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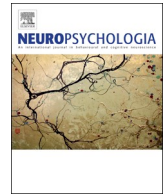
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The – weak – role of memory in tool use: Evidence from neurodegenerative diseases

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ABSTRACT

Objective: Although tool use disorders are frequent in neurodegenerative diseases, the question of which cognitive mechanisms are at stake is still under debate. Memory-based hypotheses (i.e., the semantic knowledge hypothesis and the manipulation knowledge hypothesis) posit that tool use relies solely on stored information about either tools or gestures whereas a reasoning-based hypothesis (i.e., the technical-semantic hypothesis) suggests that loss of semantic knowledge can be partially compensated by technical reasoning about the physical properties of tools and objects.

Method: These three hypotheses were tested by comparing performance of 30 healthy controls, 30 patients with Alzheimer's disease and 13 patients with semantic dementia in gesture production tasks (i.e., pantomime of tool use, single tool use, real tool use) and tool or gesture recognition tasks (i.e., functional and contextual matching, recognition of tool manipulation). Individual, item-based patterns of performance were analyzed to answer the following question: Could participants demonstrate the use of tools about which they had lost knowledge? With this aim in mind, “validation” and “rebuttal” frequencies were calculated based on each prediction.

Results: Predictions from the technical-semantic hypothesis were more frequently observed than memory-based predictions. A number of patients were able to use and demonstrate the use of tools for which they had lost either semantic or manipulation knowledge (or both).

Conclusions: These data lead to question the role of different types of memory in tool use. The hypothesis of stored, tool-specific knowledge does not predict accurately clinical performances at the individual level. This may lead to explore the influence of either additional memory systems (e.g., personal/impersonal memory) or other modes of reasoning (e.g., theory of mind) on tool use skills.

1. Introduction

1.1. Aims of the present study

Tool use disorders are a core symptom of apraxia (Goldenberg, 2009). They are frequently assessed by asking patients to use tools

under varying conditions (e.g., pantomime of tool use, single tool use, real tool use). However, the question of which cognitive mechanisms allow humans to use tools is still under debate. According to a widely accepted hypothesis, tool use depends on stored knowledge, whether about tool function (Roy and Square, 1985; Stamenova et al., 2012) or manipulation (Buxbaum, 2001, 2017; Rothi et al., 1991, 1997). These

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proposals rely on a memory-based epistemological approach, and as such they imply that loss of stored information is responsible for tool use disorders. If so, patients should be unable to use tools about which they have lost knowledge. The aim of the present study was to verify this hypothesis in Alzheimer's disease and semantic dementia since these patients are known to have long-term memory loss (Galton et al., 2001; Hodges et al., 1992a, 1992b). Besides, we contrasted this memory-based approach with a reasoning-based approach (Osiurak, 2014; Osiurak and Badets, 2016) according to which knowledge has a facilitating role but is not crucial to use actual tools. In terms of methodology, we developed an item-based methodology that is, comparing different production and recognition tasks involving the exact same tools and participants (see also Moreaud et al., 1998).

In the event of future meta-analyses or reviews of the literature, readers should be aware that this study concludes a series of studies from our research group on the topic of tool use disorders. Lesourd et al. (2013) published an extensive review of the literature on apraxia in Alzheimer's disease, demonstrating the need for more studies on this point mainly because of the discrepancy of methodologies employed in previous works. The study by Jarry et al. (2016) was the starting point of the present work for it displayed group data on a small sample of patients with Alzheimer's disease who exhibited impaired gesture recognition without clear-cut gesture production deficits. More recently, Baumard et al. (2016) compared the performance of patients with different neurodegenerative diseases (i.e., Alzheimer's disease, semantic dementia, corticobasal syndrome) on both tool use tasks and mechanical problem-solving tasks. They concluded that patients with semantic dementia demonstrated severe semantic loss but normal performance in mechanical problem-solving tasks, leading to context-dependent tool use disorders (i.e., impaired performance in pantomime of tool use, single tool use and multiple-object tasks but better performance with tool-object pairs). A second study of the same patients suggested that mechanical problem-solving deficits in Alzheimer patients are probably the consequence of general problem-solving deficits due to executive dysfunction (Baumard et al., 2018), contrary to what was previously observed in patients with left brain damage and posterior lesions (Goldenberg et al., 2007). Finally, the present work aims at testing memory-based versus reasoning-based predictions and hence focuses on differences between gesture recognition and production involving familiar tools using a more qualitative, item-based design which is a more demanding, fine-grained analysis than broad group data. To anticipate our results, this led us to conclude that none of the current hypotheses proposed in the international literature to account for tool use disorders is fully satisfying (even the one we defended in previous publications), which may pave the way for future innovative hypotheses.

1.2. The cognitive mechanisms of tool use

Overall, two theoretical approaches of tool use can be identified, that is, a memory-based approach and a reasoning-based approach (see also Osiurak and Badets, 2016). According to the memory-based approach, tool use is made possible by retrieving either explicit semantic knowledge about tool function (i.e., the semantic knowledge hypothesis; Roy and Square, 1985), or implicit manipulation knowledge about tool-related gestures (i.e., the manipulation knowledge hypothesis; Buxbaum, 2001; Rothi et al., 1997). According to the reasoning-based approach, tool use relies on online technical reasoning about the mechanical properties offered by tools and objects (i.e., the technical reasoning hypothesis; Le Gall, 1998; Osiurak et al., 2010, 2011) and semantic memory plays only a facilitating role in that it allows humans to perform canonical actions (e.g., a spoon can be used to eat, to dig or to play the battery, yet by convention it is used to eat; Baumard et al., 2016).

1.2.1. The semantic knowledge hypothesis

The semantic knowledge hypothesis posits that the core mechanism

of tool use is the ability to store and retrieve information about tool-object usual relationships (e.g., a hammer usually goes with a nail) and tool function (e.g., an axe and a saw share the same function; Roy and Square, 1985; for more recent accounts of semantic memory, see also Chen et al., 2017; Lambon Ralph et al., 2017). This type of information may extend to non-manipulable objects (e.g., a spaceship usually goes with a planet) and context (e.g., a hammer can be found in a garage or a workshop). It is thought to be stored in the ventral, temporal lobes (Goldenberg and Spatt, 2009).

Importantly, information in semantic memory has three main features (Tulving, 1972; Roy and Square, 1985). First, it is independent from context. As a consequence, it can be retrieved out of context, as in functional or contextual picture matching tasks. Second, it is relatively permanent. If information is lost, it cannot be retrieved regardless of the context (i.e., it is “permanently lost”), whether in picture matching or tool use tasks. Subsequently, impairment in picture matching tasks should always be associated with impairment in tool use tasks. Third, it is tool-specific, which means that the loss of knowledge should be observed in any task involving the same tool (e.g., if a patient does not know the function of a hammer, he should not be able to use it but he might be able to use a screwdriver; see for example Moreaud et al., 1998).

This being so, it is well known that some patients with severe semantic loss may remain able to use tools (Buxbaum and Saffran, 2002; Buxbaum et al., 1997; Hodges et al., 2000; Osiurak et al., 2008), suggesting that additional non-semantic factors may underlie tool use skills.

1.2.2. The manipulation knowledge hypothesis

The manipulation knowledge hypothesis posits that invariant features of already experienced gestures (e.g., hammering requires a broad oscillation from the elbow and a clench hand posture) are stored in a “gestural memory”, providing a processing advantage when performing familiar gestures (Buxbaum, 2001, 2017; Rothi et al., 1991, 1997). Gesture engrams are supposed to be stored in the left inferior parietal lobe (Buxbaum, 2001; Buxbaum et al., 2007; Buxbaum et al., 2003; Heilman et al., 1982; Van Elk et al., 2014; for an alternative account as to the potential role of temporal lobes in the storage of gesture engrams, see also Buxbaum, 2017).

Insofar as manipulation knowledge is hand-centered rather than tool-centered, gesture production does not depend on environmental constraints. In other words, the integrity of gesture engrams can be assessed by asking patients not only to use tools but also to demonstrate how they *would* use them (e.g., pantomime of tool use, single tool use) and to recognize their correct manipulation (i.e., recognition of tool manipulation; see for example Buxbaum et al., 2003). As for semantic memory, loss of manipulation knowledge as demonstrated by impaired recognition of tool manipulation should prevent patients from making transitive (i.e., tool-related) gestures regardless of the context (i.e., pantomime of tool use, single tool use, real tool use).

1.2.3. The technical-semantic hypothesis

Recent years have seen the emergence of the technical reasoning hypothesis according to which tool use in humans depends on the ability to infer potential mechanical actions from the structure of tools and objects (Goldenberg, 2009; Goldenberg and Hagmann, 1998; Osiurak et al., 2010, 2011). Importantly, these technical properties are abstract in nature and hence they are not tool-dependent (e.g., a wooden staff is “rigid” when used to draw in sand but “brittle” and “flammable” when used to make a fire). Neuroimaging studies (for a review, see Reynaud et al., 2016) and clinical studies on left brain-damaged patients (Goldenberg and Hagmann, 1998; Jarry et al., 2013; Osiurak et al., 2009) have reported that this mode of reasoning depends on the left inferior parietal lobe, and underlies the use of both familiar and novel tools (Goldenberg, 2009).

Actually, in this framework, technical reasoning and semantic

memory are seen as complementary cognitive mechanisms (Goldenberg, 2013; Osiurak, 2014) in that semantic memory may help individuals to select canonical tools, objects and actions among a wide range of potential tools, objects and mechanical actions (e.g., a stone, a mallet and a shoe are all technically relevant to drive a tent peg into the ground but most people would select the mallet). Besides, different tool use tasks may put differential demands on these cognitive processes depending on the transparency of mechanical constraints in the visual field (e.g., making coffee versus hammering; Hartmann et al., 2005). Pantomime of tool use and single tool use presumably put high demands on semantic knowledge so as to imagine the tool and the recipient of the action (e.g., in order to demonstrate the use of a hammer, it is necessary to imagine the nail and hence, to know that a hammer usually goes with a nail). Conversely, in real tool use technical reasoning alone may be sufficient in a number of instances (e.g., the number of potential mechanical actions is quite limited in presence of a bottle and a bottle-opener). This may explain why patients with semantic deficits have difficulties in demonstrating the use of single tools but show improved performance in presence of a recipient object (Baumard et al., 2016; Bozeat et al., 2002; Hodges et al., 2000). Since technical reasoning and semantic memory are thought to be complementary mechanisms, we shall now refer to the technical reasoning hypothesis as the “technical-semantic hypothesis” for the sake of clarity.

1.3. Tool use in neurodegenerative diseases

Tool use skills have been rarely investigated in the field of neurodegenerative diseases (e.g., Alzheimer's disease; Lesourd et al., 2013), which is a pity considering that the loss of autonomy is central to the diagnosis of dementia (McKhann et al., 2011). Besides, brain lesions are relatively circumscribed at early stages of the disease and they are slowly progressive, which may result in stable functional reorganization and allow testing for cognitive models (Felicjan et al., 2003). On this ground, it seems relevant to compare tool use skills in Alzheimer's disease and semantic dementia, especially since these patients are known to demonstrate knowledge deficits.

1.3.1. Alzheimer's disease

Patients with Alzheimer's disease may demonstrate episodic memory, language, visuo-spatial and/or executive dysfunction (McKhann et al., 2011). Semantic loss has already been documented (Hodges et al., 1992a, 1992b) even though some researchers have attributed this deficit to a failure of access rather than degraded knowledge (Rogers and Friedman, 2008). In the field of apraxia, this distinction has not been assessed, yet patients with Alzheimer's disease have difficulties in tasks designed to assess either semantic knowledge about tool function (Blondel et al., 2001; Negri et al., 2007a) or manipulation knowledge, especially recognition of tool manipulation (Chainay et al., 2006; Derouesné et al., 2000; Kato et al., 2000; Mozaz et al., 2006). Actually, it is quite logical considering that patients with Alzheimer's disease may have both temporal and parietal lesions (Braak and Braak, 1991, 1997; Foundas et al., 1997). For all that, the validity of the hypotheses mentioned in Section 1.2 has not been tested using an item-by-item analysis so far.

1.3.2. Semantic dementia

Patients with semantic dementia suffer from selective loss of semantic memory due to temporal lesions (Galton et al., 2001), which can be demonstrated in language processing (e.g., empty speech, loss of word meaning, semantic errors) and perception (e.g., loss of knowledge about the identity or the function of objects, prosopagnosia; Gorno-Tempini et al., 2011; Neary et al., 1998). At the same time, they experience a loss of semantic knowledge about tool function which has been related to impairments in Pantomime of Tool Use and Single Tool Use (Hodges et al., 2000; Moreaud et al., 1998). Interestingly,

predictions based on the technical-semantic hypothesis (i.e., better performance in real tool use than in either pantomime of tool use or single tool use, see section 1.4. Predictions) have been documented in these patients even though the authors did not relate this pattern to mechanical problem-solving skills (Bozeat et al., 2002). Surprisingly, this data has received only little attention and tool use disorders remain widely explained by a loss of either semantic or manipulation knowledge.

1.4. Predictions

In the field of apraxia, gesture production tasks (i.e., pantomime of tool use, single tool use, real tool use) assess both the conception and the production systems while picture matching and gesture recognition tasks (i.e., functional and contextual matching, and recognition of tool manipulation, respectively) assess the integrity of the conception system only (see for example Buxbaum, 2001). On this ground (and leaving aside elementary motor disorders which are not typical of Alzheimer's disease or semantic dementia), a deficit in gesture production may be observed without deficit of knowledge but loss of knowledge should always coincide with impaired gesture production.

Table 1 details predictions based on the semantic knowledge, manipulation knowledge, and technical-semantic hypotheses. According to the semantic memory hypothesis (Roy and Square, 1985), a deficit in either functional or contextual matching should lead to deficit in any tool-related production task (i.e., the “-“ symbols in Table 1). Likewise, the manipulation knowledge hypothesis posits that impaired gesture recognition will always be associated with impaired gesture production. Importantly, the reverse pattern (i.e., impaired knowledge but spared production) would stand against the memory-based approach. In particular, normal performance in real tool use should always lead to refute the memory-based hypotheses since the latter predict that real tool use relies on stored knowledge.

Pantomimes of tool use and single tool use have a more ambiguous status because they are not real tool use actions and hence they may call for additional cognitive processes (Bartolo et al., 2003; Baumard et al., 2014; Goldenberg et al., 2003). Therefore, in order to avoid excessively strict conclusions, we considered separately either “strict” or “relaxed” predictions. With regard to strict predictions, impairment in tasks assessing knowledge (i.e., picture matching or recognition of tool manipulation) was thought to provoke impairment in all production tasks

Table 1
Predictions.

| Hypothesis | | FCM | RTM | PTU | STU | RTU |
|-----------------------------------|------------|-----|-----|-------------------|-----|-----|
| Semantic knowledge hypothesis | | | | | | |
| Validation | Strict | - | - | - | - | - |
| | Relaxed 01 | - | - | - | + | - |
| | Relaxed 02 | - | - | + | - | - |
| Rebuttal | - | - | - | Any other pattern | | |
| Manipulation knowledge hypothesis | | | | | | |
| Validation | Strict | - | - | - | - | - |
| | Relaxed 01 | - | - | - | + | - |
| | Relaxed 02 | - | - | + | - | - |
| Rebuttal | - | - | - | Any other pattern | | |
| Technical-semantic hypothesis | | | | | | |
| Validation | Strict | - | - | - | - | + |
| | Relaxed 01 | - | - | - | + | + |
| | Relaxed 02 | - | - | + | - | + |
| Rebuttal | - | - | - | Any other pattern | | |

Notes. Rebuttal patterns correspond to cognitive profiles that refute the hypothesis, i.e., impaired performance in recognition tasks (i.e., either FCM or RTM) but normal performance in production tasks (i.e., PTU, STU, RTU). More detailed explanations are provided in the text. “+“: Normal performance; “-“: Impairment; FCM: Functional and Contextual Matching; RTM: Recognition of Tool Manipulation; PTU: Pantomime of Tool Use; STU: Single Tool Use; RTU: Real Tool Use.

without exception (i.e., pantomime of tool use, single tool use, real tool use). As regarded relaxed predictions, pantomime of tool use and single tool use were accepted as equivalent because both of these tasks require that participants make gestures out of context.

According to the reasoning-based approach, pantomime of tool use and single tool use put high demands on semantic memory in order to imagine absent tools. In contrast, there is no need to imagine tools and objects in real tool use so presumably this task can be solved thanks to technical reasoning. Subsequently, in case of semantic loss (as demonstrated by impaired functional and/or contextual matching), pantomime of tool use and/or single tool use should be impaired and yet real tool use may be spared thanks to compensations by mechanical problem solving skills (Hodges et al., 2000; see Table 1). This hypothesis would be refuted in other configurations, especially each time the “pure” semantic memory hypothesis is true because it would mean that semantic memory impairments are sufficient to account for tool use disorders with no need for reasoning-based mechanisms.

2. Materials and methods

2.1. Participants

A total of 73 subjects divided into three groups gave informed consent to participate in the study: **(Group 1)** 30 healthy controls (HC; 20 women, 10 men; mean age = 75.2, $SD = 6.0$; mean years of education = 12.4, $SD = 4.8$) recruited either in senior clubs or thanks to a dedicated research service. **(Group 2)** 30 patients with mild to moderate cognitive decline and probable Alzheimer's disease of the amnesic type (AD; 20 women, 10 men; mean age = 76.6, $SD = 7.1$; mean years of education = 9.1, $SD = 4.4$; mean MMSE score = 20.2/30, $SD = 2.8$; see McKhann et al., 2011); **(Group 3)** 13 patients with semantic dementia (SD; 6 women, 7 men; mean age = 67.4, $SD = 8.2$; mean years of education = 12.5, $SD = 2.9$). All patients were consecutively recruited from four neurological departments ([LOCATION REDACTED]). Patients with semantic dementia demonstrated progressive loss of meaning of words and objects and/or prosopagnosia, contrasting with relatively spared episodic memory, language processing and perception (Gorno-Tempini et al., 2011; Neary et al., 1998). The study was conducted in accordance with the Declaration of Helsinki and approved by local ethic committee (Western Protection to Persons Committee II, n° 2012/32).

Experienced neurologists dismissed vestibular, cerebellar, sensitive, pyramidal or parkinsonian syndrome in all patients. Imaging data showed no evidence of cerebrovascular damage and revealed hippocampal atrophy with or without background atrophy in Alzheimer's disease, and temporal polar atrophy or hypo-functioning in semantic dementia. Cerebro-spinal fluid biomarkers and extensive neuropsychological assessment confirmed the diagnosis. Exclusion criteria were previous history of neurological or psychiatric illnesses; a score ≤ 10 on the MMSE (Folstein et al., 1975) so as to avoid including patients with advanced neurodegenerative diseases; rheumatologic condition, mood disorders, medical treatment or comprehension impairment incompatible with performance. Patients with visual disturbances were asked to wear glasses.

Patients with dementia of the Alzheimer type and healthy participants were matched for gender and age (Mann-Whitney U test, $U = 375.0$, $p = .269$). Patients with semantic dementia were slightly younger than healthy controls and patients with Alzheimer's disease (both $ps < .009$), as is frequently the case due to differences in the age of onset (see for example Hodges et al., 1992a, 1992b; Snowden et al., 2001). Nevertheless, these differences were not prohibitive since the study was designed to assess between-item (i.e., within-subject) rather than broad between-group differences.

2.2. Neuropsychological assessment

In order to confirm diagnosis, all patients underwent a neuropsychological assessment with three standard tests:

- (1) The Mini-Mental State Examination (Folstein et al., 1975);
- (2) A French neuropsychological battery (the BEC 96 questionnaire, Signoret et al., 1989) designed to assess working memory, naming, verbal fluency, verbal reasoning, orientation, visual recognition, verbal learning, and visuo-constructive skills. Each item was scored on a 12-point scale (maximum score = 96). Any score below 9/12 revealed pathological performance according to French normative data;
- (3) A fast frontal assessment battery (FAB, Dubois et al., 2000) including word categorization, letter fluency, test of grasping reflex, deferred imitation of movement sequence and two conflict go-no-go tasks. Each item was scored on a 3-point scale (maximum score = 18). Any score below 15/18 demonstrated executive dysfunction according to French normative data.

2.3. Experimental protocol

The test battery consisted of three gesture production tasks (i.e., pantomime of tool use, single tool use, real tool use) and two recognition tasks (i.e., functional and contextual matching, recognition of tool manipulation) involving the exact same tools and objects. The order of presentation of items was fixed but different across tasks, which were administered in the following order. Each test was preceded by a practice item (i.e., pen).

2.3.1. Pantomime of tool use (PTU)

Participants were asked to demonstrate the use of ten common tools presented one at a time (i.e., electrical plug, light bulb, screwdriver, jug, scissors, match, hammer, bottle opener, key, saw). They were not allowed to grasp the tools and the examiner did name neither the tools nor the expected action. Performance was videotaped and coded in binary format: (1) the expected gesture was recognizable within the time limit (i.e., 20 s). Hesitations and “body-part-as-object” errors (e.g., demonstrating the action of scissors with the index finger and the middle finger) were accepted as correct responses (Peigneux and Van der Linden, 1999). Spatiotemporal errors (i.e., the gesture is recognizable but approximate) were accepted too even though they are not normal in apraxic patients, because the coding system focused on the content of the action rather than the form of its execution (0) the participant did not make any gesture (i.e., perplexity); or the gesture was either unexpected or unrecognizable. Both spatiotemporal errors and content errors were counted so as to provide readers with complete data. Nevertheless, the coding system focused on content errors, for two reasons. First, these have been related to semantic loss and anterior temporal damage (Hoeren et al., 2014). Second, spatiotemporal errors are thought to be caused by deficits in the production rather than the conception system, meaning that patients with normal conceptual knowledge may still make spatiotemporal errors in gesture production tasks. On the contrary, content errors are thought to be the consequence of deficits in the conceptual system (i.e., either semantic or manipulation knowledge), on which the present study focused. Two independent raters coded videos from ten healthy participants, ten patients with Alzheimer's disease and five patients with semantic dementia. Cohen's kappa coefficient indicated very good inter-rater agreement ($K = 0.91$).

2.3.2. Single tool use (STU)

Participants were asked to grasp the ten tools one at a time and to demonstrate their typical use in the absence of any recipient object (e.g., a screwdriver but no screw). The time limit and coding system were the same as for Pantomime of tool use (except for the “body-part as object” errors since participants could hold the tool). Two

independent judges coded videos from ten healthy participants, ten patients with Alzheimer's disease and five patients with semantic dementia. Inter-coder agreement was satisfying ($K = 0.80$).

2.3.3. Real tool use (RTU)

Participants were asked to use ten tool-object pairs composed of the same tools as before, plus ten recipients (i.e., electrical outlet, bulb socket, screw partially driven into a wooden board, glass, thread, matchbox, nail partially driven into a wooden board, bottle, padlock, wooden board partially cut). Here again, the examiner did not name the action to be done. The time limit was extended to 30 s because presumably the presence of recipients added visual information and mechanical constraints (e.g., using a saw to actually saw a wooden board calls for more precision than simply demonstrating a broad back-and-forth movement). The coding system was as follows: (1) the participant reached the goal (e.g., sawdust appeared on the wooden board; the participant cut the thread with the scissors); (0) he did not reach the goal. Spatiotemporal and content errors were not distinguished because in most cases the presence of a recipient makes the coding of spatiotemporal errors irrelevant (e.g., back-and-forth movements are more precise after the saw is engaged in the wooden board). Besides, the aim of this task was to assess tool use skills in “ecological” context (i.e., with both the tool and the recipient object) in order to answer the following question: Could participants use tools despite their knowledge deficits? Two independent judges coded videos from ten healthy participants, ten patients with Alzheimer's disease and five patients with semantic dementia. Inter-coder agreement was excellent ($K = 0.88$).

2.3.4. Functional and contextual matching (FCM)

This task was designed to assess the integrity of semantic knowledge about object function and context of use. Participants were asked to match a target picture (i.e., the same ten tools as in other tests) with one of four pictures. All stimuli were black-and-white line drawings (Fig. 1). The matching criterion was the function of the tool (e.g., target = match; choice = lighter, pen, coffee maker, colander) for ten items, and the context of use (e.g., target = match; choice = anniversary, wedding, Christmas day, baptism) for ten other items. The time limit was set to 20 s (based on our experience of this task; see for example Baumard et al., 2016) with a forced-choice procedure if participants did not answer within the time-limit (so that only real errors were taken into account rather than mere slowness). Performance was coded for each tool as follows: (1) The participant gave the correct answer in both conditions (i.e., functional and contextual matching); (0) The participant made at least one error.

2.3.5. Recognition of tool manipulation (RTM)

In order to assess the integrity of manipulation knowledge without actual manipulation, participants were asked to select among four color photographs the one that corresponded to the best way to use the previously proposed tool/object pairs (e.g., match/matchbox). The relative position of tools and objects remained unchanged across the four

photographs but the foils showed the tool inappropriately held, incorrectly oriented in the hand or dangerously held (Fig. 1). The time limit was set to 20 s with a forced-choice procedure upon expiry of the time limit, and 1 point was given for each correct answer.

2.4. Coding system

The aim of the present work was to test the validity of hypotheses by computing item-based comparisons with different production and recognition tasks. To this end, two measures were used: The frequency of errors so as to provide an overview of data, and the frequency of different performance patterns corresponding to either validation or rebuttal of each hypothesis (Table 1).

2.4.1. Frequency of errors

The number of participants who had a score of 0 was counted for each item of each task (e.g., the hammer in Single Tool Use). The final score was the total number of 0 scores across items in each group. For each task, the maximum number of errors was 300 in the HC and AD groups (i.e., 30 participants x 10 items) and 130 in the SD group (i.e., 13 participants x 10 items).

2.4.2. Validation and rebuttal scores

The aim of this study was to compare different gesture production and recognition tasks using an item-based methodology. There were three reasons for this unusual method. First of all, group data are classically compared using inferential statistics and p-values. However, hypothesis testing based on group comparisons tends to ignore between-subject heterogeneity. Indeed, a broad comparison of either tasks or groups does not provide information about individual, item-based performance and hence it is likely to produce misleading results as regards the relationships between gesture production and tool-related knowledge (e.g., means and medians are used to depict complex data with a single value). For example, group comparisons may allow concluding that patients with semantic dementia demonstrate both tool use disorders and severe semantic loss (Bozeat et al., 2002), yet they do not demonstrate that failure to use a specific tool (e.g., hammer) is due to the loss of knowledge related to this specific tool. For the sake of clarity, we would like to provide an additional, extensive example. Let us imagine two tasks (i.e., Recognition of Tool Manipulation, and Real Tool Use) involving two different tools: In the RTM task, 100% participants commit errors with the hammer but 0% with the scissors, while in the RTU task, 0% participants commit errors with the hammer but 100% with the scissors. If data on the hammer and scissors are grouped (which is the case in most studies), it will be concluded that the mean frequency of errors is comparable in both the RTM and RTU tasks (i.e., 50%). Although this group result would be compatible with memory-based hypotheses, an item-based analysis would rather rule out these hypotheses because obviously, participants were able to use the hammer but not to recognize its right manipulation.

Second, in the field of neuropsychology the ultimate utility of

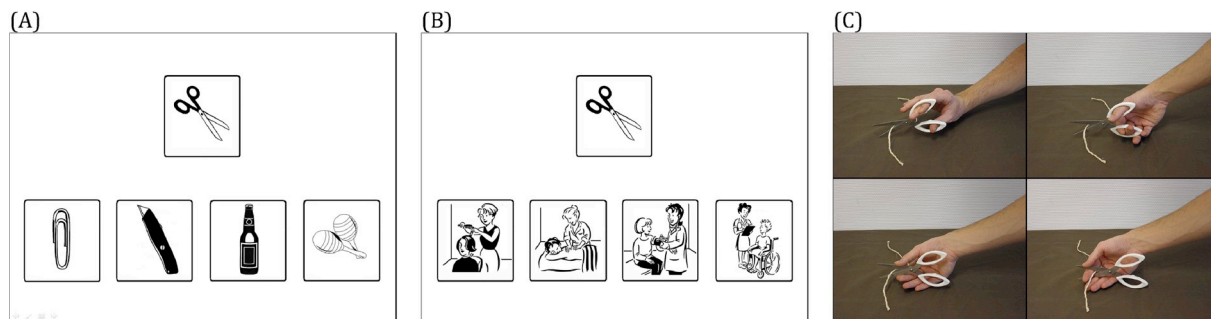


Fig. 1. Functional matching (A), contextual matching (B) and recognition of tool manipulation (C).

researches is to provide clinicians with a better comprehension of the clinical behaviors they are faced with every day. If a theory is valid at the group level (i.e., in virtual, representative individuals) but not at the individual level (i.e., in real individuals), then strictly speaking it is of little interest to clinicians and hence it would be necessary to rule out (or at least seriously discuss the validity of) the theory.

Third, using an item-based design is consistent with the current state of theories. Indeed, memory-based hypotheses predict that tool use relies on stored, tool-related knowledge. From this point of view, it is logical to consider that the loss of knowledge on a specific tool should prevent the use of the same specific tool. As an analogy, in studies focusing on episodic memory it is logical to assess encoding and retrieval/recognition of the exact same words (e.g., if the word “hammer” has not been encoded then it should be impossible to retrieve but other words may still be retrieved). Theories have been expressly proposed to account for impairments observed in a clinical setting and they are now precise enough to make predictions at the individual, item level, therefore their predictions should be verified at this very same level. Nevertheless, to our knowledge studies on apraxia have rarely addressed this issue.

For these reasons, we developed an original item-based scoring method. The aim of this method was to depict performances not only in a “2D-design” (i.e., groups x tasks) but also in a “4D-design” (i.e., groups x tasks x tools x participants) which has the advantage of reflecting real rather than estimated performances. Although this may seem either unusual or complex to readers, it is also a more demanding way to test theoretical hypotheses. In concrete terms, each prediction (Table 1) was translated into conditional language using Boolean operators (i.e., IF, AND, OR) and two scores were calculated: A validation score and a rebuttal score. A high validation score means that the hypothesis is frequently true (e.g., impairment in both gesture recognition and gesture production). Noticeably, a low score does not mean it is false. However, a high rebuttal score means that the hypothesis is frequently false in that results make the hypothesis invalid (e.g., impairment in gesture recognition but not in gesture production). Importantly, validation and rebuttal scores were calculated for each tool and each participant. For instance, a participant had a validation score of 1 as regards the semantic knowledge hypothesis (Table 1) if he consistently made errors for the item “hammer” in Functional and Contextual Matching, Pantomime of Tool Use, Single Tool Use and Real Tool Use. Conversely, he had a rebuttal score of 1 for the item “scissors” if he made an error in Functional and Contextual Matching but not in production tasks, because this would mean that he was able to use the scissors although he had lost knowledge about this tool. We shall now provide details on each hypothesis separately.

The semantic knowledge hypothesis. According to this hypothesis (Table 1), a score of 0 in either Functional or Contextual Matching should lead to score of 0 in any production task (i.e., the strict validation score). As mentioned in Section 1.4, Pantomime of Tool Use and Single Tool Use were accepted as equivalent and hence the hypothesis remained valid even if a participant had a score of 1 in one of these tasks (i.e., the two relaxed validation scores). In contrast, the hypothesis was refuted each time a participant had a score of 0 in Functional and/or Contextual Matching, but a score of 1 in Real Tool Use or in both Pantomime of Tool Use and Single Tool Use (i.e., the rebuttal scores). The score was the frequency of each performance pattern.

The manipulation knowledge hypothesis. According to this hypothesis (Table 1), a score of 0 in Recognition of Tool Manipulation should lead to score of 0 in any production task (i.e., the strict validation score). Again, Pantomime of Tool Use and Single Tool Use were accepted as equivalent (i.e., the two relaxed validation scores). The hypothesis was refuted each time a participant had a score of 0 in Recognition of Tool Manipulation, but a score of 1 in Real Tool Use or in both Pantomime of Tool Use and Single Tool Use (i.e., the rebuttal scores).

The technical-semantic hypothesis. According to this hypothesis

(Table 1), semantic memory is not critical to the use of actual tools. As a consequence, a score of 0 in either Functional or Contextual Matching may co-occur with a score of 1 in Real Tool Use, while the semantic loss should lead to impairment in both Pantomime of Tool Use and Single Tool Use (i.e., the strict validation score). As for other hypotheses, success was accepted in one of these two latter tasks because they may involve additional cognitive mechanisms (i.e., the two relaxed hypotheses). The hypothesis was refuted each time a participant: (1) Had a score of 0 in both Functional and/or Contextual Matching and Real Tool Use, because this would mean that technical reasoning did not compensate for the semantic loss; (2) Had a score of 1 in both Pantomime of Tool Use and Single Tool Use, because this was not expected in case of semantic loss (i.e., the rebuttal scores).

2.5. Statistics

The coding system relied on qualitative data (i.e., presence/absence of error) and frequencies (i.e., number of participants making errors). Since the study design focused on item-based performances, using means and standard deviations was not relevant. Therefore, in most cases significant differences were tested using Chi-Square tests, replaced by Fisher exact tests when there was a risk of error (i.e., expected frequency below 5). In some instances, quantitative data were available (e.g., within-group differences in error counts across tasks, see section 3.3). In that specific case, non-parametric statistics were preferred (i.e., Mann-Whitney U tests for between-group comparisons, and Spearman rank order correlations) seeing the non-normality of data and low sample sizes. P values were adjusted with Holm's correction for multiple tests. All analyses were performed with R statistical software.

Neuropsychological data were tested to confirm the diagnosis (section 3.1). Between-group comparisons were performed to provide an overview of group data (section 3.2). Within-group comparisons explored differences between gesture production and recognition on the one hand, and between different gesture production tasks on the other hand (section 3.3). Potential difficulty or interference effects were also controlled with this method. Item-based analyses were performed to determine whether production and recognition deficits were observed for same or different tools (section 3.4). In order to avoid data inflation, analyses focused on Real Tool Use in particular because this test reflected actual tool use skills and hence it had a (relative) “ecological” value. Crawford and Garthwaite's (2002) method for single cases in neuropsychology allowed testing for between-task dissociations in individual cases. Relationships between production and recognition were further explored by counting the number of production errors as a function of recognition deficits (section 3.5). Finally, clinical patterns reflected by the prediction-based validation and rebuttal scores (described in section 2.4.2) were calculated in both patient groups in order to test the validity of the semantic knowledge, manipulation knowledge and technical-semantic hypotheses at the individual rather than group level (section 3.6).

3. Results

3.1. Neuropsychological data

A significant effect of GROUP was found for the educational level (Kruskal-Wallis rank sum test, $H = 8.91$, $df = 2$, $p = .011$) and post-hoc analyses confirmed that it was slightly lower in AD participants (mean years of education = 9.1, standard deviation = 4.4) than in HC participants (mean = 12.4, $SD = 4.8$; Mann-Whitney U test, $U = 629.5$, $p = .021$). However, no correlation was found between age, educational level and experimental measures in the healthy control group (Spearman rank order correlations, all $ps > .24$), suggesting that demographic data had little impact on performance.

Fourteen patients with Alzheimer's disease had mild cognitive decline (MMSE 26-21) whereas sixteen had moderate to severe decline

(MMSE 20-11; see [Reisberg et al., 1982](#)). No correlation was found between the MMSE score and the number of errors in experimental tasks (all $ps > .11$). Results of the Frontal Assessment Battery yielded similar results in patients with either Alzheimer's disease (mean score = 71.3%, standard deviation = 13.1%) or semantic dementia (mean score = 75.0%, standard deviation = 12.9%; $U = 150.5$, $p = .415$). In comparison with healthy controls (mean score = 91.5%, standard deviation = 5.5%), the BEC 96 questionnaire revealed general cognitive impairment in patients with either Alzheimer's disease (mean score = 70.4%, standard deviation = 9.7%; $U = 881.0$, $p < .001$) or semantic dementia (mean score = 66.4%, standard deviation = 15.5%; $U = 350.0$, $p < .001$). Most patients with Alzheimer's disease had the amnesic form of the disease ([McKhann et al., 2011](#)) in that they had mainly memory and orientation disorders but spared language and visuospatial skills. In contrast, patients with semantic dementia had deficits in naming, verbal fluency and verbal reasoning consistent with the semantic loss. Clinical data have already been displayed in the study by [Baumard et al. \(2016\)](#).

3.2. Between-group comparisons

As shown in [Table 2](#), the frequency of errors was statistically different in patient and control groups, in production tasks and in Functional and Contextual Matching tasks. As regards production tasks, (content) errors in Pantomime of Tool Use (and to a lesser extent Single Tool Use) were significantly more frequent in semantic dementia than in Alzheimer's disease. This was not clearly the case for Real Tool Use. As regards recognition tasks, errors in Functional or Contextual Matching tasks were as frequent in both diseases whereas errors in Recognition of Tool Manipulation were more frequent in Alzheimer's disease. This pattern demonstrates a dissociation in the distribution of errors between Pantomime of Tool Use (and perhaps Single Tool Use) on the one hand, and Recognition of Tool Manipulation on the other hand, in Alzheimer's disease and semantic dementia. The same was observed at the patient level (e.g., AD 24 versus SD 02 in [Fig. 3](#)). These findings are at odds with the Manipulation knowledge hypothesis.

[Fig. 2](#) displays the frequency of both spatiotemporal and content errors in Pantomime of Tool Use and Single Tool Use. Two-by-three table analyses were performed separately for both tasks with NO/SPATIOTEMPORAL/CONTENT ERRORS and GROUP/GROUP factors with Holm's correction for multiple tests. Significant differences were found between the HC group and other groups (all $ps < .04$) but not between patient groups (both $ps > .09$). In details however, patients with Alzheimer's disease made more spatiotemporal rather than content errors whereas this was not the case for patients with semantic dementia, whether in Pantomime of Tool Use or Single Tool Use (two-by-

two table analyses with SPATIOTEMPORAL/CONTENT ERRORS and GROUP/GROUP factors, both $ps < .003$).

3.3. Within-group comparisons

As regards within-group comparisons, two-by-two table analyses performed on the total number of errors (all items and participants together) revealed a significant difference between Pantomime of Tool Use and Real Tool Use in the AD group ($\chi^2 = 4.43$, $df = 1$, $p = .035$) and in the SD group ($\chi^2 = 9.77$, $df = 1$, $p = .001$). In the AD group, errors were significantly more frequent in either FCM or RTM than in RTU (both $ps < .001$; see [Table 2](#)). In the SD group, errors were significantly more frequent in FCM than in RTU ($\chi^2 = 48.44$, $df = 1$, $p < .001$) but there was no difference between RTM and RTU ($\chi^2 = 3.66$, $df = 1$, $p = .055$; see [Table 2](#)).

These differences between gesture production and recognition could be interpreted as a difficulty effect seeing that even HC participants made more errors in recognition than in production tasks ([Supplementary Fig. 1](#)). In order to control this effect, between-task differences were calculated for each item (e.g., in the HC group, [errors in RTM for the hammer] – [errors in RTU for the hammer]) and absolute values were compared between groups. In comparison with healthy controls, the RTM-RTU difference was significantly more important in the AD group (mean difference across items = 8.5, $SD = 3.2$) than in either the HC group (mean = 2.5, $SD = 2.5$) or the SD group (mean = 1.5, $SD = 1.2$; Mann-Whitney U-tests, both $ps < .002$). No difference was found between the SD and HC groups ($U = 61.0$, $p = .416$). Likewise, in comparison with healthy controls, the FCM-RTU difference was significantly more important in the AD group (mean difference across items = 10.0, $SD = 3.5$) than in either the HC group (mean = 3.3, $SD = 1.9$) or the SD group (mean = 5.1, $SD = 2.7$; both $ps < .006$). No difference was found between the SD and HC groups ($U = 30.0$, $p = .138$). On ground of these data and seeing [Tables 3 and 4](#) and [Fig. 3](#), within-group differences are not likely to be accounted for by a mere difficulty effect.

Differences in performance between different gesture production tasks might be an effect of task order seeing that Pantomime of Tool Use was always performed before Single, then Real Tool Use. This effect cannot be completely ruled out and would deserve further studies especially since list effects have been demonstrated in the field of apraxia ([Cubelli et al., 2006](#)). However, this effect is unlikely in the present work, for five reasons. First, the loss of knowledge should prevent gesture production independently of the order of trials and tasks because if tool knowledge is lost, it should not be retrieved regardless of the order of presentation of tools. Second, we tested for item effects by splitting the data in half and there was no statistical effect of the items on the frequency of errors (see [Supplementary Table 1](#)). Third, in healthy controls all of the production tasks had identical levels of difficulty ([Supplementary Fig. 1](#)). Fourth, the higher difficulty of pantomime of tool use and to a lesser extent, single tool use, over real tool use is now well documented (for a review, see [Baumard et al., 2014](#)). The reason for this is probably that pantomime of tool use calls for additional cognitive mechanisms like either working memory ([Bartolo et al., 2003](#)), or the ability to retrieve information in memory and to make it comprehensible to the examiner (i.e., the symbolic hypothesis, [Goldenberg et al., 2003](#)). So, the different levels of difficulty between pantomime of tool use, single tool use and real tool use in patients may partly be explained by the fact that these are actually quite different tasks. Fifth, the hypothesis of a proactive interference of task A on task B does not fully make sense regarding gesture production tasks and apraxia. Indeed, if patients have difficulties performing the “hammering” gesture (for example), it means that they lack information to perform this gesture, then why should repetition help to retrieve missing information (and hence improve performance)? Actually, if the mere repetition of gestures was sufficient to improve gesture production, then it should always be an efficient rehabilitation of apraxia,

Table 2
Frequency of errors.

| Number of errors (%) | PTU | STU | RTU | FCM | RTM |
|---------------------------------------|-----------|-----------|----------|------------|------------|
| HC | 0 (0.0) | 0 (0.0) | 3 (1.0) | 36 (12.0) | 28 (9.3) |
| AD | 36 (12.0) | 16 (5.3) | 20 (6.7) | 120 (40.0) | 103 (34.3) |
| SD | 29 (22.3) | 16 (12.3) | 10 (7.7) | 61 (46.9) | 21 (16.2) |
| AD versus SD (Fisher test, p value) | .047 | .079 | .859 | .438 | .001 |

Notes. Values correspond to the number of errors observed across all items and participants. Values between brackets correspond to the percentage of errors that is, the number of errors out of the number of observations (i.e., number of subjects x number of tools). For example, in Pantomime of Tool Use AD patients made 36 errors out of 300 items (i.e., 30 subjects x 10 tools). Bold values are non-significant differences to healthy controls (Chi-square tests on two-by-two tables with ERROR/NO ERROR and GROUP/GROUP factors, p -values corrected with Holm's method for multiple testing, significant at $p < .05$).

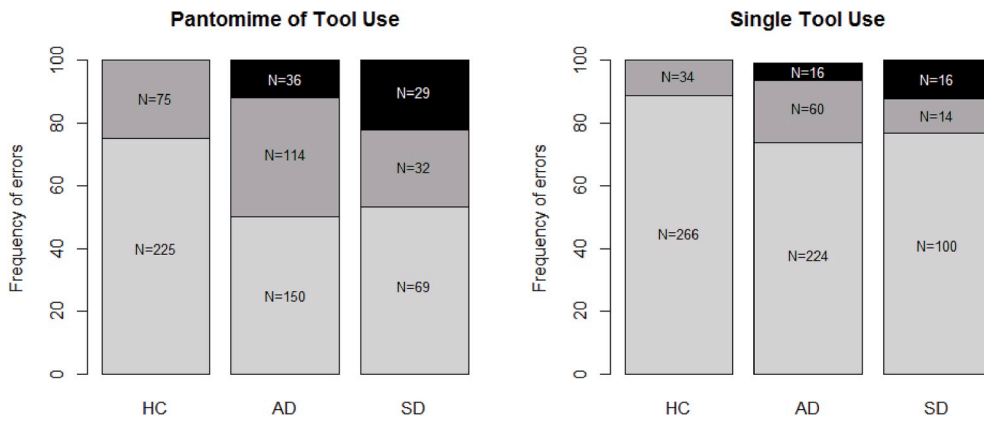


Fig. 2. Frequency of spatiotemporal and content errors in gesture production tasks. Note. N: Number of errors. HC: Healthy Controls. AD: Alzheimer’s Disease. SD: Semantic dementia. Black: Content errors (i.e., unrecognizable gestures or perplexity). Dark grey: Spatiotemporal errors (i.e., recognizable but approximate gesture). Light grey: No error.

meaning that apraxia should always recover spontaneously (because patients perform gestures in everyday life). Obviously, this is not the case seeing that many patients remain apraxic in long-term follow-up.

3.4. Item-based analysis

Overall, errors were more frequent in recognition rather than in production tasks even for one and the same tool. Two-by-two table analyses were performed with ERROR/NO ERROR and either RTM/RTU or FCM/RTU factors. In the AD group, the RTM/RTU difference was significant (or there was a tendency after p-value adjustment) for six out of ten tools (i.e., light bulb, screwdriver, scissors, match, bottle-opener, key; all $ps < .07$). The FCM/RTU difference was significant (or there was a tendency) for eight tools with the exception of scissors and match (all $ps < .07$). These differences were not calculated with PTU and STU to avoid data inflation. In the SD group, the RTM/RTU differences were not significant (all $ps > .95$) whereas the FCM/RTU differences were significant (or there was a tendency after p-value adjustment) for five tools (i.e., electric plug, light bulb, screwdriver, hammer, saw; all $ps < .08$). So, overall, impairment in both Real Tool Use and recognition tasks (i.e., either Functional/Contextual Matching or Recognition of Tool Manipulation) with one and the same tool was

the exception rather than the rule.

It should be noted that the abovementioned analyses focus on errors distribution patterns in a whole group (i.e., the number of errors made, irrespective of the performance that each single participant made in each task). Therefore, two distinct factors intervene, that is, the higher number of errors that even a single participant can make one the one hand, and the higher number of participants who make at least one error on the other hand. For this reason, the repartition of errors across tools and tasks in individual cases is displayed separately for the AD and SD groups in Fig. 3, Tables 3 and 4. As can be seen, dissociations between impaired recognition and spared production were consistently observed at both the individual and the item level.

3.5. Relationships between production and recognition

Table 5 displays the number of errors in production tasks as a function of errors in recognition tasks, for each item (see Supplementary Table 2 for more details). This table compares performance in different tasks for one and the same tool. For example, if a participant made an error in both Pantomime of Tool Use and Recognition of Tool Manipulation for the “Hammer” item, then a score of 1 was given in the “PTU impaired/RTM impaired” cell. With this

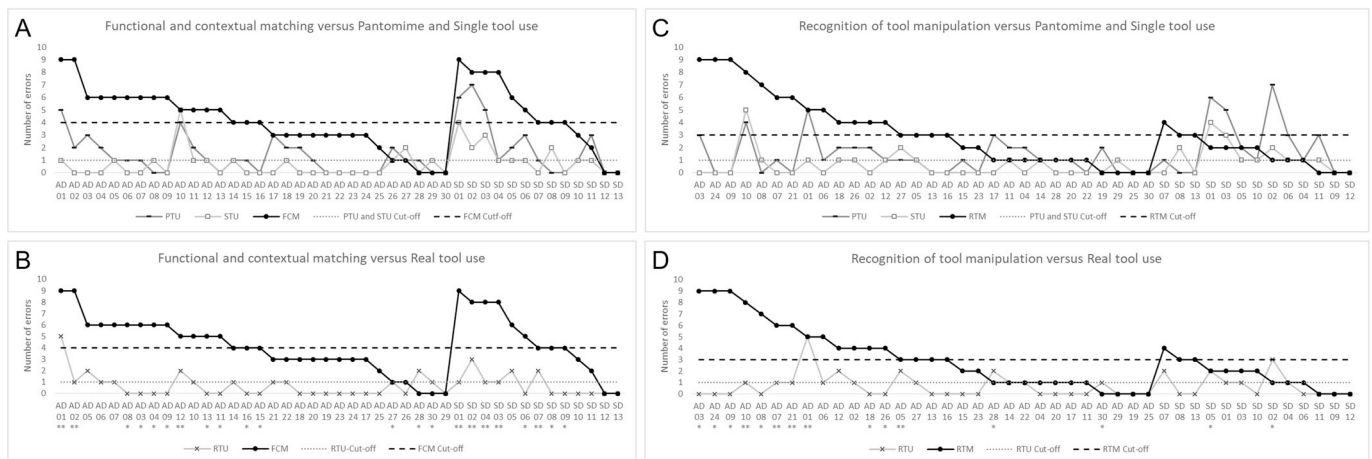


Fig. 3. Dissociations between gesture production and recognition in individual cases. Notes. In the PTU and STU tasks, only content errors are displayed (i.e., unrecognizable gestures or perplexity). In the FCM task, one error corresponded to an observed error in either Functional or Contextual Matching, or both (see Table 6 for more details). Dotted lines correspond to the cut-off, which was defined based on Crawford and Garthwaite’s (2002) statistics for single cases in neuropsychology. Because of a ceiling effect in the PTU and STU tasks (i.e., 0 error in the HC group), the cut-off was arbitrarily set to 1 error. * Classical between-task dissociation: The case’s score significantly differs between two tasks ($p < .05$) but the score on only one of the tasks qualify as a deficit. ** Strong between-task dissociation: The case’s score significantly differs between two tasks ($p < .05$) and both scores qualify as deficits in comparison with healthy controls. This method is based on the means, standard deviations, and correlations between task 1 and 2 in the HC group, hence similar absolute values (e.g., 1 error in both tasks) may correspond to dissociations. For the same reason, it could not apply to the PTU and STU tasks, and panels A and C are purely descriptive. PTU: Pantomime of Tool Use; STU: Single Tool Use; RTU: Real Tool Use; FCM: Functional and Contextual Matching; RTM: Recognition of Tool Manipulation; AD: Alzheimer’s disease; SD: Semantic dementia.

Table 3
Individual profiles across tasks and items in the AD group.

| Profile | Task | | | | | Tool | | | | | | | | | | Mean N (%) | Mean % HC group) | |
|---------|-------------|-----|-----|-------------|-----|-----------|------------|-------------|-----|-----------|-------|-----------|-----------|-----|-----------|------------|------------------|-------------|
| | Production | | | Recognition | | El. Plug | Light bulb | Screwdriver | Jug | Scissors | Match | Hammer | B. opener | Key | Saw | | | |
| | PTU | STU | RTU | FCM | RTM | | | | | | | | | | | | | |
| A1 | + | + | + | - | - | 4 | 4 | 5 | 2 | 2 | 3 | 4 | 3 | 6 | 1 | 3.4 | (11.3) | 1.0 |
| A2 | - | + | + | - | - | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 2 | 0 | 0 | 0.5 | (1.7) | na |
| A3 | - | - | + | - | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | (Na) | na |
| A4 | - | - | - | - | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | (Na) | na |
| A5 | + | + | - | - | - | 1 | 0 | 0 | 0 | 1 | 2 | 0 | 0 | 1 | 0 | 0.5 | (1.7) | na |
| A6 | - | + | - | - | - | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0.2 | (0.7) | na |
| A7 | + | - | - | - | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | Na | na |
| A8 | + | - | + | - | - | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.1 | (0.3) | na |
| B1 | + | + | + | - | + | 6 | 5 | 4 | 2 | 5 | 4 | 12 | 6 | 4 | 7 | 5.5 | (18.3) | 10.3 |
| B2 | - | + | + | - | + | 1 | 0 | 3 | 2 | 2 | 0 | 0 | 1 | 0 | 1 | 1 | (3.3) | na |
| B3 | - | - | + | - | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 1 | 0.3 | (1.0) | na |
| B4 | - | - | - | - | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | Na | na |
| B5 | + | + | - | - | + | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0.3 | (1.0) | 0.7 |
| B6 | - | + | - | - | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.1 | (0.3) | na |
| B7 | + | - | - | - | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | Na | na |
| B8 | + | - | + | - | + | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0.1 | (0.3) | na |
| C1 | + | + | + | + | - | 3 | 4 | 2 | 2 | 7 | 9 | 2 | 2 | 8 | 3 | 4.2 | (14.0) | 8.3 |
| C2 | - | + | + | + | - | 0 | 2 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0.4 | (1.3) | na |
| C3 | - | - | + | + | - | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0.2 | (0.7) | na |
| C4 | - | - | - | + | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | Na | na |
| C5 | + | + | - | + | - | 1 | 0 | 0 | 0 | 1 | 2 | 0 | 0 | 0 | 1 | 0.5 | (1.7) | na |
| C6 | - | + | - | + | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | Na | na |
| C7 | + | - | - | + | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | Na | na |
| C8 | + | - | + | + | - | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0.3 | (1.0) | na |
| Other | Any pattern | | | + | + | 11 | 15 | 11 | 20 | 10 | 7 | 12 | 14 | 9 | 15 | 12.4 | (41.3) | 79.7 |
| Total | Na | Na | Na | Na | Na | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | (100) | 100 |

Notes. Values correspond to number of participants. Bold values correspond to significant patient-control differences (Chi-Square tests with the variables AD/HC and PRESENCE/ABSENCE of the considered profile). A profiles: Impairment in both FCM and RTM. B profiles: Impairment in FCM. C profiles: Impairment in RTM. Although AD patients showed a deficit in the recognition tasks, the A1 profile was frequent while the A4 profile was not observed. Data are available on the HC group in [Supplementary Table 3](#). PTU: Pantomime of Tool Use; STU: Single Tool Use; RTU: Real Tool Use; FCM: Functional and Contextual Matching; RTM: Recognition of Tool Manipulation.

method, relationships between tasks are considered at the item rather than the group level. As can be seen, patients were frequently able to demonstrate the use of tools (even without the usual recipient) about which they had lost either manipulation or semantic knowledge.

Likewise, [Table 6](#) shows that even patients with severe semantic loss (i.e., who had lost both functional and contextual knowledge) were able to demonstrate the use of tools. These data contradict all the hypotheses.

3.6. Validation and rebuttal scores

[Fig. 4](#) displays the repartition of the prediction-based validation and rebuttal scores ([Table 1](#)), for one and the same tool. Data of patients with either Alzheimer's disease or semantic dementia have been grouped to test the relevancy of each hypothesis in neurodegenerative diseases as a whole. Patients ($n = 43$) made a total of 181 errors in the Functional and Contextual Matching task, and a total of 124 errors in the Recognition of Tool Manipulation task. As can be seen, in these situations the “validation” patterns predicted in [Table 1](#) were rarely observed for one and the same tool. In more details, predictions based on the semantic knowledge hypothesis were confirmed in 5.5% cases. Predictions based on the manipulation knowledge hypothesis were confirmed in 3.2% cases. Predictions based on the technical-semantic predictions were confirmed in 19.9% cases. The technical-semantic hypothesis was significantly more frequently confirmed than either the “pure” semantic knowledge hypothesis ($\chi^2 = 8.09$, $df = 1$, $p = .004$) or the manipulation knowledge hypothesis ($\chi^2 = 12.06$, $df = 1$, $p < .001$). That being said, all of the hypotheses were more frequently rebutted than validated, meaning that patients were able not only to use but also to demonstrate the use of tools about which they had lost either semantic or manipulation knowledge. This was not predicted by any

hypothesis (including the Technical-semantic hypothesis that is defended in this study).

4. Discussion

4.1. Main results

The aim of the present work was to test both memory-based and reasoning-based assumptions in a clinical setting. According to the memory-based hypothesis, tool use depends on stored knowledge about properties of either tools/objects ([Roy and Square, 1985](#)) or gestures ([Buxbaum, 2001, 2017](#); [Rothi et al., 1991, 1997](#)). In contrast, the reasoning-based approach acknowledges the role of semantic memory in imagining absent tools (as in Pantomime of Tool Use and Single Tool Use) but it posits that Real Tool Use also depends on specific technical reasoning skills ([Osiurak, 2014](#)). According to our results, dissociations were consistently found at both the patient and item level. Besides, predictions from the technical-semantic hypothesis tended to be more frequently observed than memory-based predictions in both patient groups. For all that, all of the hypotheses were frequently rebutted so none can be reasonably validated. These results have serious implications for the main assumptions recently made about tool use skills in humans, on the one hand, and for the potential nature of tool-related knowledge and semantic memory, on the other hand.

4.2. The semantic knowledge hypothesis

The semantic knowledge hypothesis predicted that loss of knowledge about specific tools would prevent patients from producing the corresponding tool-related gestures. Our results are not in line with this hypothesis, whether in the AD or SD group. It is true that patients made

Table 4
Individual profiles across tasks and items in the SD group.

| Profile | Task | | | | | Tool | | | | | | | | | | Mean N (%) | Mean % (HC group) | |
|---------|-------------|-----|-----|-------------|-----|----------|------------|-------------|-----|----------|-------|--------|-----------|-----|-----|------------|-------------------|-----|
| | Production | | | Recognition | | El. Plug | Light bulb | Screwdriver | Jug | Scissors | Match | Hammer | B. opener | Key | Saw | | | |
| | PTU | STU | RTU | FCM | RTM | | | | | | | | | | | | | |
| A1 | + | + | + | - | - | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0.3 (2.3) | 1.0 |
| A2 | - | + | + | - | - | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.1 (0.8) | na |
| A3 | - | - | + | - | - | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0.2 (1.5) | na |
| A4 | - | - | - | - | - | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0.1 (0.8) | na |
| A5 | + | + | - | - | - | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0.1 (0.8) | na |
| A6 | - | + | - | - | - | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0.1 (0.8) | na |
| A7 | + | - | - | - | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | na |
| A8 | + | - | + | - | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | na |
| B1 | + | + | + | - | + | 6 | 3 | 4 | 2 | 2 | 1 | 7 | 1 | 1 | 6 | 3.3 (25.4) | 10.3 | |
| B2 | - | + | + | - | + | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0.6 (4.6) | na | |
| B3 | - | - | + | - | + | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 2 | 0 | 0 | 0.5 (3.8) | na | |
| B4 | - | - | - | - | + | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 1 | 1 | 0 | 0.4 (3.1) | na | |
| B5 | + | + | - | - | + | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0.1 (0.8) | 0.7 | |
| B6 | - | + | - | - | + | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0.1 (0.8) | na | |
| B7 | + | - | - | - | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | na |
| B8 | + | - | + | - | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0.2 (1.5) | na | |
| C1 | + | + | + | + | - | 1 | 2 | 2 | 0 | 1 | 2 | 0 | 1 | 3 | 0 | 1.2 (9.2) | 8.3 | |
| C2 | - | + | + | + | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | na |
| C3 | - | - | + | + | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | na |
| C4 | - | - | - | + | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | na |
| C5 | + | + | - | + | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | na |
| C6 | - | + | - | + | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | na |
| C7 | + | - | - | + | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | na |
| C8 | + | - | + | + | - | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Na | na |
| Other | Any pattern | | | + | + | 5 | 5 | 4 | 11 | 8 | 3 | 5 | 6 | 6 | 4 | 5.7 (43.8) | 79.7 | |
| Total | Na | Na | Na | Na | Na | 13 | 13 | 13 | 13 | 13 | 13 | 13 | 13 | 13 | 13 | 13 | (100) | 100 |

Notes. Values correspond to number of participants. Bold values correspond to significant patient-control differences (Chi-Square tests with the variables SD/HC and PRESENCE/ABSENCE of the considered profile). A profiles: Impairment in both FCM and RTM. B profiles: Impairment in FCM. C profiles: Impairment in RTM. Although SD patients showed a deficit in the recognition tasks, the B1 profile was frequent while the A4 profile was rare. Data are available on the HC group in [Supplementary Table 3](#). PTU: Pantomime of Tool Use; STU: Single Tool Use; RTU: Real Tool Use; FCM: Functional and Contextual Matching; RTM: Recognition of Tool Manipulation.

more errors than healthy controls in Functional/Contextual Matching and in all production tasks. On this ground, it could be assumed that their inability to use tools properly was due to the semantic loss, which corresponds to a widely accepted point of view in the field of dementia (see for example [Blondel et al., 2001](#); [Ochipa et al., 1992](#)). Nevertheless, several results contradict this hypothesis. First, Pantomime of Tool Use was more difficult than Real Tool Use so these production tasks are not superimposable and presumably call for different cognitive mechanisms as already discussed. Second, patients made more errors in Functional/Contextual Matching than in Real Tool Use so

recognition was more difficult than production. Third, predictions based on the semantic knowledge hypothesis were rarely observed in that patients could use and demonstrate the use of tools although they had lost functional and/or contextual information about these same tools. Fourth, many patients made errors in both Functional and Contextual Matching and yet had normal performance with the same tools in Pantomime of Tool Use, Single Tool Use or Real Tool Use, meaning that in these patients success in production tasks did not depend on a specific subtype of semantic knowledge (i.e., functional or contextual). For these reasons, performance of both AD and SD patients in gesture

Table 5
Errors in production tasks as a function of errors in recognition tasks.

| Alzheimer's disease | PTU Normal | PTU Impaired | STU Normal | STU Impaired | RTU Normal | RTU Impaired |
|--------------------------|-------------------|---------------------|-------------------|---------------------|-------------------|---------------------|
| RTM Normal | 174 | 23 | 187 | 10 | 189 | 8 |
| RTM Impaired | 90 | 13 | 97 | 6 | 91 | 12 |
| Fisher tests (p value) | 1. | | 1. | | 0.20 | |
| FCM Normal | 165 | 15 | 169 | 11 | 171 | 9 |
| FCM Impaired | 99 | 21 | 115 | 5 | 109 | 11 |
| Fisher tests (p value) | 0.20 | | 1. | | 1. | |
| Semantic dementia | PTU Normal | PTU Impaired | STU Normal | STU Impaired | RTU Normal | RTU Impaired |
| RTM Normal | 85 | 24 | 96 | 13 | 102 | 7 |
| RTM Impaired | 16 | 5 | 18 | 3 | 18 | 3 |
| Fisher tests (p value) | 1. | | 1. | | 1. | |
| FCM Normal | 61 | 8 | 67 | 2 | 68 | 1 |
| FCM Impaired | 40 | 21 | 47 | 14 | 52 | 9 |
| Fisher tests (p value) | .033 | | .012 | | .060 | |

Notes. Values correspond to the number of observations. An observation is defined as one item of one task in one patient. In the AD group, the maximum number of observations was 300 for each 2 × 2 table (i.e., 30 participants x 10 tools). In the SD group, the maximum number of observations was 130 for each 2 × 2 table (i.e., 13 participants x 10 tools). Bold values correspond to significant differences (Chi-square tests with Holm's correction for multiple tests).

Table 6
Errors in production tasks as a function of the semantic loss.

| Number of errors in FCM | PTU | | STU | | RTU | |
|----------------------------|------|-----|------|-----|------|-----|
| Alzheimer's disease | - | + | - | + | - | + |
| No error | 15 | 165 | 11 | 169 | 9 | 171 |
| 1 error | 13 | 83 | 2 | 94 | 6 | 90 |
| 2 errors | 8 | 16 | 3 | 21 | 5 | 19 |
| Fisher tests (p value) | .012 | | .077 | | .059 | |
| Semantic dementia | - | + | - | + | - | + |
| No error | 8 | 61 | 2 | 67 | 1 | 68 |
| 1 error | 14 | 33 | 12 | 35 | 6 | 41 |
| 2 errors | 7 | 7 | 2 | 12 | 3 | 11 |
| Fisher tests (p value) | .011 | | .005 | | .012 | |

Notes. “+”: Normal performance; “-”: Impairment; “No error”: The participant obtained 1 in both Functional and Contextual Matching for one and the same tool; “1 error”: The participant made one mistake in either Functional or Contextual Matching; “2 errors”: The participant made errors in both Functional and Contextual Matching. Fisher exact tests were performed on contingency tables with 0/1/2 ERRORS IN FCM and +/-IN PRODUCTION TASKS. P-values are corrected values with Holm's method for multiple tests.

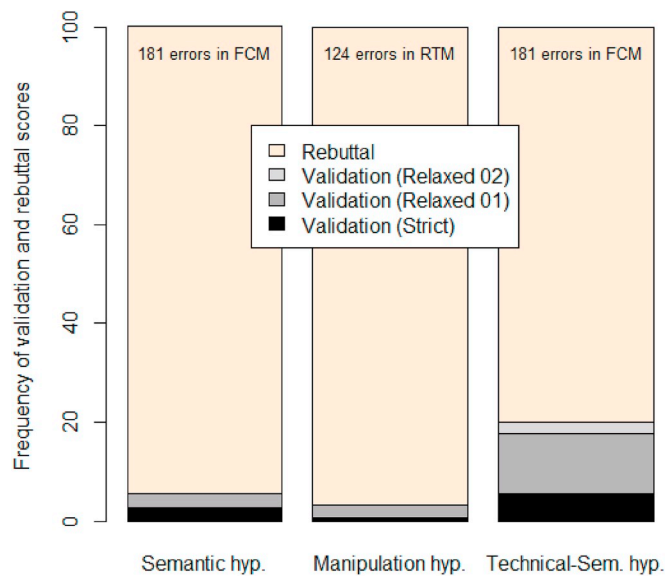


Fig. 4. Validation and rebuttal of each hypothesis in neurodegenerative diseases. Notes. Data of patients with either Alzheimer's disease or semantic dementia have been grouped to test the relevancy of each hypothesis in neurodegenerative diseases. Detailed cognitive profiles corresponding to Validation and Rebuttal scores are provided in Table 1. Values at the top of bars (i.e., 181 and 124) correspond to the total number of errors in recognition tasks. Example: Patients made 181 errors in the Functional and Contextual Matching task (out of 10 items x 43 patients = 430 observations). On these 181 observations, predictions based on either the semantic or the technical-semantic hypotheses were observed in 5.5% and 19.9% of cases, respectively (for one and the same tool). FCM: Functional and Contextual Matching; RTM: Recognition of Tool Manipulation.

production tasks cannot be explained merely by loss of tool-specific stored representations.

Cognitive models of apraxia (Roy and Square, 1985) predict that tool use relies on specific tool-related knowledge about function. Recently, it has been proposed that knowledge about the context of use is another key component of normal tool use actions (Osiurak, 2014). Nevertheless, using a within-item design we observed a clear dissociation between tool knowledge and tool use skills, even in case of severe semantic loss. In other words, patients were frequently able to make tool-related actions although they could not recognize properties of the involved tools. These data are consistent with the two-way hypothesis (Milner and Goodale, 1995; Ungerleider and Mishkin, 1982) that makes

a distinction between a ventral pathway providing information about characteristics of objects, and a dorsal pathway providing information about goal-directed actions. It also echoes previous works which suggested that SD patients may demonstrate normal or subnormal tool use skills despite severe semantic loss (Baumard et al., 2016; Bozeat et al., 2002). Interestingly, the reverse pattern has also been documented, that is, impaired tool use but spared tool recognition (Lunardelli et al., 2011).

With this in mind, it can be assumed that in Alzheimer's disease and semantic dementia, characteristics of objects may be lost but this loss does not prevent normal or subnormal tool use. In line with previous findings according to which semantic memory is not necessary to use tools (Baumard et al., 2016; Buxbaum et al., 1997; Buxbaum and Saffran, 2002; Hodges et al., 2000; Osiurak et al., 2008), these results lead us to conclude that semantic tool-related knowledge is not primarily dedicated to action. This dichotomy between knowledge and action contradicts classical models of apraxia (Roy and Square, 1985; Rothi et al., 1991, 1997), yet it is actually quite intuitive. For example, one may know that a bookbinder is part of office equipment and is made to bind documents, and still have difficulties in actually binding documents (at least for neophytes). Likewise, instruction in Newtonian mechanics is not sufficient to accurately predict the motion of objects in space (McCloskey, 1983). Conversely, “humans did not have to wait for Newton's discovery of the law of gravity to apply it in everyday life” (Osiurak and Badets, 2016, pp. 26). This does not mean, however, that semantic memory and temporal lobes on the one hand, and goal-directed processes and the left parietal lobe on the other hand, are totally independent. In all likelihood, semantic memory provides a processing advantage for tool use skills when goal-directed actions concern usual tools (see also Van Polanen and Davare, 2015). Noticeably, it may be useful so as to imagine absent tools (e.g., if I need to drive a nail into a wooden board I may look for a hammer if it is not present in the visual field), to select usual tools (e.g., in presence of a rock, a saw and a hammer I may select only the latter to drive a nail) and to arrange them in daily life (e.g., tidying a house; see Osiurak, 2017). In contrast, our findings show that manipulation itself does not depend on semantic knowledge.

The discussion then boils down to whether tool use actions depend on either stored knowledge about manipulation, or technical reasoning skills. Indeed, it has been suggested that visual representations of tools are stored in temporal lobes whereas motor representations (i.e., manipulation knowledge) would be stored in the left parietal lobe (Binkofski and Buxbaum, 2013), but the latter brain region has also been found to be critical in mechanical problem-solving tasks involving technical reasoning skills (Goldenberg, 2009).

4.3. The manipulation knowledge hypothesis

Over the last thirty years, this relative independence between semantic memory and action has led researchers to make a distinction between declarative knowledge stored in the semantic system in the ventral temporal lobes on the one hand, and implicit manipulation knowledge stored in a gestural memory in the left parietal lobe (Buxbaum, 2001, 2017; Buxbaum and Kalénine, 2010) on the other hand. In this framework, manipulation knowledge underlies both gesture production and gesture recognition, meaning that the loss of manipulation knowledge as demonstrated by impaired recognition of tool-related gestures should coincide with impaired production of the same gestures. In addition, performance should not vary depending on context enrichment (i.e., Pantomime of Tool Use, Single Tool Use, Real Tool Use) since gesture engrams are body-centered rather than tool-centered. Our results are not in line with these predictions.

Patients with semantic dementia did not have significant difficulties in recognizing tool use actions so the manipulation knowledge hypothesis can be neither validated nor rebutted in this group. In contrast, AD patients made frequent errors in the Recognition of Tool

Manipulation task, and yet they demonstrated performance patterns which contradict the manipulation knowledge hypothesis. First, different levels of performance were observed in production tasks in both patient groups. Second, Recognition of Tool Manipulation was more difficult than Real Tool Use for AD patients. Third, patients were able to use tools and to demonstrate the use of tools properly even when they could not recognize the correct use of the same tools on photographs. Again, difficulties in gesture production could not be accounted for by loss of stored motor representations. This finding corroborates previously documented double dissociations between tool use and pantomime recognition (Negri et al., 2007b) while it is inconsistent with memory-based approaches of apraxia (Buxbaum, 2001, 2017).

Other models of apraxia made a distinction between an action input and an action output lexicon, with the former being devoted to action recognition and the latter to action production (Rothi et al., 1997; for a revision of this model, see Cubelli et al., 2000). On this ground, one could argue that AD patients could not recognize tool manipulation because they had lost representations specifically stored in the action input lexicon. However, this explanation is not fully satisfying. The first reason is that the specificity of each lexicon remains to be demonstrated (e.g., differences in contents or involved brain regions). More importantly, this assumption raises a critical epistemological issue. Indeed, manipulation knowledge is thought to contain information about how to perform tool-related actions, yet the dissociation between input and output lexicon posits that this information may be lost without consequence for action production. That amounts to considering that manipulation knowledge is not necessary for actual manipulation, which is paradoxical because the existence of gesture engrams has just been posited so as to explain how humans may use tools. As De Vignemont (2007) already noted regarding body schema, defining representations based on their function (i.e., action-oriented or recognition-oriented) rather than their content is not heuristic, and there is a risk of infinite multiplication of specific representations.

This being so, the problem remains why AD patients, but not SD patients, had impaired performance in Recognition of Tool Manipulation (see also Jarry et al., 2016). If this task does not assess manipulation knowledge, then why is it difficult for these patients? First of all, this may depend on methodological choices. For example, one could consider that some of the foils used in the Recognition of Tool Manipulation task corresponded to spatiotemporal rather than content errors (i.e., the action can still be performed even though the position of the hand on the tool is incorrect), which might explain dissociations between this task and content errors in gesture production tasks. This possibility cannot be ruled out though it is indicative of the arbitrary dimension of any error-based analysis (e.g., considering “temporal” errors in static-picture selection may sound odd to some researchers). Another possible explanation would be that it is actually not a “recognition” task but a “reconstruction” task. Indeed, the term “recognition” is not theory neutral (Negri et al., 2007b) since it automatically refers to memory-based approaches of cognition in general, and apraxia in particular. However, in a reasoning-based approach, other cognitive processes may be invoked. For discussion, let us assume that this task can be solved without need of specific memory but rather by way of action simulation. This would mean that correct answers are not the result of a comparison between presented and stored information, but rather of a mental simulation of the presented action (see also Reynaud et al., 2016). In the present study, participants were presented with photographs of someone else performing a tool-use action (i.e., third-person perspective) so presumably this mental simulation required allo-/egocentric conversion mechanisms for participants to imagine what they would do themselves (i.e., first-person perspective). Interestingly, difficulties in this type of translation have been documented in AD patients (see Serino et al., 2014). So, perhaps difficulties of these patients in the Recognition of Tool Manipulation task arose from general impairment of allo-/egocentric conversion mechanisms rather than of a specific praxis system. A participation of technical

reasoning so as to mentally simulate the action of the tool with the object is also plausible. Further studies are needed on the cognitive mechanisms needed to perform gesture recognition tasks.

4.4. The technical-semantic hypothesis

The technical-semantic hypothesis predicted that in case of semantic loss, Pantomime of Tool Use and/or Single Tool Use would be impaired while Real Tool Use would be preserved thanks to compensations by technical reasoning. This assumption is partially validated by the facts. First, Real Tool Use was easier than Pantomime of Tool Use and Functional/Contextual Matching in both patient groups. Second, patients frequently demonstrated normal performance in Real Tool Use despite impaired performance in Functional/Contextual Matching. Third, the technical-semantic hypothesis was more frequently valid than other hypotheses. Nevertheless, it was also more frequently rebutted than validated. Besides, in most cases patients were able to demonstrate the use of tools even in the absence of tools and/or objects (i.e., Pantomime of Tool Use, Single Tool Use), which was expected to be impossible due to the semantic impairment. This result shows that not only Real Tool Use, but also Pantomime of Tool Use and Single Tool Use, may call for non-semantic cognitive mechanisms. Again, semantic memory is likely to play a facilitating role but is not critical to these tasks. So, the question remains of which other cognitive processes are at stake.

Classically, Pantomime of Tool Use and Single Tool Use are thought to assess the integrity of manipulation knowledge (see for example Buxbaum, 2001, 2017). Nevertheless, our results are not consistent with this hypothesis (see Section 4.3. The manipulation knowledge hypothesis). Previous works already demonstrated that these tasks are actually complex, composite tasks. Bartolo et al. (2003) suggested that working memory is necessary to maintain information about how to hold and use a tool with the corresponding, imaginary object. Although this is probably the case, working memory alone cannot be sufficient. In particular, this hypothesis does not explain how participants select which tool-use action they should perform. For example, when presented with a hammer, participants may hold it in different ways (e.g., by the “head” or the handle) and they may perform many different actions (e.g., pushing, hammering, levering, rubbing) so they must first select these hold and use components, and only then working memory is useful to maintain this configuration over time. Besides, a deficit in working memory should have led to impairment in almost all items of Pantomime of Tool Use and Single Tool Use, which was far from being the case. In fact, both AD and SD patients performed canonical, recognizable actions (e.g., hammering) in most items despite the semantic loss so they were able to select the hold and use components without relying on semantic knowledge.

Another possibility is that participants who demonstrated semantic impairment actually imagined non canonical objects and thus performed actions that only *seemed* canonical. As a reminder, our coding system did not take hesitations and spatiotemporal errors into account but rather content errors (i.e., unrecognizable gestures or perplexity). With this in mind, perhaps participants reconstructed a non-conventional technical device and demonstrated the use of the presented object thanks to technical reasoning. It is true that SD patients tend to rely on mechanical rather than semantic cues (Bozeat et al., 2002; Osieurak et al., 2008). For example, when presented with a hammer, one may analyze that the hammer is suitable to ring a bell or to stomp insects, and hence perform the expected gesture (i.e., repeated movement of the elbow). In this case, the performed action would only incidentally correspond to the examiner's expectation. Since approximations are not considered by the coding system, this type of response would have been judged correct. However, a participation of technical reasoning is plausible but not sufficient. Indeed, even so there are many potential technical actions that do not correspond to the expected action (e.g., rubbing, pushing or pulling instead of hammering). Even though AD

and SD patients made errors in Pantomime of Tool Use and Single Tool Use, most gestures were recognizable so their performance must have been driven by other cognitive mechanisms.

So, on the one hand, memory-based approaches cannot account for gesture production disorders and on the other hand, the technical-semantic hypothesis is not sufficient to explain the observed dichotomy between impaired semantic knowledge and subnormal performance in Pantomime of Tool Use and Single Tool Use. In more details, the technical-semantic hypothesis is actually both reasoning- and memory-based, and although reasoning-based assumptions were frequently confirmed (e.g., better performance in Real Tool Use than in other gesture production tasks), there was no correspondence between gesture production and knowledge assessed by the Functional/Contextual Matching task. This raises important issues as to the role of memory in tool use.

4.5. The role of memory in tool use

Although apraxia has long been defined as a disorder of learned, skilled gestures (Geschwind, 1975; Rothi et al., 1991), the nature of the underlying memory system remains unspecified or ambiguous. Results reported here suggest that neither semantic nor manipulation knowledge may explain performance in Pantomime of Tool Use, Single Tool Use and Real Tool Use. For all that, most patients made recognizable gestures so that their performance was probably driven by prior experience. The question is therefore which memory system allowed for normal gesture production, seeing that semantic knowledge, manipulation knowledge and working memory have been ruled out (see section 4. Discussion). As currently framed the role of two other memory systems may be invoked (i.e., episodic memory and autobiographical memory).

Patients with semantic dementia are known to have impaired semantic memory but relatively preserved episodic memory (Hodges et al., 1992a, 1992b) and autobiographical memory, at least for recent years (Westmacott et al., 2001). This dissociation may lead to cognitive egocentrism (i.e., better preservation of naming and recovery of meaning for personally experienced items), which might also result from a disorganization of the semantic system itself (Belliard et al., 2013). Likewise, Snowden et al. (2010) argued that in these patients, the distinction between personal, autobiographical memory (preserved) and impersonal memory (impaired) is as important as the one between episodic and semantic memory. For example, they better recognize relatives than famous people (Péron et al., 2015). In the same vein, patients with dementia tend to use their own tools in a more effective way compared to other exemplars of the same tools (i.e., the personal object advantage, Giovannetti et al., 2006). On the whole, personal experience seems to be a powerful compensation method for patients with semantic deficits.

Pending future publications, let us pool these different elements under the same “personal habits” label. Perhaps most patients could demonstrate the use of tools by invoking personal habits rather than impersonal knowledge. Since personal habits tend to coincide with semantic knowledge within a given culture (e.g., most people put their toothbrush in the bathroom and use it in the same way), our coding system which focused on semantic knowledge (i.e., the content of the action) recorded mainly correct answers in Pantomime of Tool Use and Single Tool Use. Put differently, perhaps patients could demonstrate the use of tools properly by relying on their own bodily experience while they could not fulfill Functional/Contextual Matching because this task rather assesses collective, shared semantic knowledge. Indeed, patients were presented with relatively frequent tools (e.g., hammer, light bulb, bottle opener) so they were likely to have prior experience of different exemplars of the same tools. This may explain why patients had pathological yet relatively preserved performance in production tasks compared with Functional/Contextual Matching. If this hypothesis is correct, then poor performance is expected when demonstration of tool

use relies on impersonal memory (e.g., many people broadly know how to use a book-binder but only few of them have experienced it) whereas performance would increase when demonstration can rely on personal experience (e.g., fork and knife, light bulb). It should be acknowledged that this explanation may be valid for SD, but not AD patients for the latter do have episodic and autobiographical memory disorders (see for example Westmacott et al., 2001) so that explicit self-reference is unlikely to enhance performance, or at least not in the same proportions as in SD patients. Perhaps personal habits drive performance implicitly seeing that the personal object advantage has been observed even when patients do not recognize the object as “personal” (Giovannetti et al., 2006). Further studies are needed on this point.

Another approach would be to consider different types of semantic impairments rather than impairments of different memory systems. In the framework of the controlled semantic cognition (Rogers et al., 2015), successful retrieval of semantic knowledge not only requires the integrity of stored conceptual representations, but it also requires cognitive control to access context-relevant information. So, one could consider that we do not know whether the included patients had either a true degradation of semantic representations, or a semantic access deficit. For instance, the latter could have made it difficult to process and/or inhibit the foils in recognition tasks, while in production tasks there was only one item for the participant to attend to. Although this issue was beyond the scope of the present study – which design was based on classical tasks used in the field of apraxia – this inaccurate representation of semantic access in the patients tested might explain why none of the hypotheses were satisfying. However, this seems unlikely in the SD group because patients with semantic dementia typically show a degradation of semantic representations (Jefferies and Lambon Ralph, 2006; Jefferies et al., 2010). Besides, semantic control and general executive dysfunction may be superimposable (Thompson et al., 2018). Executive scores of the patients included here have already been published showing that 7% of SD patients, and 47% of AD patients, showed a deficit in the Tower of London test (Baumard et al., 2018). No correlation was found between this score and the experimental measures, suggesting that the executive score does not predict different patterns of performance in semantic versus tool use tests (Supplementary Table 4). On ground of these additional data, it can be assumed that degraded semantic knowledge rather than semantic control deficit, explained the semantic impairments observed in the SD group, and to a lesser extent in the AD group. However, future works may discuss the semantic, manipulation and technical-semantic hypotheses in light of the dichotomy between semantic representation and semantic control with more specific pre-semantic tasks (e.g., uni-versus multimodal tests, cueing effects).

That being said, these memory-based assumptions should be weighed against additional, interactionist hypotheses. So far, we considered that Functional/Contextual Matching did actually assess pure knowledge, which led us to discuss the dissociation between impaired knowledge and preserved gesture production. Nevertheless, it could also be suggested that impairment in this task was not due to a loss of stored information but rather to impairment in what we would call “sociological reasoning”.

4.6. Towards sociological reasoning

Semantic memory has two main characteristics: It is a long-term memory in which knowledge is stored, but it is also a symbolic, collective memory. So, matching tools on ground of their function or context of use may be viewed as a complex task requiring at least three steps: 1) Gathering stored information about the item (e.g., the name and shape of a hammer, its typical function and location); 2) Understanding the examiner's intentions so as to use the expected criterion (e.g., in the Functional Association task the corrected, practice item implicitly informs participants that a “shape” criterion is not considered as relevant); 3) Inhibiting personal habits in order to use this

criterion. On this ground, one could imagine that depending on cases difficulties in tasks assessing semantic knowledge are due to a real loss of knowledge preventing recollection of information; to a deficit of theory of mind preventing patients from understanding the examiner's expectations (e.g., inhibiting their own perspective to adopt the examiner's perspective); or to the inability to consciously and voluntarily adhere to these expectations (e.g., cognitive egocentrism). Interestingly, similar hypotheses have been made in stroke patients suggesting that pantomime of tool use is a creative task that requires to extract core features of tools and actions so as to be able to communicate them to the examiner (Goldenberg et al., 2003). Although this hypothesis was not clearly confirmed in stroke patients, SD patients are known to have both communication deficits due to cognitive egocentrism, and theory of mind impairments (Duval et al., 2012). Interestingly, some of these patients are able to make jokes (in a stereotypical and/or inappropriate manner) although they do not understand other people's jokes (see Clark et al., 2015). As an analogy, could they have difficulties in recognizing semantic information which they otherwise would be able to evoke and reuse spontaneously? This amounts to considering that access to semantic information can be compromised specifically in social situations. Interestingly, previous works suggested that children with autism can use tools and imitate the result of a technical action (e.g., rubbing, pulling) but not the style of the examiner (e.g., smooth movement; Hobson and Hobson, 2008; Hobson and Lee, 1999), as if the sociological component of the action was defaulted.

To sum up, this work (and future works) could lead to replace the mere dichotomy between stored, tool-specific semantic knowledge and immediate technical reasoning, by a dichotomy between two modes of reasoning: Sociological reasoning based on theory of mind and personal/impersonal differentiation, and technical reasoning grounded in differentiating mechanical features and potential actions. Similar proposals have been made in developmental psychology between a teleological rationality and a mentalistic rationality (Gergely and Csibra, 2003). So, perhaps difficulties of AD and SD patients in Pantomime of Tool Use, Single Tool Use and Functional/Contextual Association were due to a deficit in sociological reasoning while technical reasoning allowed them to understand expectations in Real Tool Use (and in Recognition of Tool Manipulation as regards SD patients). This would mean that the apparent loss of knowledge was not item-specific but rather corresponded to a broad impairment of the ability to share information. This may explain why we did not find systematic concordance between production and recognition in an item-by-item analysis. At the moment this interpretation might seem quite putative but we hope it will open up a range of new perspectives to understand why some memory-based approaches were proved to be unreliable in the present work.

5. Conclusion and clinical relevance

The aim of the present work was to test memory-based and reasoning-based hypotheses in neurodegenerative diseases. Memory-based hypotheses predicted consistent errors across recognition and production tasks whereas the reasoning-based hypothesis rather predicted a dissociation between recognition tasks and, at least, Real Tool Use. In order to investigate these assumptions, we developed an original design including both item-based and prediction-based quantitative analyses. Results suggest that memory-based hypotheses are far from satisfying to understand tool use disorders in neurodegenerative diseases. In contrast, predictions from the reasoning-based approach were more frequently observed. However, even the latter approach (although defended here) was not sufficient. One of the reasons might be that even the reasoning-based predictions admitted the existence of tool-related stored knowledge in this item-by-item analysis, which is why we proposed a potential role of “sociological reasoning” (e.g., theory of mind).

At the theoretical level, these findings have three main implications.

First, they confirm that tool-related knowledge is not sufficient to use tools, which is already well admitted (e.g., Buxbaum et al., 1997). Second, they demonstrate the weak role of manipulation knowledge in tool use, at least in neurodegenerative diseases. Third, they provide more evidence for the technical-semantic hypothesis (see also Baumard et al., 2016; Jarry et al., 2013) that, although still more reliable than other hypotheses, nevertheless fails to fully account for tool use disorders in these diseases. Fourth, they question the very type of knowledge that might underlie the use of familiar tools (e.g., personal versus impersonal memory). On the whole, they question the relative roles of knowledge and reasoning in the field of apraxia.

At the clinical level, we would like to propose recommendations for clinicians that work in the field of neurodegenerative diseases. First of all, performance in recognition tasks (whether it concerns picture matching or recognition of tool manipulation tasks) is a poor predictor of actual tool use skills, even though it should be acknowledged that this conclusion applies only to tool-object pairs in a laboratory setting for we did not assess naturalistic multi-step actions. On this ground, clinicians might be tempted to assess tool use skills with Pantomime of Tool Use and/or Single Tool Use for these are convenient bedside indicators of apraxia. However, this study also demonstrates that performance in either Pantomime of Tool Use or Single Tool Use does not accurately predict the performance with actual tool-object pairs. Note that strictly speaking these findings apply to patients with neurodegenerative diseases but not to patients with stroke and apraxia. It appears that decontextualized tasks (i.e., recognition tasks and production tasks in which a part of the device is lacking) are particularly difficult for patients with either Alzheimer's disease or semantic dementia, which is why we would like to recommend the use of real technical devices in neuropsychological assessment when possible.

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Appendix A. Supplementary data

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