 2.2.3. Experimental protocol) is expected to result in low performance in both Single Tool Use and Real Tool Use (whether with or without choice). Indeed, the technical reasoning hypothesis predicts consistent correlations between mechanical problem-solving and both of these conditions, as previously found in patients with left brain-damage (Jarry et al., 2013). The rationale is as follows. In case of isolated abnormal technical reasoning, patients may be able to match pictures of a tool and its corresponding, usual object in some instances. However, in presence of real tools and objects, selecting which technical potentials are relevant to perform the action should be especially difficult. As a consequence both tool selection and tool application deficit should be observed (tool application is defined as the efficient interaction between a tool and an object), as it has been described in stroke patients (Goldenberg & Hagmann, 1998). For example, patients may know that a screw and a screwdriver usually fit together while being unable to analyze which tool, which part of the tool and which actions are relevant to perform the expected action.

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As mentioned above, patients with semantic dementia have lesions in the temporal lobes and semantic memory deficit so the semantic memory hypothesis is expected to apply to this group. Patients with corticobasal degeneration have lesions in the parietal lobes so the technical reasoning hypothesis is expected to be true in this group. Patients with Alzheimer's disease may have lesions in both of these brain regions so both predictions may be observed. Considering that both semantic memory and technical reasoning may be involved in familiar tool use, these patients may exhibit particularly severe tool use disorders.

II. Materials and Methods

2.1. Participants

Four groups of French participants (Table 1) were exposed to the same fixed testing procedure: three groups of patients with Alzheimer's disease (AD, n = 31), semantic dementia (SD, n = 16) or corticobasal syndrome (CBS, n = 7), and a group of healthy control participants (HC, n = 31). It should be noticed that the clinical diagnosis of corticobasal syndrome may be associated with cytopathological changes of either Alzheimer's disease or corticobasal degeneration depending on the presence of either memory impairments or behavioral changes, respectively (Shelley, Hodges, Kipps, Xuereb, & Bak, 2009). In the CBS group, five patients had normal cognitive functioning but two patients had memory, language, visuoconstructive and executive dysfunction. In the absence of post-mortem confirmation, the label "corticobasal syndrome" rather than "corticobasal degeneration" was considered to be more rigorous. Patients from other groups did not exhibit corticobasal syndrome. All patients were consecutively recruited from four neurological departments (Angers, Lyon, Rennes, Grenoble). They lived at home and had no previous history of neurological or psychiatric illnesses. The study was conducted in conformity with the Declaration of Helsinki and

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approved by local ethical committee (Western Protection to Persons Committee II, n° 2012/32).

Participants were excluded in the following situations: severe dementia as disclosed by a score ≤ 10 on the MMSE (Folstein, Folstein, & McHugh, 1975), rheumatologic condition, mood disorders, medical treatment or comprehension impairment that could interfere with performance. All patients underwent neurological examination and extensive neuropsychological assessment. Cerebro-spinal fluid biomarkers were collected to confirm diagnosis in most patients. Imaging data did not show evidence of cerebrovascular damage. Patients with Alzheimer's disease fulfilled the criteria for diagnosis of probable Alzheimer's disease (McKhann et al., 2011) and imaging demonstrated hippocampal atrophy with or without background cerebral atrophy. The clinical diagnosis of semantic dementia required progressive loss of meaning of words, objects and/or faces in the context of relatively spared episodic memory, perceptual and language abilities (Gorno-Tempini et al., 2011; Neary et al., 1998). Cortical atrophy and/or hypoperfusion circumscribed to (or at least predominant in) the temporal polar regions were consistently observed. In both of these groups, vestibular, cerebellar, sensitive, pyramidal and parkinsonian syndrome were dismissed. Corticobasal syndrome was diagnosed in patients with a parkinsonian syndrome coupled with cortical signs such as orobuccal, limb and/or limb-kinetic apraxia, sensory deficit, alien limb phenomena, executive dysfunction or moderate visuospatial deficit (Armstrong et al., 2013; Litvan et al., 1997). In this group, vestibular and cerebellar syndromes were dismissed. Imaging data confirmed asymmetric atrophy in both frontoparietal cortical areas and basal ganglia.

The HC group was a control group for patients. It was matched with the AD group for gender and age (Table 1). A Kruskal-Wallis rank sum test revealed significant age differences (H = 16.8, df = 3, p < .001). Pairwise Wilcoxon comparisons with Holm's correction confirmed that patients with semantic dementia were slightly younger than those with

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Alzheimer's disease (W = 406.0, p = .002) and healthy controls (W = 402.5, p .002), which makes sense because the age of onset is frequently earlier in semantic dementia than in Alzheimer's disease (see for example Hodges, Patterson, Oxbury, & Funnell, 1992; Snowden et al., 2001). No other age differences were significant. The educational level was significantly lower in the Alzheimer group compared with other groups (Table 1) but no correlation was found between this variable and experimental measures in healthy participants (Spearman rank order correlations with Holm's correction for multiple tests, all ps > .24).

< Insert Table 1 about here >

2.2. NEUROPSYCHOLOGICAL TESTING

Neuropsychological data were collected in all participants with three standard tests:

(1) The Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975);

(2) A French neuropsychological battery (the BEC 96 questionnaire, Signoret et al., 1989) composed of eight subtests ordered as follows: working memory (i.e., saying the days of the week in reverse order), orientation questions, general verbal reasoning (i.e., arithmetic problem-solving, word-categorization, proverb comprehension), verbal fluency (i.e., providing as many animal names as possible in 2 minutes), visual recognition (i.e., 10-min recall and recognition of six black and white depicted objects), verbal learning (i.e., three immediate recalls of eight words), naming and visuo-constructive skills (i.e., copying two 3D and 2D geometrical drawings). Maximum score per subtest is twelve (total score = 96) with any score below nine indicating pathological performance according to French normative data.

(3) A fast frontal assessment battery (FAB, Dubois, Slachevsky, Litvan, & Pillon, 2000) which includes word-categorization, letter fluency, assessment of grasping, deferred imitation of movement sequence and two conflict go-no-go tasks. Each subtest is scored on a 3-point

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scale (total score = 18). Any score below fifteen demonstrates executive dysfunction according to French normative data.

2.3. Experimental protocol

Very similar procedures have already been used in previous works (Goldenberg et al., 2007; Jarry et al., 2013). Patients were allowed to use both hands in all experimental tasks, which were administered in the following order.

2.3.1. Single tool use (STU)

Ten common tools (plus one corrected, practice item) were presented one at a time on a vertical panel (Supplementary Fig. 1). Participants were asked to grasp the tool and to demonstrate its typical use. The examiner did not name the tools. The time limit was set to 20 seconds per item. Performance was videotaped and rated on a 3-point scale (maximum = 20): (2) the expected action was clearly recognizable and performed without hesitation; (1) the gesture was recognizable but with hesitations or errors (i.e., spatiotemporal errors); (0) unrecognizable gesture (i.e., content error). Two independent judges coded videos from 10 Alzheimer patients and 10 control participants who were not included in the HC group. Inter-coders agreement was high for scores (Pearson's product moment correlation, r = 0.95, $p < .001$) and completion time (r = 0.82, $p < .001$).

2.3.2. Real tool use (RTU)

Participants were asked to actually use ten tool-object pairs (Supplementary Fig. 1) plus one practice pair. The examiner did not name tools, objects or actions to be done. There were two versions of this test. In the Choice condition, participants were asked to select one of the ten tools and to use it with the presented object. In the No-choice condition, the participant was given only a tool/object pair. The time limit was set to 60 seconds per item in the Choice condition and 30 seconds in the No-choice condition because the need to select tools presumably called for additional cognitive processing. One point was given if the participant

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produced the expected action with the expected tool (maximum = 10 in each condition). In addition, in the Choice condition the number of unexpected tools removed from the panel by the participant was summed up across all items.

2.3.3. Mechanical problem solving (MPS)

This test assessed tool use abilities with novel tools and objects, that is, without reference to semantic knowledge. Experimental materials included three transparent boxes (one per item) and eight rods (Supplementary Fig. 2) that differed on material, length, diameter, bendability and friability. Participants were asked to extract a red wooden target (a cube or a bead) from each box using the rods. Each problem called for different mechanical actions (e.g., pushing, pulling, levering) and could be solved in two stages but not by hand, by chance or by random selection of the rods. A fourth box and one additional rod were used as a practice item.

In the Choice condition, participants were presented with the eight rods and one box at a time. They could use and combine as many rods as necessary although for each box, two rods allowed solving the whole problem. Some other rods could be relevant depending on the status of the problem. In the No-choice condition, participants were given only one relevant rod. The time limit was set to 3 minutes per item in both conditions. Performance was rated on a 4-point scale (maximum score = 9 for each condition): (3) The target is extracted from the box within the time limit; (2) The participant goes beyond the first stage of the problem (e.g., for box 1, he inserts a long rod into the “chimney” and pushed the cube so that it falls into the box; see Supplementary Fig. 2); (1) The participant reaches the target with a rod but he does not fulfill the first stage; (0) The participant does not reach the target with a rod.

2.3.4. Functional and contextual association (FCA)

Two tests were proposed to assess semantic knowledge about tools without effective tool manipulation. In both tests, participants were asked to select among an array of four

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pictures the one that best matched the picture of a tool (the same ten tools employed in tool use tasks). In Functional Association, the matching criterion was the function of the tool (e.g., target = match; choice = *lighter*, pen, coffee maker, colander). In Contextual Association, the criterion was its usual context of use (e.g., target = match; choice = *anniversary*, wedding, Christmas day, baptism). There were ten items in each condition (plus two corrected, practice items). Each correct answer given within 20 seconds was worth 1 point (maximum score = 20).

2.4. General scoring system

Ceiling effects are very frequent in the field of apraxia, whether in healthy participants, in stroke patients or in patients with dementia (Baumard et al., 2014; Lesourd et al., 2013). Yet, they can minimize the differences between groups so that data only indicate the presence or absence of impairment but not its severity. In order to overcome such problems, we adopted an original scoring procedure that is close to the one employed in the Wechsler Adult Intelligence Scale (Wechsler, 1997). The method took three steps: (1) Completion time (i.e., the time period between the presentation of an item and the moment the participant obtained the best possible score) was collected from videos in each item; (2) The 5^{th}, 25^{th}, 75^{th} and 95^{th} percentile ranks were calculated for completion time for each item in the control group; (3) Additional points were given to all participants depending on completion time (Supplementary Table 1). This procedure was tested in a group of seventy-two healthy participants before use in the present work, demonstrating that time-based scores were normally distributed in all experimental tests (Supplementary Fig. 3).

Besides, processing speed was assessed in all participants using a paper-and-pencil tracking task (Baddeley, 1996) so as to control for general cognitive slowing. Participants were presented with a chain of 0.5-cm-square boxes forming an irregular path on a sheet of paper. They were asked to draw a cross in each box in turn, following the path and working as

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rapidly as possible. The score was the number of crosses made within a two-minute time limit.

2.5. Statistical analysis

Despite normal distribution of data, non-parametric tests were preferred because of small sample sizes. We employed a three-step, non-Bayesian data analysis approach. First, we examined between-group differences using Kruskall-Wallis tests and post-hoc Mann-Whitney U-tests, and within-group differences using Wilcoxon tests. Second, the correlational structure was explored with Spearman rank order correlations. Holm's correction for multiple tests was applied. With the idea to infer general factors from experimental measures, we conducted a principal component analysis with the active variables (i.e., variables used to infer components) Mechanical Problem Solving (both conditions) and Functional/Contextual Associations. Age, Educational level, Processing speed, Single Tool Use and Real Tool Use in both conditions were included as additional quantitative variables and the factor GROUP as an additional qualitative variable. Data were standardized so that all variables had the same weight. Next, we examined correlations between dimensions, active variables and additional variables. All analyses were performed with R statistical software. Third, single cases were examined using a dedicated statistical method (Crawford & Garthwaite, 2002, 2005).

III. Results

3.1. Effects of demographic data and neuropsychological testing

No linear relationship was observed between age, educational level and experimental measures in the control group (all *p*s > .08). Sixteen Alzheimer patients had mild cognitive decline (MMSE 26-21; subgroup 1, mean score = 22.3/30, SD = 1.2/30) whereas fifteen had moderate to severe decline (MMSE 20-11; subgroup 2, mean score = 18.0/30, SD = 2.3/30; see Reisberg et al., 1982). Both groups obtained similar results in Real Tool Use, choice

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condition (subgroup 1: mean score = 28.4 %, SD = 13.3 %; subgroup 2: mean score = 21.4 %, SD = 13.3 %; U = 158.5, p = .13) and even subgroup 1 was significantly impaired when compared to healthy controls (mean MMSE score = 27.2/30, SD = 1.7/30; mean Real Tool Use score = 60.6 %, SD = 12.0 %; U = 453.5, $p < .001$).

Results of the Frontal Assessment Battery yielded comparable results in patients with Alzheimer's disease (mean score = 71.1 %, SD = 12.8 %), semantic dementia (mean score = 75.0 %, SD = 12.2 %, 3 missing values due to comprehension deficits) and corticobasal syndrome (mean score = 67.2 %, SD = 22.8 %; H = 0.94, df = 2, p = .62).

With respect to the BEC 96 questionnaire, significant general cognitive impairment was observed in comparison with healthy controls (mean score = 91.3 %, SD = 5.5 %), in Alzheimer's disease (mean score = 70.3 %, SD = 9.7 %; U = 939.0, $p < .001$), semantic dementia (mean score = 70.8 %, SD = 9.4 %; U = 392.0, $p < .001$) and corticobasal syndrome (mean score = 79.6 %, SD = 14.3 %; U = 172.0, p = .017). As shown in Figure 1, Alzheimer patients had mainly severe memory and orientation disorders. In contrast, patients with semantic dementia performed worse in tasks assessing language and semantic memory but they could answer orientation questions. Patients with corticobasal syndrome had constructional deficits due to motor disorders but other dimensions were spared in most patients.

Finally, in the tracking task, Alzheimer patients (mean score = 74.9, SD = 34.0) were slower than healthy controls (mean score = 107.6, SD = 37.2; U = 629.5, $p < .001$) while this was not the case for patients with semantic dementia (mean score = 85.9, SD = 39.6; U = 141.5, p = .22). Missing data for three out of seven cases (due to motor deficits) did not allow reliable comparison as regards patients with corticobasal syndrome but they appeared clearly

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slower than healthy controls (mean score = 59.0, SD = 33.1). In the healthy control group, no correlation was found between processing speed and experimental measures (all *p*s > .26).

< Insert Figure 1 about here >

3.2. Comparisons between groups

As shown in Figure 2, all patient groups exhibited tool use disorders, whether in Single Tool Use or Real Tool Use. Compared to healthy controls, patients with semantic dementia had difficulties in Functional/Contextual Associations but not in Mechanical Problem Solving. The reverse pattern was observed in patients with corticobasal syndrome. On average, healthy controls selected 0.7 irrelevant tools in the Real Tool Use task (range = 0-3) against 1.8 in Alzheimer patients (range = 0-6; U = 660.5, p = .04) and 3.1 in patients with semantic dementia (range = 0-13; U = 367.5, p = .027); the difference was not significant as regards corticobasal syndrome (mean = 0.7, range = 0-2; U = 113.0, p = .92). Besides, SD patients scored significantly higher than AD patients in Mechanical Problem Solving (U = 384.5, p = .011) but tended to have lower scores than other patients groups in Functional/Contextual Associations (both *p*s = .084). Other differences were not significant (all *p*s > .08).

In Real Tool Use (Choice), all patient groups had lower performance than healthy controls (all *p*s < .022). In the No-choice condition, the difference was significant only in CBS and AD patients (both *p*s < .011) but not in SD patients despite a tendency toward significance (W = 138.5, p = .057). In the Choice condition of Mechanical Problem Solving, AD and CBS patients performed worse than healthy controls (both *p*s < .02), contrary to SD patients (W = 167.0, p = .20). The same pattern was observed in the No-choice condition.

< Insert Figure 2 about here >

3.3. Comparisons within groups

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Within-subject differences were calculated in order to highlight the following effects: 1) presence/absence of objects (i.e., Single Tool Use versus Real Tool Use, No-choice condition); 2) choice versus no-choice conditions, in both Real Tool Use and Mechanical Problem Solving; 3) familiarity versus novelty of tools and objects (i.e., Real Tool Use versus Mechanical Problem Solving). To this end, we used the following formula: [(Task 2 – Task 1) / Task 1]. With this method, each case was compared to himself or herself. Results are displayed in Figure 3. Within-group comparisons were performed on composite scores (with Wilcoxon tests) in order to assess simple task effects, then between-group comparisons were performed on this difference (with Mann-Whitney U-tests) in order to determine whether task effects were specific to a certain group.

The choice/no-choice difference was significantly higher in SD patients than in CBS patients ($U = 107.5$, $p = .002$) and healthy controls ($U = 467.0$, $p < .001$) and there was a trend toward a significant difference when comparing SD and AD patients ($U = 343.0$, $p = .067$). Likewise, this difference was higher in the AD group than in the CBS group ($U = 189.5$, $p = .007$). As regards Mechanical Problem Solving, the mean improvement between choice and no-choice conditions was virtually the same in all groups (Kruskal-Wallis test, $p = .31$). The difference of performance between Real Tool Use and Mechanical Problem Solving was significantly higher in the SD group than in healthy controls ($U = 400.0$, $p < .001$) or Alzheimer patients ($U = 329.5$, $p = .06$), while no difference was found between CBS patients and healthy controls ($U = 140.5$, $p = .23$). Besides, as can be seen in Figure 2, patients with Alzheimer's disease performed slightly better in Functional/Contextual Associations than in Mechanical Problem Solving ($W = 371.0$, $p = .016$) whereas patients with semantic dementia exhibited the reverse pattern ($W = 11.0$, $p = .001$). The difference did not reach significance in the CBS group ($W = 24.0$, $p = .10$).

< Insert Figure 3 about here >

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3.4. Correlational structure and factor analysis

3.4.1. Correlation matrixes

Correlation matrixes are displayed in Table 2 for patients with Alzheimer's disease and semantic dementia. No significant correlation was found in patients with corticobasal syndrome after application of Holm's adjustment for multiple tests (all *p*s > .14). No correlation was found between processing speed assessed by the tracking task and experimental measures, in none of the patients groups (all *p*s > .068).

< Insert Table 2 about here >

3.4.2. Principal component analysis

Before going further, it should be acknowledged that due to number of measurements the use of Principal Component Analysis is illustrative at most. Three components were found (eigenvalues = 1.97, 0.67 and 0.34). The first one could be interpreted as the overall performance and explained 66.0 % of data dispersion. It was correlated with all quantitative variables (all *p*s < .001), and it distinguished the AD group from the HC group ($p < .001$). The second dimension accounted for 22.5 % of data dispersion and opposed on the one hand, Mechanical Problem Solving (No-choice) and on the other hand, Functional/Contextual Associations and Single Tool Use. This dimension distinguished the SD group from other groups ($p < .001$). Finally, the third component explained 11.4 % of data dispersion and opposed the Choice and No-choice conditions of Mechanical Problem Solving ($p < .001$). Loadings are available in Supplementary Table 2.

Results of the PCA are displayed in Figure 4. On the variables factor map, long vectors are variables for which data dispersion is well explained by the two axes, and the relative directions of vectors indicate associations or dissociations between variables. In this case, Mechanical Problem Solving and Functional/Contextual Associations are clearly dissociated, with Real Tool Use and Single Tool Use being in an intermediate position between these

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tasks. On the individuals factor map, groups located on the left had poor overall performance, while groups located at the top performed better in Functional/Contextual Associations than in Mechanical Problem Solving. Here, it is clear that SD patients had better performance in the latter than in the former.

< Insert Figure 4 about here >

3.5. PROFILES

As clinical heterogeneity may lead to power problems and distorted inferences in statistical group analyses, a profile analysis was performed. Table 3 provides three key pieces of information: 1) patients with Alzheimer's disease are more frequently impaired in Mechanical Problem Solving than patients with semantic dementia; 2) dissociations between problem solving and picture matching are more frequent in the SD than in the AD group; 3) Real Tool Use and Functional/Contextual Associations are often concurrently impaired in the SD group but not in the CBS group. In addition, Table 4 reveals a double dissociation between semantic dementia and corticobasal syndrome as regards Mechanical Problem Solving and Functional/Contextual Associations (Fisher exact test on 2x4 table, $p = .035$). The same is true between semantic dementia and Alzheimer's disease (Fisher exact test on 2x4 table, $p = .001$) so group effects are confirmed at the individual level. Finally, a deficit in both Mechanical Problem Solving and Functional/Contextual Associations is always associated with tool use disorders, regardless of the disease.

< Insert Table 3 about here >

< Insert Table 4 about here >

IV. DISCUSSION

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The purpose of the present study was to describe tool use disorders in Alzheimer's disease, semantic dementia and corticobasal syndrome with regard to the semantic and technical reasoning hypothesis. We shall now discuss the main results in each patient group and their relationship with neuropsychological data.

4.1. Relationships between clinical data and tool use disorders

Patients were recruited with reference to international consensus criteria and the neuropsychological assessment produced data consistent with diagnosis (Figure 1). All patient groups exhibited tool use disorders so they were all likely to have reduced autonomy when using tools in everyday life. However, demographic data and the MMSE score failed to predict tool use abilities, as previously suggested (Lesourd et al., 2013). Although it is intuitive that as the disease progresses, the growing number of cognitive defects may generate tool use disorders (see for example Ochipa et al., 1992), our data imply that some patients may exhibit tool use disorders even in the very beginning of the disease. In Alzheimer's disease, it might depend on the presence/absence of non-memory cognitive disorders but here, most patients exhibited the amnestic type of the disease (see McKhann et al., 2011). Future studies may compare different phenotypes of Alzheimer's disease.

Within-group comparisons and correlations also confirm that Single Tool Use alone cannot predict real tool use abilities (Baumard et al., 2014; Lesourd et al., 2013). In all likelihood, this task is a simulation of real tool use, and hence calls for technical reasoning and semantic memory, but also for additional cognitive mechanisms that were beyond the scope of this study. For example, working memory might be needed to imagine and maintain the object to be used with the tool, as it has been demonstrated for pantomime of tool use (Bartolo, Cubelli, Della Sala, & Drei, 2003). In addition, it must be acknowledged that the clinical rating is frequently more ambiguous for Single Tool Use than for Real Tool Use since only the latter provides clinicians with objective evidence of success or failure. For all these

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reasons, the most reliable way to detect tool use disorders is probably to ask patients to actually use tools and objects.

4.2. TOOL USE DISORDERS IN SEMANTIC DEMENTIA

4.2.1. CONFORMITY OF DATA WITH HYPOTHESES

The semantic memory hypothesis predicted positive correlations between performance in Functional/Contextual Associations on the one hand, and performance in Single Tool Use and Real Tool Use (Choice condition) on the other hand. In contrast, Real Tool Use (No-choice condition) was expected to be easier. The technical reasoning hypothesis predicted positive correlations between performance in Mechanical Problem Solving tasks and both Single Tool Use and Real Tool Use (both conditions). Regarding these predictions, the fact that patients with semantic dementia had normal performance in Mechanical Problem Solving immediately rules out the technical reasoning hypothesis in this group, while results are consistent with the semantic memory hypothesis. In comparison with healthy controls, patients with semantic dementia have difficulties with Single Tool Use, Real Tool Use and Functional/Contextual Associations but not with Mechanical Problem Solving. In Real Tool Use, the Choice condition was more difficult than the No-choice condition. This deficit in tool selection seems to be specific to familiar tools since it was not observed, or not in the same proportions, in Mechanical Problem Solving (Figure 3). Furthermore, the latter was easier than both Real Tool Use and Functional/Contextual Associations so it is reasonable to assume that the core deficit is at the level of semantic memory rather than technical reasoning or tool application. To sum up, patients with semantic dementia had difficulties in selecting present tools as well as in imagining absent objects.

4.2.2. SEMANTIC MEMORY VERSUS TECHNICAL REASONING

In the framework of the technical reasoning hypothesis, tool application is a synonym for utilization and depends on this type of reasoning. In our design, Real Tool Use (choice)

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implied tool selection and tool application while Real Tool Use (no choice) called for tool application only. On this ground, the following results may be highlighted. First, patients with semantic dementia had tool selection deficit. Second, they significantly improved in the No-choice condition compared with the Choice condition. Third, they did not demonstrate tool application deficit in Mechanical Problem Solving. As a conclusion, it can be argued that tool selection is lost whereas tool application is relatively spared. In the field of apraxia, dissociations have already been demonstrated between tool application and knowledge about tool function in stroke patients (see Buxbaum & Saffran, 2002) and Alzheimer patients (Moreaud et al., 1998). It has been proposed that the former relies on technical reasoning while the latter relies on semantic memory, and that both are involved in the use of familiar tools (Goldenberg & Hagmann, 1998; Osiurak, 2014; Osiurak et al., 2011; Randerath, Goldenberg, Spijkers, Li, & Hermsdörfer, 2011). Indeed, previous studies found that some tool use tasks call for semantic memory whereas other call for problem solving skills depending on transparency of mechanical relationships between tools and objects or between different elements of the same device (Hartmann et al., 2005). Notably, technical reasoning may be important to use tool/object pairs (Goldenberg & Hagmann, 1998). Besides, patients with severe semantic loss may remain able to produce tool-related actions that do not correspond to the prototypical use but that are still compatible with the tool's physical properties (Hodges et al., 2000; Osiurak et al., 2008). Consistent with this hypothesis, our data revealed a semantic memory/technical reasoning axis that distinguished patients with semantic dementia from other groups.

In all likelihood, patients with semantic dementia had tool selection disorders due to the semantic memory loss but spared tool application thanks to compensations by technical reasoning. The latter may inform individuals about *how to* carry out the action by bringing out possible tasks (e.g., inserting, turning, lifting the key; Osiurak, 2014; Osiurak et al., 2010,

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2011). However, taken in isolation these tasks are meaningless in that they do not have any purpose *per se*; they are only technical potentials (e.g., participants could rub or strike the padlock with the key, or even lift the padlock and push the key). On the contrary, semantic memory, which is certainly highly culture-dependent, may inform individuals about *what* to do (or why) but not about how to do it, thus indicating which technical potentials should be considered relevant or irrelevant when using familiar tools and objects, particularly in light of the examiner's expectations (Osiurak, 2014; Osiurak & Badets, 2016). In this view, patients with semantic dementia may be able to identify technical potentials but not the purpose of actions (of which they were not informed). Subsequently, they may select tools depending on tool/object technical complementarity but not in accordance with cultural expectations. As an analogy, these patients are known to process common words as unfamiliar words while reading or writing irregular words and doing so they make errors (e.g., "caught" written as "cort"; Neary et al., 1998), but they remain able to read regular words. Interestingly, the two-way hypothesis (Milner & Goodale, 1995; Ungerleider & Mishkin, 1982) distinguished a dorsal, parietal stream dedicated to the guidance of action and a ventral, temporal stream dedicated to object recognition and representation. Back to our topic, technic-based actions may rely at least on the left parietal lobe (Goldenberg, 2009) whereas culture-based choices may rely on ventral, temporal lobes (see also Hodges et al., 1999).

4.3. Tool use disorders in corticobasal syndrome

4.3.1. Conformity of data with hypotheses

As with other groups, patients with corticobasal syndrome exhibited tool use disorders but the underlying reasons are different. This group showed significant impairment in Mechanical Problem Solving but not in Functional/Contextual Associations. Besides, at the individual level, deficits were less frequent in the former than in the latter (i.e., 29 % against 72 %, respectively). Correlations did not reach significance, perhaps because of the low

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sample size. However, single-case analyses demonstrated that problem solving deficits were always associated with impairment in Real Tool Use. In addition, dissociation was more frequent between Real Tool Use and Functional/Contextual Associations than between the former and Mechanical Problem Solving (Table 4). Interestingly, in Real Tool Use, the impairment did not take the form of tool selection deficits (Figure 3) suggesting tool application was at stake. On the whole, the technical reasoning hypothesis is more plausible than the semantic memory hypothesis, which is logical considering that lesions are more frequent in the frontal and parietal lobes than in the temporal lobes (Litvan et al., 1997). Interestingly, this cognitive pattern demonstrates a double dissociation of problem solving skills and semantic knowledge in corticobasal syndrome and semantic dementia. Notwithstanding, this finding should be interpreted with caution because tool application deficits can be explained in different ways.

4.3.2. TOOL APPLICATION VERSUS TECHNICAL REASONING

Difficulties in tool application can be the consequence of technical reasoning deficits following parietal lobe lesions as it has been described in stroke patients (Goldenberg, 2009; Jarry et al., 2013). Such patients are neither able to select nor to use familiar tools (Goldenberg & Hagmann, 1998). Interestingly, Spatt et al. (2002) described five patients with corticobasal syndrome who had deficits in the selection of novel tools, which may suggest that they did have technical reasoning deficits. However, we did not distinguish scores for tool application and tool selection in Mechanical Problem Solving, and we used combined scores including raw scores and time completion. It turns out that corticobasal degeneration is characterized by bilateral, asymmetric motor deficits due to frontal lobe lesions (Armstrong et al., 2013; Litvan et al., 1997). In addition, according to conception/production models of apraxia (Osiurak, 2014; Rothi et al., 1991, 1997; Roy & Square, 1985), efficient application of tools is not possible in case of conception deficits, and errors in tool application may be

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accounted for either by isolated motor deficits or technical reasoning deficits, depending on patients. Indeed, it has been demonstrated that the kinematic features of movement depend on the type of gesture to be done (Hermsdörfer, Hentze, & Goldenberg, 2006). Therefore, tool application deficits in this population could be due to either motor deficit or conception (i.e., technical reasoning) deficit. We shall now discuss these two hypotheses.

According to the motor hypothesis, the deficit should be exclusively at the level of tool application while tool selection should be spared. Motor deficits should lead to poor performance in any task involving tool use while other tasks should be spared. Likewise, the "motor" dimension should play a role in both choice and no-choice conditions since both scores took tool application into account. Our data are consistent with this prediction since patients had impaired performance in Single Tool Use, Real Tool Use and Mechanical Problem Solving but not in Functional/Contextual Associations. Besides, the Choice/No-choice difference was not significant in Mechanical Problem Solving. From this point of view, the motor hypothesis is sufficient to explain tool use disorders in corticobasal syndrome.

A deficit in technical reasoning should prevent patients from using as well as selecting both novel and familiar tools, as is the case in stroke patients (Goldenberg & Hagmann, 1998; Jarry et al., 2013). Some of our results are in line with this interpretation since CBS patients had impairment in both conditions of Mechanical Problem Solving and Real Tool Use. However, they remained able to select familiar tools, yet this would be very unlikely to occur in case of technical reasoning deficit (see Goldenberg & Hagmann, 1998). On this ground, it can be assumed that their difficulties in tool application were due to motor deficit rather than conception (i.e., technical reasoning) deficit.

At this point, our results do not confirm previous findings (Spatt et al., 2002), perhaps because of intrinsic difficulties in diagnosing corticobasal degeneration. We tended to select

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patients with relatively isolated motor deficits: Five out of seven patients had normal cognitive functioning, and two additional patients were excluded from the sample due to diagnosis uncertainty. In contrast, Spatt et al. found a semantic knowledge breakdown in three out of five patients, which is not typical of the disease. So, lesions were presumably more diffuse in their patients and hence they were more likely to have tool selection deficit due to semantic loss or technical reasoning disorders. To conclude, in order to overcome methodological limitations, future research may analyze problem-solving strategies independently from motor deficits in order to disentangle the motor and technical dimensions.

4.4. Tool use disorders in Alzheimer's disease

4.4.1. Conformity of data with hypotheses

Results regarding Alzheimer patients were more delicate to interpret. Based on the technical reasoning hypothesis, a deficit in Mechanical Problem Solving should be associated with a deficit in Single Tool Use and Real Tool Use. This hypothesis appears relevant seeing low performance of Alzheimer patients in Mechanical Problem Solving and correlations between the latter and Real Tool Use. For all that, the semantic memory hypothesis prediction is also relevant seeing positive correlations between Real Tool Use and Functional/Contextual Associations. Besides, these patients exhibited tool selection deficits, although these were not clearly specific to Real Tool Use and less dramatic than in semantic dementia. As a whole, the performance pattern of Alzheimer patients can fit either the semantic memory or the technical reasoning hypotheses (or both).

Two conclusions may nonetheless be drawn. First, in the Alzheimer group, deficits are slightly more frequent in Mechanical Problem Solving than in Functional/Contextual Associations (i.e., 66 % against 45 %, respectively). Second, Mechanical Problem Solving deficits are more frequent in Alzheimer's disease than in semantic dementia (i.e., 66 % against 31 %, respectively) but they are not specific since such deficits are even more frequent in

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corticobasal degeneration (i.e., 72 %). In view of these data, even though tool use disorders in Alzheimer's disease have long been considered to result from semantic memory loss (see for example Blondel et al., 2001), the recently proposed concept of technical reasoning (Osiurak et al., 2010, 2011) puts this interpretation into perspective. Actually, using a semantic memory/technical reasoning axis, Alzheimer's disease is closer to corticobasal syndrome than to semantic dementia (Figure 4).

Nonetheless, it is not certain that Alzheimer patients consistently exhibit technical reasoning disturbances. Historically, this type of deficit has been studied in stroke patients with lesions in the left hemisphere (Goldenberg, 2009; Jarry et al., 2013). Clinically, these patients cannot manipulate simple tool/object pairs, and they may grasp tools in an ineffective way (e.g., the blade of a knife; see also Randerath, Goldenberg, Spijkers, Li, & Hermsdörfer, 2010) and commit "serious" errors (e.g., a fork to eat soup; see Goldenberg & Hagmann, 1998; Sirigu, Duhamel, & Poncet, 1991). Yet, the same has not been observed in neurodegenerative diseases, and nor did we. Interestingly, qualitative analyses of mechanical problem solving strategies in stroke patients (Osiurak et al., 2013) and patients with neurodegenerative diseases (Lesourd et al., 2016) revealed that Alzheimer patients use the same strategies as healthy controls while patients with left brain-damage cannot engage in any problem-solving strategy. So, it can be assumed that mechanical problem solving deficits in Alzheimer patients are not the result of tool-specific cognitive impairments but rather of a broad impairment of problem solving skills. Future research may investigate this distinction.

4.4.2. The issue of heterogeneity

In our results, high heterogeneity and double dissociations were observed within the Alzheimer group, which is quite logical as this disease is characterized by a high degree of heterogeneity whether in progression, imaging or clinical manifestations (Komarova & Thalhauser, 2011; Lam, Masellis, Freedman, Stuss, & Black, 2013). Heterogeneity can be

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understood in three ways. First, tool use disorders in Alzheimer patients may be the consequence of cognitive impairments that were not taken into account in the present work (e.g., general problem solving skills). Second, heterogeneity between patients might be the consequence of heterogeneity *within* patients in that cognitive mechanisms cannot be reliably measured with a single assessment in Alzheimer's disease (Knotek, Bayles, & Kaszniak, 1990). Unfortunately, in our design, patients were assessed only once, as is the case in most studies. Third, a lot of patients had various cognitive impairments (i.e., in both Mechanical Problem Solving and Functional/Contextual Associations) and global slowness. This echoes recent studies that consider Alzheimer's disease as a disconnection syndrome between brain regions that remain relatively operational (Delbeuck, Van der Linden, & Collette, 2003). According to this hypothesis, patients with Alzheimer's disease may have a deficit of access to cognitive functions that are altogether spared, and this may prevent the substitution of altered functions by spared ones. This may lead to global hypo-functioning and slowness as well as to high heterogeneity seeing that brain connectivity is likely to be altered in a very singular way between patients.

4.5. Conclusion

The most startling results of the present work can be summarized as follows: (1) We developed an innovative methodology which overcomes the issue of ceiling effects in the field of apraxia (Lesourd et al., 2013); (2) All patients may have tool use disorders and the latter may appear even in the first stages of Alzheimer's disease, but the underlying reasons are different depending on the disease, which implies that future attempts to maintain autonomy should be grounded in detailed evaluation of tool use skills; (3) Tool use disorders can be described with a semantic memory/technical reasoning axis (see also Goldenberg & Spatt, 2009; for a similar dual-route hypothesis, see Hoeren et al., 2013, 2014). Although conceptual apraxia has been proposed to be the consequence of impairment of different types

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of knowledge (Ochipa et al., 1992), our results can be interpreted in light of a dichotomy between culture-based (ie., semantic memory) and performance-based (i.e., technical reasoning) mechanisms, which is close to the classical distinction between fluid and crystallized intelligence (Cattel, 1963; see also Osiurak et al., in press, for discussion about the link between technical reasoning skills and fluid/crystallized intelligence).

In semantic dementia, the loss of tool knowledge leads to difficulties in both imagining absent tools and selecting present tools while tool application is relatively spared thanks to mechanical problem solving skills (see also Hodges et al., 1999, 2000). In other words, patients may use tools in an unusual but effective way (see for example Osiurak et al., 2008) so perhaps caregivers should not expect them to conform to the prototypical use of tools as long as their method is technically relevant (e.g., buttering bread with the handle of a fork). Likewise, in these patients (and only them), pre-selection of tools by caregivers would be highly beneficial. In corticobasal degeneration, the reverse pattern was found, that is, tool application deficits without loss of semantic knowledge. Additional research is needed to disentangle the relative contributions of motor and technical reasoning deficits to tool use disorders. Finally, in Alzheimer's disease, both the technical reasoning and the semantic memory hypotheses appeared relevant depending on patients. Difficulties were frequent in Mechanical Problem Solving but not of the same nature as in stroke patients. All that being said, we found dissociations within each patient group and some patients exhibited tool use disorders without loss of semantic knowledge or problem solving deficits, therefore the technical/semantic axis is not sufficient and additional factors are likely to determine tool use skills in patients with neurodegenerative diseases (e.g., general problem solving skills, the singularity of brain organization and lesion patterns).

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REFERENCES

Armstrong, R.A., Cairns, N.J., & Lantos, P.L. (1999). Clustering of cerebral cortical lesions in patients with corticobasal degeneration. *Neuroscience Letter, 268*(1), 5-8.

Armstrong, M.J., Litvan, I., Lang, A.E., Bak, T.H., Bhatia, K.P., Borroni, B., … Weiner, W.J. (2013). Criteria for the diagnosis of corticobasal degeneration. *Neurology, 80*(5), 496-503.

Baddeley, A. (1996). Exploring the central executive. *The Quarterly Journal of Experimental Psychology, 49A*(1), 5-28.

Bartolo, A., Cubelli, R., Della Sala, S., & Drei, S. (2003). Pantomimes are special gestures which rely on wordking memory. *Brain and Cognition, 53,* 483-494.

Baumard, J., Osiurak, F., Lesourd, M., & Le Gall, D. (2014). Tool use disorders after left brain damage. *Frontiers in Psychology, 5,* 473. doi: 10.3389/fpsyg.2014.00473

Bieńkiewicz, M.M., Brandi, M.L., Goldenberg, G., Hughes, C.M., & Hermsdörfer, J. (2014). The tool in the brain: Apraxia in ADL. Behavioral and neurological correlates of apraxia in daily living. *Frontiers in Psychology, 5*, 353. doi: 10.3389/fpsyg.2014.00353

Blondel, A., Desgranges, B., De la Sayette, V., Schaeffer, S., Benali, K., Lechevalier, F., … & Eustache, F. (2001). Disorders in intentional gestural organization in Alzheimer's disease: Combined or selective impairment of the conceptual and production systems? *European Journal of Neurology, 8*(6), 629-641.

Boeve, B.F., Lang, A.E., & Litvan, I. (2003). Corticobasal degeneration and its relationship to progressive supranuclear palsy and frontotemporal dementia. *Annals of Neurology, 54*(5), S15-S19.

Bozeat, S., Lambon Ralph, M.A., Patterson, K., & Hodges, J.R. (2002). When objects lose their meaning: What happens to their use? *Cognitive, Affective and Behavioral Neurosciences, 2,* 236-251.

Braak, H, & Braak, E. (1991). Neuropathological stageing of Alzheimer-related changes. *Acta Neuropathologica, 82*(4), 239-259.

Braak, H, & Braak, E. (1995). Staging of Alzheimer's disease-related neurofibrillary changes.

ACCEPTED MANUSCRIPT

Neurobiology of Aging, 16(3), 278-284.

Braak, H., & Braak, E. (1997). Staging of Alzheimer-related cortical destruction. *International Psychogeriatrics, 9*(S1), 257-261.

Buxbaum, L.J., Kyle, K.M., Grossman, M., & Coslett, H.B. (2007). Left inferior parietal representations for skilled hand-object interactions: Evidence from stroke and corticobasal degeneration. *Cortex, 43*(3), 411-423.

Buxbaum, L.J., & Saffran, E.M. (2002). Knowledge of object manipulation and object function: Dissociations in apraxic and nonapraxic subjects. *Brain and Language, 82,* 179-199.

Buxbaum, L.J., Schwartz, M.F., & Carew, T.G. (1997). The role of memory in object use. *Cognitive Neuropsychology, 14,* 219-254.

Buxbaum, L.J., Shapiro, A.D., & Coslett, H.B. (2015). Reply: Apraxia: A gestural or a cognitive disorder? *Brain, 138*(3), e334.

Cattell, R.B. (1963). Theory of fluid and crystallized intelligence: A critical experiment. *Journal of Educational Psychology, 54*(1), 1-22.

Crawford, J.R., & Garthwaite, P.H. (2002). Investigation of the single case in neuropsychology: Confidence limits on the abnormality of tests scores and test scores differences. *Neuropsychologia, 40,* 1196-1208.

Crawford, J.R., & Garthwaite, P.H. (2005). Testing for suspected impairments and dissociations in single-case studies in neuropsychology: Evaluation of alternatives using Monte Carlo simulations and revised tests for dissociations. *Neuropsychology, 19,* 318-331.

Crutch, S.J., Rossor, M.N., & Warrington, E.K., (2007). The quantitative assessment of apraxic deficits in Alzheimer's disease. *Cortex, 43,* 976-986.

Delbeuck, X., Van der Linden, M., & Collette, F. (2003). Alzheimer's disease as a disconnection syndrome? *Neuropsychology Review, 13*(2), 79-92.

Derouesné, C., Lagha-Pierucci, S., Thibault, S., Baudoin-Madec, V., & Lacomblez, L. (2000).Apraxic disturbances in patients with mild to moderate Alzheimer's disease. *Neuropsychologia, 38,*1760–1769.

Dubois, B., Slachevsky, A., Litvan, I., & Pillon, B. (2000). The FAB: A Frontal Assessment

ACCEPTED MANUSCRIPT

Battery at bedside. *Neurology, 55*(11), 1621-1626.

Dumont, C., Ska, B., & Joanette, Y. (2000). Conceptual apraxia and semantic memory deficit in Alzheimer's disease: Two sides of the same coin? *Journal of the International Neuropsychological Society, 6*, 693-703.

Félician, O., Ceccaldi, M., Didic, M., Thinus-Blanc, C., & Poncet, M. (2003). Pointing to body parts: A double dissociation study. *Neuropsychologia, 41*(10), 1307-1316.

Folstein, M.F., Folstein, S.E., & McHugh, P.R. (1975). Mini-Mental State: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12,* 189-198.

Foundas, A.L., Leonard, C.M., Mahoney, S.M., Agee, O.F., & Heilman, K.M. (1997). Atrophy of the hippocampus, parietal cortex, and insula in Alzheimer's disease: A volumetric magnetic resonance imaging study. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology, 10*(2), 81-89.

Gagnepain, J. (1990). *Du vouloir dire. Du signe, de l'outil*. Bruxelles: De Boeck Université.

Galton, C.J., Patterson, K., Graham, K., Lambon-Ralph, M.A., Williams, G., Antoun, N., … Hodges, J.R. (2001). Differing patterns of temporal atrophy in Alzheimer's disease and semantic dementia. *Neurology, 57*(2), 216-225.

Goldenberg, G. (2009). Apraxia and the parietal lobes. *Neuropsychologia, 47,* 1449-1459.

Goldenberg, G., & Hagmann, S. (1998). Tool use and mechanical problem solving in apraxia. *Neuropsychologia, 36,* 581-589.

Goldenberg, G., Hartmann-Schmid, K., Sürer, F., Daumüller, M., & Hermsdörfer J. (2007). The impact of dysexecutive syndrome on use of tools and technical devices. *Cortex, 43,* 424–435.

Goldenberg, G., & Spatt, J. (2009). The neural basis of tool use. *Brain, 132,* 1645-1655.

Gorno-Tempini, M.L., Hillis, A.E., Weintraub, S., Kertesz, A., Mendez, M., Cappa, S.F., …& Grossman, M. (2011). Classification of primary progressive aphasia and its variants. *Neurology, 76*(11), 1006-1014.

Graham, N.L., Zeman, A., Young, A.W., Patterson, K., & Hodges, J.R. (1999). Dyspraxia in a patient with corticobasal degeneration: The role of visual and tactile inputs to action. *Journal of Neurology, Neurosurgery and Psychiatry, 67,* 334-344.

Hartmann, K., Goldenberg, G., Daumüller, M., & Hermsdörfer, J. (2005). It takes the whole brain to make a cup of coffee. *Neuropsychologia, 43*(4), 625-637.

Heilman, K.M., Maher, L.M., Greenwald, M.L., & Rothi, L.J.G. (1997). Conceptual apraxia from lateralized lesions. *Neurology, 49,* 457-464.

Hermsdörfer, J., Hentze, S., & Goldenberg, G. (2006). Spatial and kinematic features of apraxic movement depend on the mode of execution. *Neuropsychologia, 44*(10), 1642-1652.

Hodges, J.R., Bozeat, S., Lambon Ralph, M.A., Patterson, K., & Spatt, J. (2000). The role of conceptual knowledge in object use: evidence from semantic dementia. *Brain, 123*(9), 1913-1925.

Hodges, J.R., Patterson, K., Oxbury, S., & Funnell, E. (1992). Semantic dementia. Progressive fluent aphasia with temporal lobe atrophy. *Brain, 115,* 1783-1806.

Hodges, J.R., Spatt, J., & Patterson, K. (1999). "What" and "how": Evidence for the dissociation of object knowledge and mechanical problem-solving skills in the human brain. *Proceedings of the National Academy of Sciences of the United States of America, 96,* 9444-9448.

Hoeren, M., Kaller, C.P., Glauche, V., Vry, M.-S., Rijntjes, M., Hamzei, F., & Weiller, C. (2013). Action semantics and movement characteristics engage distinct processing streams during the observation of tool use. *Experimental Brain Research, 229,* 243-260.

Hoeren, M., Kümmerer, D., Bormann, T., Beume, L., Ludwig, V.M., Vry, M.-S., … & Weiller, C. (2014). Neural bases of imitation and pantomime in acute stroke patients: Distinct streams for praxis. *Brain, 137*(10), 2796-2810.

Jarry, C., Osiurak, F., Delafuys, D., Chauviré, V., Etcharry-Bouyx, F., & Le Gall, D. (2013). Apraxia of tool use: More evidence for the technical reasoning hypothesis. *Cortex, 49*(9), 2322-2333.

Knotek, P.C., Bayles, K.A., & Kaszniak, A.W. (1990). Response consistency on a semantic memory task in persons with dementia of the Alzheimer type. *Brain and Language, 38*(4), 465-475.

Komarova, N.L., & Thalhauser, C.J. (2011). High degree of heterogeneity in Alzheimer's disease progression pattern. *PLoS Computational Biology, 7*(11). Published online 2011 November 3. doi: 10.1371/journal.pcbi.1002251

ACCEPTED MANUSCRIPT

Lam, B., Masellis, M., Freedman, M., Stuss, D.T., & Black, S.E. (2013). Clinical, imaging, and pathological heterogeneity of the Alzheimer's disease syndrome. *Alzheimer's Research & Therapy, 5I*(1), 1. doi: 10.1186/alzrt155

Le Gall, D. (1998). *Des apraxies aux atechnies:* Propositions pour une ergologie clinique. Bruxelles: De Boeck Université.

Lesourd, M., Baumard, J., Jarry, C., Etcharry-Bouyx, F., Belliard, S., Moreaud, O., … & Osiurak, F. (2016). Mechanical problem-solving strategies in Alzheimer's Disease and Semantic Dementia. *Neuropsychology.*

Lesourd, M., Le Gall, D., Baumard, J., Croisile, B., Jarry, C., & Osiurak, F. (2013). Apraxia and Alzheimer's disease: Review and perspectives. *Neuropsychology Review, 23*, 234-256.

Litvan, I., Agid, Y., Goetz, C., Jankovic, J., Wenning, G.K., Brandel, J.P., … Bartko, J.J. (1997). Accuracy of the clinical diagnosis of corticobasal degeneration: A clinicopathologic study, *Neurology, 48*(1), 119-125.

McKhann, G.M., Knopman, D.S., Chertkow, H., Hyman, B.T., Jack, C.R., Kawas, C.H., … & Phelps, C.H. (2011). The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia, 7*(3), 263-269.

Milner, A.D., & Goodale, M.A. (1995). *The visual brain in action.* Oxford: Oxford University Press.

Moreaud, O., Charnallet, A., & Pellat, J. (1998). Identification without manipulation: A study of the relations between object use and semantic memory. *Neuropsychologia, 36,* 1295-1301.

Mummery, C.J., Patterson, K., Price, C.J., Ashburner, J., Frackowiak, R.S., & Hodges, J.R. (2000). A voxel-based morphometry study of semantic dementia: Relationship between temporal lobe atrophy and semantic memory. *Annals of Neurology, 47*(1), 36-45.

Neary, D., Snowden, J.S., Gustafson, L., Passant, U., Stuss, D., Black, S., …Benson, D.F. (1998). Frontotemporal lobar degeneration: A consensus on clinical diagnostic criteria. *Neurology, 51,* 1546-1554.

Ochipa, C., Rothi, L.J.G., & Heilman, K.M. (1992). Conceptual apraxia in Alzheimer's

ACCEPTED MANUSCRIPT

disease. *Brain, 115,* 1061-1071.

Okazaki, M., Kasai, M., Meguro, K., Yamaguchi, S., & Ishii, H. (2009). Disturbances in everyday life activities and sequence disabilities in tool use for Alzheimer disease and vascular dementia. *Cognitive and Behavioral Neurology, 22,* 215-221.

Orban, G., & Caruana, F. (2014). The neural basis of human tool use. *Frontiers in Psychology, 5,* 310.

Osiurak, F. (2014). The four constraints theory of human tool use: Mechanics, space, time, and effort. *Neuropsychology Review, 24,* 88-115.

Osiurak, F., Aubin, G., Allain, P., Jarry, C., Richard, I., & Le Gall, D. (2008). Object usage and object utilization: A single-case study. *Neurocase, 14,* 169-183.

Osiurak, F. & Badets, A. (2016). Tool use and affordance: Manipulation-based versus reasoning-based approaches. *Psychological Review*.

Osiurak, F., De Oliveira, E., Navarro, J., Lesourd, M., Claidière, N., & Reynaud, E. (in press). Physical intelligence does matter to cumulative technological culture. *Journal of Experimental Psychology: General.*

Osiurak, F., Jarry, C., & Le Gall, D. (2010). Grasping the affordances, understanding the reasoning: Toward a dialectical theory of human tool use. *Psychological Review, 117,* 517-540.

Osiurak, F., Jarry, C., & Le Gall, D. (2011). Re-examining the gesture engram hypothesis: New perspectives on apraxia of tool use. *Neuropsychologia, 49,* 299-312.

Osiurak, F., Jarry, C., Lesourd, M., Baumard, J., & Le Gall, D. (2013). Mechanical problem-solving strategies in left brain damaged patients and apraxia of tool use. *Neuropsychologia, 51,* 1964-1972.

Osiurak, F., & Le Gall, D. (2014). Apraxia: A gestural or a cognitive disorder? *Brain, 138,* e333.

Pillon, B., Blin, J., Vidailhet, M., Deweer, B., Sirigu, A., Dubois, B., & Agid, Y. (1995). The neuropsychological pattern of corticobasal degeneration: Comparison with progressive supranuclear palsy and Alzheimer's disease. *Neurology, 45*(8), 1477-1483.

Randerath, J., Goldenberg, G., Spijkers, W., Li, Y., & Hermsdörfer, J. (2010). Different left brain regions are essential for grasping a tool compared with its subsequent use.

ACCEPTED MANUSCRIPT

NeuroImage, 53, 171-180.

Randerath, J., Goldenberg, G., Spijkers, W., Li, Y., & Hermsdörfer, J. (2011). From pantomime to actual tool use: How affordances can facilitate actual tool use. *Neuropsychologia, 49,* 2410-2416.

Rapcsak, S.Z., Crosswell, S.C., & Rubens, A.B (1989). Apraxia in Alzheimer's disease. *Neurology, 39*(5), 664-668.

Reynaud, E., Lesourd, M., Navarro, J., & Osiurak, F. (2016). On the neurocognitive origins of human tool use: A critical review of neuroimaging data. *Neuroscience & BioBehavioral Reviews, 64,* 421-437.

Rothi, L.J.G., Ochipa, C., & Heilman, K.M. (1991). A cognitive neuropsychological model of limb praxis. *Cognitive Neuropsychology, 8,* 443-458.

Rothi, L.J.G., Ochipa, C., & Heilman, K.M. (1997). A cognitive neuropsychological model of limb praxis and apraxia. In L.J.G. Rothi & K.M. Heilman (Eds.), *Apraxia: The neuropsychology of action* (pp. 29-49). Hove: Psychology Press.

Roy, E.A. (1996). Hand preference, manual asymmetries, and limb apraxia. In D. Elliott & E.A. Roy (Eds.), *Manual asymmetries in motor performance* (pp. 215-236). Boca Raton: CRC Press.

Roy, E.A., & Square, P.A. (1985). Common considerations in the study of limb, verbal and oral apraxia. In E.A. Roy (Ed.), *Neuropsychological studies of apraxia and related disorders* (pp. 111-161). Amsterdam: Elsevier.

Shelley, B.P., Hodges, J.R., Kipps, C.M., Xuereb, J.H., & Bak, T.H. (2009). Is the pathology of corticobasal syndrome predictable in life? *Movement Disorders, 24*(11), 1593-1599.

Signoret, J.-L., Allard, M., Benoit, N., Bolgert, F., Bonvarlet, M., & Eustache, F. (1989). *Batterie d'Evaluation Cognitive – BEC 96.* Paris: Fondation IPSEN.

Silveri, M.C., & Ciccarelli, N. (2009). Semantic memory in object use. *Neuropsychologia, 47,* 2634-2641.

Sirigu, A., Duhamel, J.-R., & Poncet, M. (1991). The role of sensorimotor experience in object recognition. A case of multimodal agnosia. *Brain, 114,* 2555-2573.

Snowden, J., Bathgate, D., Varma, A., Blackshaw, A., Gibbons, Z., & Neary, D. (2001). Distinct behavioral profiles in frontotemporal dementia and semantic dementia. *Journal*

ACCEPTED MANUSCRIPT

of Neurology, Neurosurgery and Psychiatry, 70(3), 323-332.

Spatt, J., Bak, T., Bozeat, S., Patterson, K., & Hodges, J.R. (2002). Apraxia, mechanical problem solving and semantic knowledge. Contributions to object usage in corticobasal degeneration. *Journal of Neurology, 249*(5), 601-608.

Tsuchiya, K., Ikeda, K., Uchihara, T., Oda, T., & Shimada, H. (1997). Distribution of cerebral cortical lesions in corticobasal degeneration: A clinicopathological study of five autopsy cases in Japan. *Acta Neuropathologica, 94*(5), 416-424.

Ungerleider, L.G., & Mishkin, M. (1982). Two cortical visual systems. In D.J. Ingle, M.A. Goodale & R.J.W. Mansfield (Eds.). *Analysis of visual behaviour* (pp. 549-586). Cambridge, MA: The MIT Press.

Wechsler, D. (1997). *Wechsler Adult Intelligence Scale – 3rd Edition (WAIS-3).* San Antonio, TX: Harcourt Assessment.

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LEGENDS FOR FIGURES AND TABLES

Table 1

Data between brackets are standard deviations. Bold values are significant differences between patients and healthy controls.

Table 2

Bold values are significant correlations. RTU = Real Tool Use; MPS = Mechanical Problem Solving; FCA = Functional/Contextual Associations; Irr. T. = Number of irrelevant tools selected in Real Tool Use, Choice condition.

Table 3

Bold values are significant differences.

[a] A deficit means that individual's scores are significantly different ($p < .05$) from that of healthy controls.

[b] Classical and strong dissociations have been grouped to summarize the findings.

[c] All analyses were performed using two-by-two tables and Fisher exact test.

STU = Single Tool Use; RTU = Real Tool Use; MPS = Mechanical Problem Solving; FCA = Functional/Contextual Associations; AD = Alzheimer's disease; SD = Semantic dementia; CBS = Corticobasal syndrome.

Table 4

Values between brackets represent the percentage of these patients who exhibit a deficit in Real Tool Use (e.g., 32 % of Alzheimer patients had normal performance in Mechanical

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Problem Solving and Functional/Contextual Associations but 60 % of these 32 % exhibited deficits in Real Tool Use).

Figure 1

Black lines represent the mean performance of patient groups. Grey dotted lines represent the cut-off in healthy controls according to French normative data.

Figure 2

The boxplots display the interquartile range (minimum, first quartile, median, third quartile, and maximum). Cases with values more than 1.5 box lengths from the upper or lower edge of the box are displayed as outliers. The width of boxplots is proportional to the sample size. Results in the choice and no-choice conditions were averaged for Real Tool Use and Mechanical Problem Solving. HC = Healthy controls ; AD = Alzheimer's disease ; SD = Semantic dementia ; CBS = Corticobasal syndrome. Comparisons with healthy controls are significant with * $p < .05$; ** $p < .01$; *** $p < .001$.

Figure 3

Bars represent the percentage of improvement between task 1 and task 2 (e.g., patients with semantic dementia dramatically improved in the No-choice condition of Real Tool Use). It is called an improvement because task 1 has always been proposed before task 2. Between-group comparisons are detailed in the text. Within-group comparisons (Wilcoxon tests) performed on composite scores were significant with * $p < .05$; ** $p < .01$; *** $p < .001$.

Figure 4

Right panel: Solid lines are active variables whereas dotted lines are additional variables. Details are provided in the text. STU = Single Tool Use; RTU.C = Real Tool Use

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(choice); RTU.NC = Real Tool Use (no choice); MPS.C = Mechanical Problem Solving (choice); MPS.NC = Mechanical Problem Solving (no choice); PS = Processing speed.

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FOOTNOTES

There is no footnote in the manuscript.

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TABLE 1. DEMOGRAPHIC DATA

	Healthy controls n = 31	Alzheimer's disease n = 31	Semantic dementia n = 16	Corticobasal syndrome n = 7
Gender (women/men)	21/10	21/10	8/8	3/4
Age (years)	75.6 (6.4)	77.1 (7.5)	**67.3 (7.4)**	71.3 (8.6)
Education (years)	12.4 (4.7)	**9.0 (4.4)**	12.1 (2.9)[a]	10.3 (3.4)

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TABLE 2. CORRELATION MATRIXES

	Alzheimer's disease				Semantic dementia			
	RTU	MPS	FCA	Irr. T.	RTU	MPS	FCA	Irr. T.
Single Tool Use	**.49**	.43	.35	.14	.52	.03	.51	**- .65**
Real Tool Use		**.75**	**.61**	- .28		.31	**.95**	**- .77**
Mechanical Problem Solving			**.69**	- .31			.14	- .23
Functional/Contextual Assoc.				.15				**- .68**

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TABLE 3. PATIENTS IMPAIRMENTS AND DISSOCIATIONS ACCORDING TO CRAWFORD AND GARTHWAITHE'S (2002, 2005) CRITERIA

	Per cent of patients showing a deficit[a]				Per cent of dissociations[b]		
	STU	RTU	MPS	FCA	RTU-MPS	RTU-FCA	MPS-FCA
AD (%)	17/31 (55)	25/31 (81)	20/31 (65)	14/31 (45)	6/31 (19)	8/31 (26)	1/31 (03)
SD (%)	10/16 (63)	10/16 (63)	5/16 (31)	12/16 (75)	7/16 (44)	1/16 (06)	7/16 (44)
CBD (%)	4/7 (57)	6/7 (86)	5/7 (71)	2/7 (29)	1/7 (14)	4/7 (57)	1/7 (14)
AD vs SD (*p*)[c]	.758	.289	**.037**	.067	.095	.138	**.001**
AD vs CBS (*p*)[c]	1	1	1	.675	1	.176	.338
SD vs CBS (*p*)[c]	1	.366	.168	.065	.345	**.017**	.345

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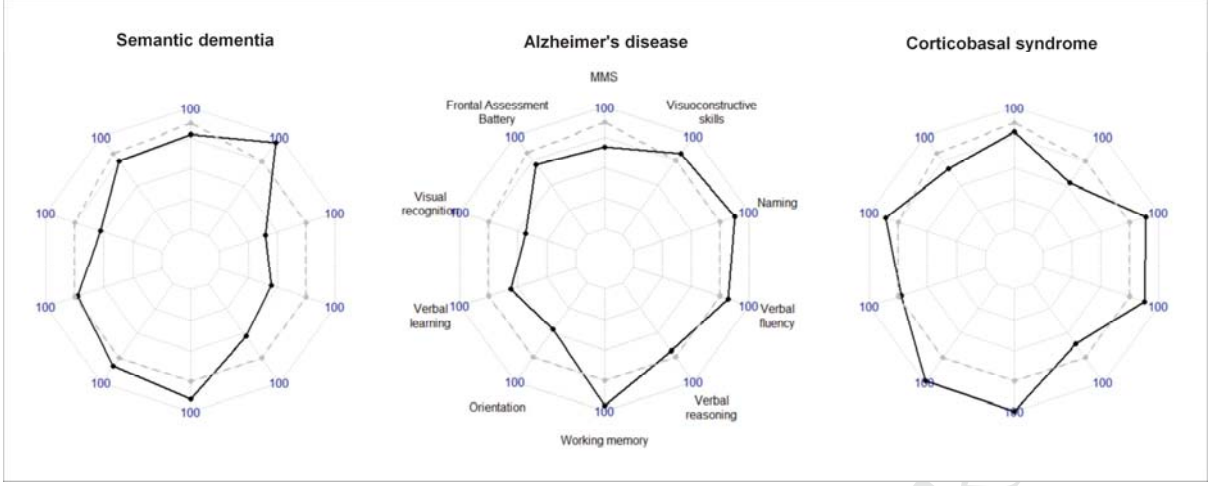
12 # TABLE 4. EFFECTS OF COGNITIVE PROFILES ON TOOL

13 # USE ABILITIES

Mechanical Problem Solving	Functional/Contextual Associations	Per cent of patients corresponding to this profile					
		Alzheimer's disease		Semantic dementia		Corticobasal syndrome	
Impaired	Normal	23 %	(71 %)	6 %	(0 %)	43 %	(100 %)
Normal	Impaired	3 %	(100 %)	50 %	(75 %)	0 %	(-)
Impaired	Impaired	42 %	(100 %)	25 %	(100 %)	29 %	(100 %)
Normal	Normal	32 %	(60 %)	19 %	(50 %)	29 %	(50 %)

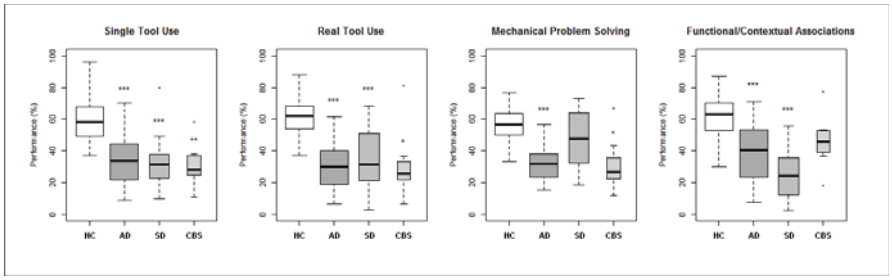
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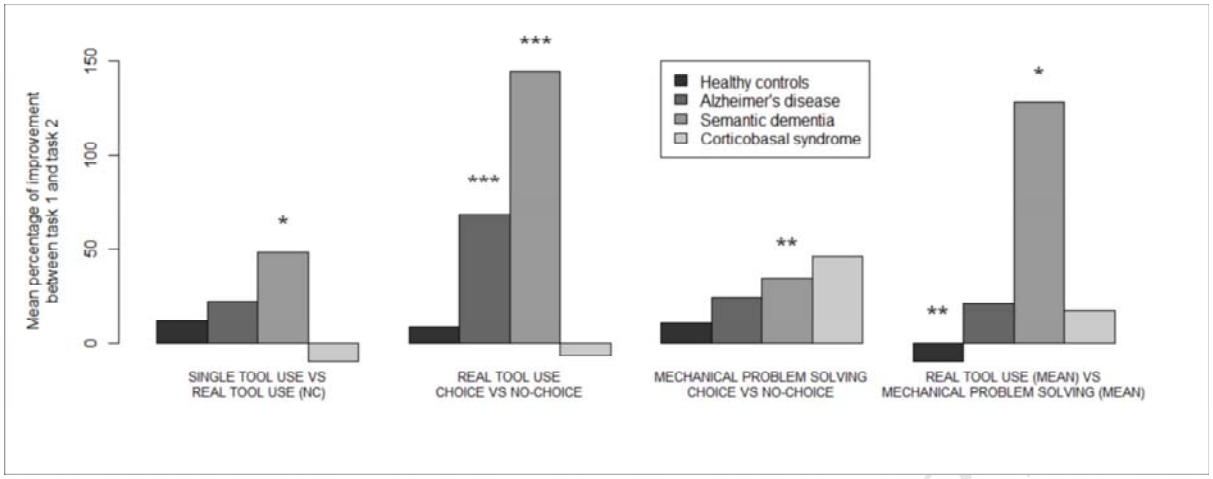


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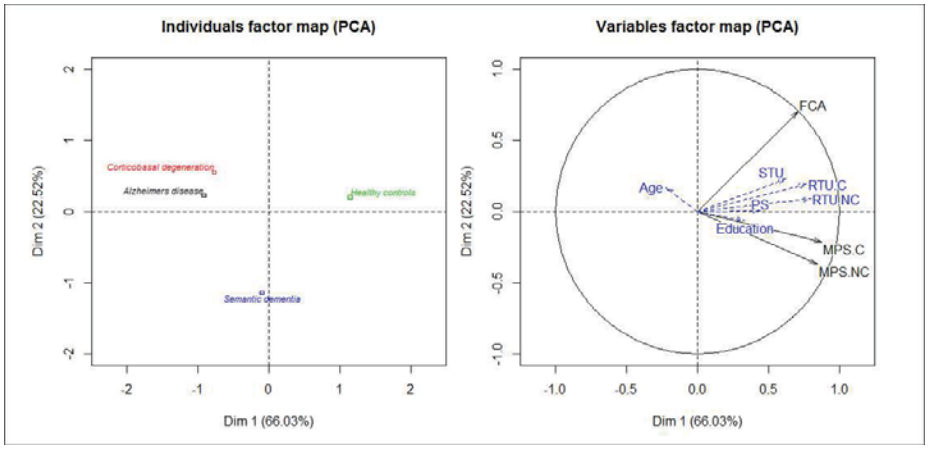


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