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Influence des représentations d'action et des représentations sémantiques lors de l'utilisation d'objets : une approche neurocognitive

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"May the force be with you"

an old Master

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Published studies

The published studies I will present all along this manuscript are listed below according to the chapters they belong. All these published works are proposed at the end of the manuscript (only in the pdf version of the manuscript).

Lesourd, M., Servant M., Baumard J., Reynaud E., Ecochard, C., Trari Medjaoui F., Bartolo, A., & Osiurak, F. (2021). Semantic and action tool knowledge in the brain: identifying common and distinct networks. *Neuropsychologia*. https://doi.org/10.1016/j.neuropsychologia.2021.107918 **(Chapter 2 and 3)**

Lesourd, M., Näegelé, B., Jaillard, A., Jarry, C., Detante, O., & Osiurak, F. (2020). Using tools efficiently despite defective hand posture: a case-study. *Cortex*, *129*, 406-422. https://doi.org/10.1016/j.cortex.2020.04.023 **(Chapter 4)**

Lesourd, M., Budriesi, C., Osiurak, F., Nichelli, P. F., & Bartolo, A. (2019). Mechanical knowledge does matter to tool use even when assessed with a non-production task: evidence from left brain-damaged patients. *Journal of Neuropsychology, 13,* 198-213. https://doi.org/10.1111/jnp.12140 **(Chapter 4)**

Lesourd, M., Baumard, J., Jarry, C., Etcharry-Bouyx, F., Belliard, S., Moreaud, O., Croisile, B., Chauviré, V., Granjon, M., Le Gall, D., & Osiurak, F. (2017). Rethinking the cognitive mechanisms underlying pantomime of tool use: evidence from Alzheimer's disease and semantic dementia. *Journal of International Neuropsychology Society, 23,* 128-138. https://doi.org/10.1017/S1355617716000618 **(Chapter 4)**

Lesourd, M., Osiurak, F., Navarro, J., & Reynaud E. (2017). Involvement of the left supramarginal gyrus in manipulation judgment tasks: contributions to theories of tool use. *Journal of International Neuropsychology Society, 23,* 685-691. https://doi.org/10.1017/S1355617717000455 **(Chapter 3)**

Baumard, J., **Lesourd, M.**, Jarry, C., Merck, C., Etcharry-Bouyx, F., Chauviré, V., Belliard, S., Moreaud, O., Croisile, B., Osiurak, F., & Le Gall, D. (2016). Tool use disorders in neurodegenerative diseases: roles of semantic memory and technical reasoning. *Cortex, 82*, 119-132. https://doi.org/10.1016/j.cortex.2016.06.007 **(Chapter 4)**

Lesourd, M., Baumard, J., Jarry, C., Le Gall, D., & Osiurak, F. (2016). A cognitive-based model of tool use in normal aging. *Aging, Neuropsychology and Cognition, 24,* 363-386. https://doi.org/10.1080/13825585.2016.1218822 **(Chapter 2 and 4)**

Lesourd, M., Baumard, J., Jarry, C., Etcharry-Bouyx, F., Belliard, S., Moreaud, O., Croisile, B., Chauviré, V., Granjon, M., Le Gall, D., & Osiurak, F. (2016). Mechanical problem-solving strategies in Alzheimer's Disease and Semantic Dementia. *Neuropsychology, 30,* 612-623. https://doi.org/10.1037/neu0000241 **(Chapter 4)**

Reynaud, E., **Lesourd, M.**, Navarro, J., & Osiurak, F. (2016). On the neurocognitive origins of human tool use: A critical review of neuroimaging data. *Neuroscience and Biobehavioural Reviews*, *64*, 421-437. https://doi.org/10.1016/j.neubiorev.2016.03.009 **(Chapter 3)**

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Introduction

This manuscript includes 5 chapters. In chapter 1, I present a brief historical overview of models of apraxia of tool use, and the debate existing between two current neurocognitive approaches on the use of tools, namely, the manipulation-based approach and the reasoning-based approach. I present several theoretical issues with predictions derived from the two approaches, focusing on three forms of representations supporting the use of tools, that is, manipulation, mechanical and semantic tool knowledge. Then, I present in the following chapters (chapter 2-4) some of my works conducted in the last decade to answer to these theoretical points.

In chapter 2, I examined the way manipulation, mechanical and semantic tool knowledge are defined and assessed. With neuropsychological data, I confirmed that manipulation, mechanical, and semantic tool knowledge are relatively independent. I also demonstrated that tasks assessing manipulation knowledge can bring contradictory findings in left brain-damaged patients, pointing out that manipulation knowledge needs to be more specified. I also found that normal aging had differential effect on mechanical and semantic knowledge, the former being more robust to age-related effect that the latter. In chapter 3, I examined the cerebral correlates of each of these representations, by investigating particularly the role of the left inferior parietal lobe (IPL) and the lateral occipitotemporal cortex (LOTC). I found that mechanical knowledge is supported mainly by the left IPL (supramarginal gyrus) whereas manipulation knowledge engaged the intraparietal sulcus and the left LOTC. Finally, in chapter 4, according to the reasoning-based approach, I demonstrated that mechanical knowledge, but not manipulation knowledge, is a good predictor of several tool use tasks in patients presenting apraxia of tool use (i.e., in stroke and neurodegenerative patients).

Finally, in chapter 5, I introduce future directions. Reasoning-based approach and manipulation-based approach are exclusive approaches both rejecting the strong form of the other one. I propose an alternative hypothesis, in which both forms of representations may co-exist, but if mechanical knowledge is mandatory in our interaction with tools, manipulation knowledge gives only an economic advantage by storing pre-existing hand-tool representations, while not being of first importance to use tools. To test this hypothesis, I propose to study the temporal dynamics of activation of mechanical and manipulation representations in healthy subjects. I also propose to explore the functional reorganization of manipulation and mechanical representations in LBD patients and how these representations can predict apraxic outcomes from acute to chronic stage.

1. Apraxia of tool use: a brief overview

1.1. The precursors

1.1.1. Karl Hugo Liepmann

In the early XXth century, K.H. Liepmann was one of the first to give a detailed description of apraxia, based on the observation of brain-damaged patients. In a group study including 42 right-brain damaged (RBD) patients and 47 left brain-damaged (LBD) patients, Liepman (1908) reported several interesting observations. First, he found that apraxia was never present in RBD patients whereas 48% patients (n = 20/42) suffered from apraxia following a lesion in the left hemisphere. From this first result, Liepmann suggested that the left hemisphere should be dominant for gestural functions. Second, among the 20 patients presenting apraxic deficits, 70% of them (n = 14/20) were aphasic. For Liepmann this result indicates that apraxia and aphasia are two autonomous manifestations and although the cerebral substrates of language and gestures are close, they remain distinct.

Liepman (1908, 1920) proposed also a clinical synthesis in which he introduced several concepts that are still used to classify apraxic deficits (see **Figure 1**). To explain the production of intentional gestures, he introduced the notion of "*movement formulae*", created in posterior parietal cortices and translated in "*cinetic formulae*" within motor centers. Three forms of apraxia may be observed following a perturbation occurring at different steps of the model. The first form is called ideational apraxia, which may occur following a deficit of the *movement formulae*, the representation of the action on its whole is impaired. This deficit is observed in actual use of tools and pantomime of tool use, but can be compensated, at least in part, if a model of the gesture is given to the patient (i.e., imitation). Lesions in posterior parietal cortex and particularly the left hemisphere may be responsible for such apraxia. The second form of apraxia, called ideomotor apraxia, disrupts the relation between the *movement formulae* and the *cinetic formulae*, as the *movement formulae* can no longer guide motor center, patient will meet difficulties in imitating gestures or pantomiming the use of tools on verbal command. However, the actual use of tools can be spared because of the physical constraints imposed by the tool. This apraxia may be caused by the interruption of white fibers associating parietal structures with motor centers. Finally, the third form of apraxia, *melokinetic apraxia* is a loss of the *cinetic formulae* and is effector specific. The deficit will not vary according to the context of assessment and will be present in all the gestural activities. *Melokinetic apraxia* has been attributed to lesions occurring in sensorimotor cortices.

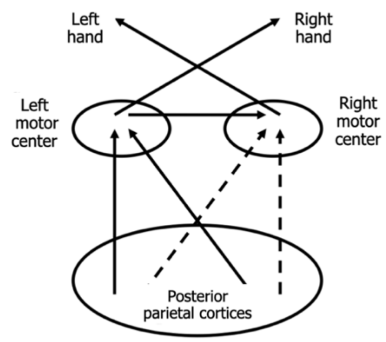

Figure 1. Model proposed by Liepmann (1908, 1920). *Movement formulae* is created in posterior parietal cortices and transferred in motor cortices in order to guide the *cinetic formulae*.

1.1.2. The neo-associationism of Norman Geschwind

Far away from Liepmann, in the 1970's, Geschwind, (1975) has proposed a connexionist model which rejected the existence of a specific praxis center, as it was initially proposed by Liepmann. For Geschwind, the processing of gestural information is mainly depending on the nature of the sensory input (i.e., visual input or auditory input). This model posits the existence of two main pathways originating from associative sensory cortices and projected to associative motor centers (see **Figure 2**). Thus, a direct connection between auditive cortices and associative motor cortices allows producing gestures on verbal command. A second direct connection between visual associative areas and associative motor cortices allows imitating gestures and pantomiming the use of tools on visual presentation. Apraxia can be observed in only one sensory modality and will occur because of an interruption between sensory cortices and motor centers. This model explains the dissociation observed in patients that showed preserved gestures on verbal command and impaired production on visual presentation, and the inverse dissociation. The presence of both deficits is also explained by the simultaneous interruption of the two pathways.

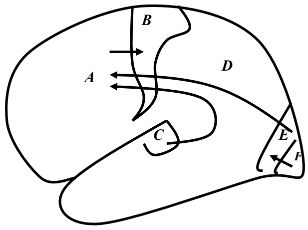

Figure 2. Neo-associationist model of Geschwind (1975). A, associative motor cortex; B, motor cortex; C, Wernicke area; D, arcuate fasciculus; E, associtaive visual cortex; F, visual cortex.

1.2. Cognitive models of apraxia

1.2.1. Conceptual and production systems (Roy & Square, 1985)

Roy and Square (1985) are the first to propose a distinction between a conceptual and a production system to produce a gesture. The conceptual system allows the emergence of an abstract representation of the action, which is supported by the activation of two forms of knowledge, namely, action knowledge and knowledge about object function. Knowledge about object function contains relations existing between objects, based on their function, their perceptual properties (size, shape, etc.) and their context of use (in relation to the body, to other objects or to the location of the objects). Action knowledge links limb movements with actions (e.g., screwing requires the rotation of the wrist), but the actions are non-specific of a particular object, a same action can be achieved with distinct objects (e.g., screwing can be done with a screw or with a knife), thus actions exist independently from the objects. Once elaborated, the action is translated to the production system in the form of a generalized motor program. These programs are not effector-specific, as an action can be made with the hand, a finger or even a foot. The selection of the effector represents the final step of the model.

1.2.2. Action lexicon and semantic system

1.2.2.1. Gonzalez Rothi et al. (1991)

In their model, largely inspired by the cognitive models of language, Gonzalez Rothi, Ochipa, and Heilman, (1991) proposed a dissociation between semantic memory and action knowledge (**Figure 3**). The existence of an input (gesture recognition) and output (gesture production) action lexicon in which known gestures are stored as visuokinestesic engrams. A deficit of these lexicon may be associated with an ideomotor apraxia (i.e., spatial and temporal errors during gesture production). The model includes several input modalities, inspired by the neo-associationist model of Geschwind, and can explain the dissociations observed in patients between different kind of gestures (pantomime on verbal command vs on visual presentation of the tool). The model includes also two routes, a lexical route which allows the production of meaningful gestures and a non-lexical route which allows to imitate meaningless gestures. The semantic system, common to both language and gesture parts, contains an action sub-system which stores function and mechanical associations between objects. A deficit of this sub-system may lead to a "conceptual apraxia", that is, an incapacity to produce the correct action (e.g., hammering at the sight of a screw).

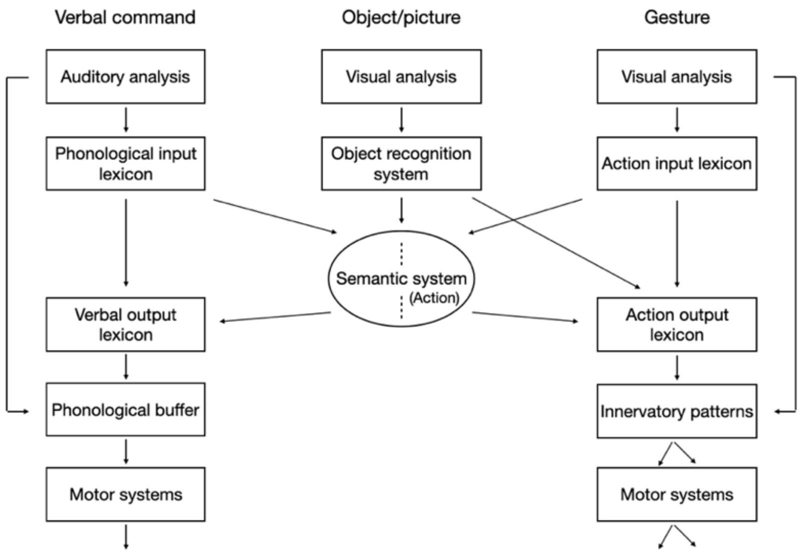

Figure 3. The model of Gonzalez Rothi et al. (1991).

1.2.2.2. Cubelli et al. (2000)

Cubelli et al. (2000) proposed a revision of the model of Gonzalez Rothi et al. (1991). First, they introduced an intermediate step in the direct route of imitation called visuo-motor conversion mechanism. Indeed, it has been demonstrated that imitation of meaningless gestures may call upon body representations (i.e., conceptual mediation; Goldenberg 1995; see also Lesourd et al. 2017). This intermediate step suggests that the direct route is not as direct as initially proposed by Rothi et al. (1991) but includes many cognitive processes distributed across several brain regions of both hemispheres (Goldenberg 2013; for a review see Lesourd et al. 2018). Second, the direct path between action input lexicon and action output lexicon has been removed given the lack of empirical observations. Third, the term "innervatory patterns" is replaced by "gestural buffer" to remove the confusion introduced in the model of Rothi et al. (1991) between neural and psychological level.

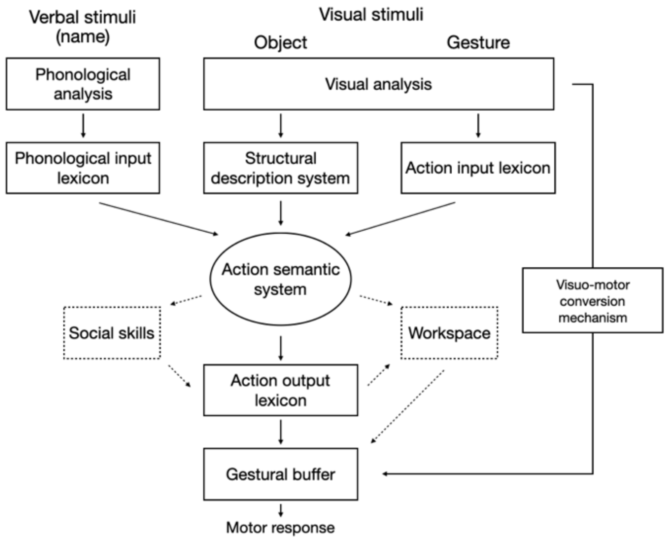

Figure 4. Model of Cubelli et al. (2000).

Two modules have been added in a recent version of the model (see Bartolo & Stieglitz Ham, 2016): (1) a Workspace module between the action semantic system and action output lexicon to account for the deficit in pantomiming the use of tools in the presence of working memory impairment (Bartolo, Cubelli, Della Sala, & Drei, 2003); and (2) a Social skills module to account for the deficit of producing meaningful gestures in association with theory of mind deficit (Stieglitz Ham, Bartolo, Corley, Swanson, & Rajendran, 2010).

1.2.3. The importance of gesture engrams

Buxbaum (2001) proposed a modified version of the model of Gonzalez Rothi et al. (1991), which includes 3 distinct systems (**Figure 5**). First, the dorsal system contains dynamic body representations which guide the gestures to the constraints imposed by the environment. Thus, patients with dynamic apraxia met difficulties while pantomiming the use of tools but can use tools successfully, as they have tools in hand. Second, the ventral system stores conceptual knowledge about tools and patients could produce conception errors and can be impaired in tool semantic matching tasks, as it can be observed in patients with semantic dementia (Baumard et al., 2016; Bozeat, Lambon Ralph, Patterson, & Hodges, 2002; Hodges, Bozeat, Lambon Ralph, Patterson, & Spatt, 2000). Third, the praxis central system contains gesture engrams and is particularly involved in the recognition of pantomimes and in the tasks assessing manipulation knowledge. A deficit of this system leads to representational apraxia, which is associated with lesions in the left inferior parietal lobe (Buxbaum, Kyle, Grossman, & Coslett, 2007; Buxbaum, Kyle, & Menon, 2005). According to Buxbaum (2001), gesture engrams are effector-specific motor representations that characterize hand-tool relationships:

> "The gesture engram is thought to contain the features of gestures which are invariant and critical in distinguishing a given gesture from others. For a hammering movement, for example, a broad oscillation from the elbow joint is critical, as is a clenched hand posture, and these and other similar gestural features are construed as forming the "core" of the gesture representation. In other words, the schema for "hammering" specifies a range of values for the features (or parameters) "elbow joint angle," "shoulder joint angle," "grip aperture," and so forth." (Buxbaum, 2001; p.452)

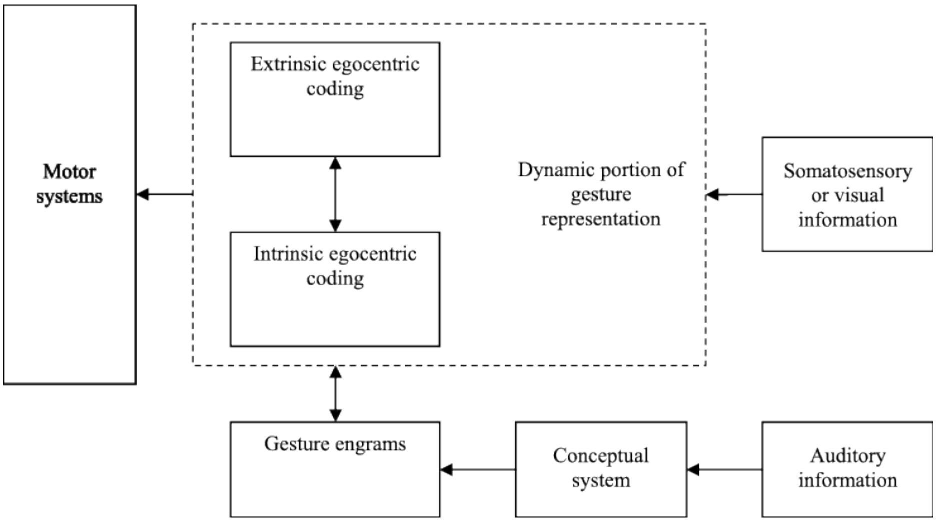

Figure 5. Model of Buxbaum (2001).

In a recent account of the two visuo-motor pathways (Goodale & Milner, 1992; Ungerleider & Mishkin, 1982), Binkofski and Buxbaum (2013) proposed an anatomical and functional subdivision of the dorsal pathway into a ventro-dorsal pathway (the "use" system) and a dorso-dorsal pathway (the "grasp" system). While the dorso-dorsal pathway is mainly involved in online monitoring of action (e.g., reaching/grasping; Rossetti et al., 2005; Tunik, Frey, & Grafton, 2005), the ventral and the ventro-dorsal pathways underpin the main representations about tool use. The ventral pathway supports semantic tool knowledge, and the ventro-dorsal pathway supports manipulation knowledge. More recently, with the 2AS+ model, Buxbaum and colleagues showed that the left posterior middle temporal gyrus is also playing a key role in manipulation knowledge. The left posterior middle temporal gyrus (pMTG) is involved in retrieving hand posture associated with the use of familiar tools and the recognition of pantomiming the use of tools whereas the kinematic component of the gesture is associated with left inferior parietal lobe (IPL; Buxbaum, Shapiro, & Coslett, 2014; Kalénine & Buxbaum, 2016; Kalénine, Buxbaum, & Coslett, 2010; Tarhan, Watson,

& Buxbaum, 2015). Thus, retrieving manipulation knowledge may be possible from the functional interactions between brain regions of the inferior parietal lobe and the lateral temporal cortex. In agreement with these data, the lateral occipital temporal cortex (LOTC) has been found to be largely involved in action understanding (Wurm, Ariani, Greenlee, & Lingnau, 2016; Wurm, Caramazza, & Lingnau, 2017; Wurm & Caramazza, 2019; for review see Lingnau & Downing, 2015).

If the MBA has largely focused on hand-tool relationships for explaining the use of tools, in a more recent account of the MBA, manipulation knowledge may contain the whole action event, that is, hand-tool and tool-object relationships:

> "we store knowledge that hammers and nails 'go together' in a common 'hammering event', and thus, tools and nails are linked in memory in part via manipulation knowledge". (Buxbaum, 2017; p.351)

1.3. The role of reasoning

1.3.1. Inferring structure from function

Goldenberg and Hagmann (1998) observed the presence of errors in apraxic patients that cannot be explained only by a semantic deficit (e.g., eat a soup with a fork). They proposed that these patients may suffer from not being able to retrieve the function of objects based on their structure. Using tools does not need stored knowledge, as the function of tools can be directly inferred from the analysis of its structure. According to Goldenberg, gesture engrams are not required to use tools as this representation can be replaced by functional knowledge (i.e., semantic tool knowledge) and mechanical knowledge (Goldenberg, 2013). The ability of inferring structure from function can be assessed with mechanical problem-solving tasks, in which patients are asked to select among several rods with distinct characteristics (e.g., shape), the one that can be combined with a cylinder to lift it. Goldenberg and Hagmann (1998) found that mechanical problem solving was invariably defective in apraxic patients who commit errors when using simple tools. Thus, using tools would be irremediably linked to the ability to infer function from structure. Moreover, lesions in left inferior parietal lobe would impair the ability to infer function from structure (Goldenberg & Spatt, 2009). Other approaches have been inspired by Goldenberg's model while presenting their own specificity.

1.3.2. The technical reasoning hypothesis

The technical reasoning hypothesis assumes that people reason about the physical object properties to solve everyday life activities (Le Gall, 1998; Osiurak, Jarry, & Le Gall, 2010; Osiurak, Lesourd, Navarro, & Reynaud, 2020). This reasoning is based on mechanical knowledge (e.g., cutting, lever, or percussion), which is thought to be non-declarative (Osiurak, Jarry, & Le Gall, 2010, 2011; Osiurak & Lesourd, 2014). Mechanical knowledge is based on the understanding of opposition existing between properties of tools and objects. For example, understanding the cutting action relies on the understanding of the relative opposition between one thing possessing the properties "abrasiveness" and "hardness" versus another one possessing the opposite properties (e.g., Lesourd, Baumard, Jarry, Le Gall, & Osiurak, 2016). This knowledge does not store functional properties of tools but rather functional compatibility of their parts (Vaina & Jaulent, 1991) in that mechanical knowledge is assumed to be abstract (Gagnepain, 1990; Le Gall, 1998; for a discussion see Osiurak, 2014). The reasoning-based approach posits that in a situation where a tool has to be used with an object, the technical reasoning process generates a mental simulation of how the tool has to be used with an object (i.e., expected perceptual effect) and is followed by a simulation of the potential motor actions (i.e., motor simulation) which evaluate the costs associated with the intended tool-use actions (Osiurak, 2014; Osiurak, Lesourd, Navarro, & Reynaud, 2020).

Mechanical knowledge has been traditionally considered to support novel tool use, the use of familiar tools in a non-conventional way (e.g., using the blade of a knife to drive a screw) and in a conventional way (Jarry et al., 2013; Osiurak et al., 2010, 2011; for a review see Baumard, Osiurak, Lesourd, & Le Gall, 2014). Mechanical knowledge is commonly assessed with mechanical problem-solving tasks (e.g., Goldenberg & Hagmann, 1998; Jarry et al., 2013; Ochipa, Rothi, & Heilman, 1992) in which participants have to carry out specific actions to extract an element out from a box. More recently, mechanical knowledge has been also assessed with non-production tasks (Lesourd, Budriesi, Osiurak, Nichelli, & Bartolo, 2019). This kind of knowledge is required for allocentric relationships (i.e., tool-object relationship), that is, when we have to focus on the relation between a tool and an object. The left inferior parietal lobe has been shown to be crucial for mechanical knowledge (Goldenberg & Hagmann, 1998; Goldenberg & Spatt, 2009; Jarry et al., 2013; Osiurak, Jarry, Lesourd, Baumard, & Le Gall, 2013).

1.4. The reasoning-based approach versus the manipulation-based approach

During this first brief overview, we reported that classical cognitive models of apraxia have focused mainly on two forms of representations to explain tool use interactions, that is manipulation knowledge and semantic tool knowledge (Buxbaum, 2001; Cubelli et al., 2000; Gonzalez Rothi, Ochipa, & Heilman, 1991; Roy & Square, 1985). We also acknowledged a third kind of representation, mechanical knowledge, which may also occupy a central role in tool use interactions. How these representations interact together to produce object-related actions is a matter of intense debate between two theories of tool use, namely the reasoning-based approach (RBA) and the manipulation-based approach (MBA). These two theories make distinct predictions concerning the role of the representations that underlie tool use (**Figure 6)**. According to the RBA, it is the idea of how to use the tool via mechanical knowledge which guides the movement. By contrast, the MBA posits that it is the idea of the movement which guides the use of tool. These two approaches are conceptually distinct in the manner they model the use of tools, but they both accept the existence of representations underlying the use of tools (i.e., mechanical and manipulation knowledge). To simply model the interactions between tools and objects, one may posit the existence of two kinds of relationships: hand-tool relationships and tool-object relationships (**Figure 6**). RBA posits a clear distinction between these two kinds of relations and the role they play in using tools: mechanical knowledge concerns tool-object relationships, that is the understanding of the physical principles that allow to use a tool with an object, whereas hand-tool relationships are rather a matter of motor simulation (i.e., by-product of technical reasoning). For MBA, manipulation knowledge contains mainly hand-tool relationships (Buxbaum et al., 2007; Buxbaum, Sirigu, Schwartz, & Klatzky, 2003; Buxbaum, 2001) but may also contains tool-object relationships (Buxbaum, 2017). The concept of manipulation has evolved along the years and may be more underspecified in its current form, as it is far from being clear that manipulation is associated to hand-tool relationships or both hand-tool and tool-object relationships.

RBA and MBA are traditionally exclusive approaches that criticize each other on several theoretical points (see Buxbaum, 2017; Osiurak & Badets, 2016; Osiurak et al., 2011; Osiurak & Badets, 2017). For instance, the RBA in its strong form rejects the existence of manipulation knowledge whereas the MBA accepts a point of contact between the two theories by proposing that technical reasoning may be supported by the dorso-dorsal pathway (Buxbaum, 2017). However, this proposition disagrees with the key prediction of the RBA, which hypothesis that technical reasoning is supported by the left IPL (Orban & Caruana, 2014; Osiurak, 2014; Osiurak et al., 2011). Thus, mechanical knowledge should be processed within the dorso-ventral pathway and not in the dorso-dorsal pathway.

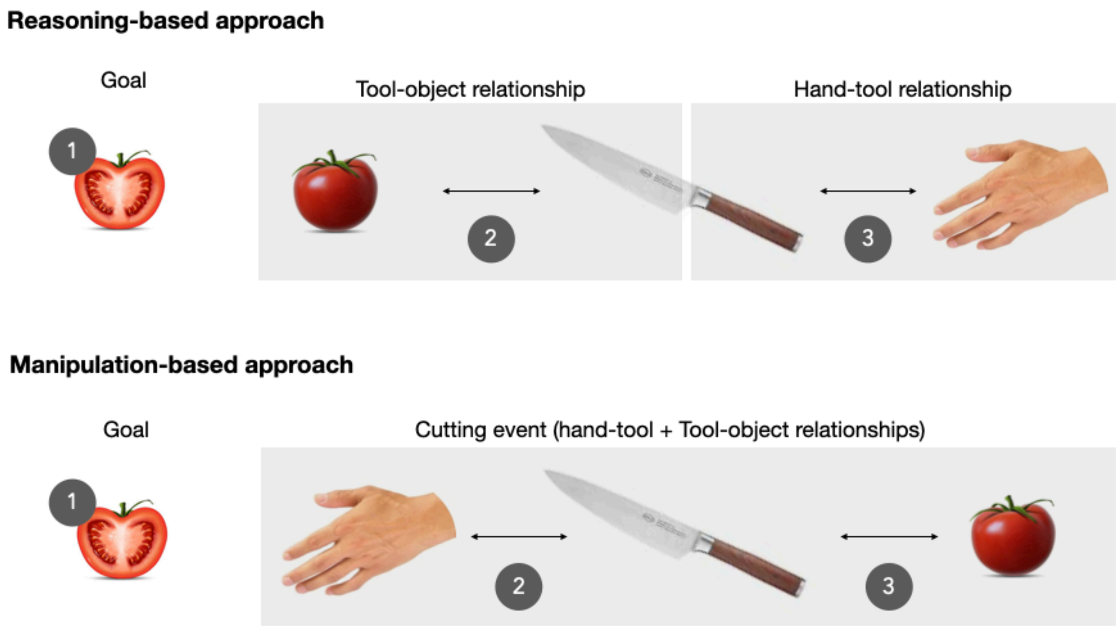

Figure 6. The manipulation-based approach versus the reasoning-based approach. Each number represents the order of the mental process occurring during the use of tool. For the MBA, the step 2 and 3 may also be simultaneous.

MBA and RBA are agree on the role of semantic knowledge in using familiar tools which is neither sufficient nor required but may play a useful role in using tools (Buxbaum, Schwartz, & Carew, 1997; Negri, Lunardelli, Reverberi, Gigli, & Rumiati, 2007).

1.5. Synthesis and predictions

The aim of this work was to better understand (1) the neurocognitive organization of the conceptual tool knowledge (independence and hierarchy); and (2) how these representations can explain actual use of familiar tools. To do that, we tested some of the predictions made by the MBA and the RBA at the light of neuropsychological and neuroimaging data. Although RBA questions the relevance of manipulation knowledge; and MBA, in a lesser extent, questions the relevance of mechanical knowledge, we hypothesis that manipulation and mechanical knowledge could both coexist in the conceptual tool system. Hereafter, we will consider mechanical and manipulation knowledge as part of action tool knowledge.

I will consider several theoretical questions (detailed below) in the three following chapters: the cognitive organization of the conceptual tool knowledge (Chapter 2); the cerebral correlates supporting the conceptual tool knowledge (Chapter 3); and the link between conceptual tool knowledge and the actual use of tool (chapter 4). Finally, I will propose several perspectives in the last part of this manuscript (Chapter 5).

1.5.1. The issue of cognitive organization (Chapter 2)

In this chapter, I will investigate the links between action tool knowledge and semantic tool knowledge. I will test the independence of semantic tool and action tool representations by examining the neuropsychological dissociations obtained in LBD patients. To do that, I will explore some of the tasks used to assess mechanical, manipulation and semantic tool knowledge. Tasks assessing mechanical knowledge are classically focusing on tool-object relationships whereas tasks assessing manipulation knowledge are focusing on hand-tool relationships. Moreover, I will investigate the tasks that targeted two components of manipulation knowledge, that is hand posture and kinematics. If dissociations have been observed between hand posture and kinematics in apraxic patients, they remain rare in the literature of apraxia (Hayakawa, Fuji, Yamadori, Meguro, & Suzuki, 2015; Lesourd, Naëgelé, Jaillard, Detante, & Osiurak, 2020; Sirigu et al., 1995), questioning the real nature of a fractionated manipulation knowledge.

1.5.2. The issue of cerebral correlates (Chapter 3)

RBA and MBA make distinct predictions according to the cerebral correlates of hand-tool and tool-object relationships. According to the RBA, tool-object relationships are stored mainly in the left IPL (area PF; Orban & Caruana, 2014) whereas hand-tool relationships are processed in the left IPS. Moreover, mechanical knowledge may support both familiar and unfamiliar use of tools, but more particularly unfamiliar use of tools (Osiurak, 2014; Osiurak et al., 2011; Osiurak et al., 2009). Initially, the MBA predicted that manipulation knowledge was stored in the left IPL (Buxbaum, 2001; van Elk, 2014; Haaland, Harrington, & Knight, 2000), in a more recent account of the MBA, manipulation knowledge is distributed across the left IPL (kinematic component) and the left pMTG (hand posture) (Buxbaum, Shapiro, & Coslett, 2014; Garcea, Greene, Grafton, & Buxbaum, 2020; Kalénine, Buxbaum, & Coslett, 2010). In the last version of the MBA, the left pMTG is involved in the retrieval of the visual appearance of tool use action and the left IPL aggregates visual attributes of a tool and its associated action (e.g., a hammer is swung along a particular trajectory to pound in a nail). It is therefore more difficult to make precise predictions between hand-tool and tool-object relationships.

1.5.3. The issue of context of use (Chapter 4)

Cognitive models of apraxia have mainly focused on pantomime of tool use tasks but not on actual use of tools. LBD patients are traditionally impaired in pantomiming the use of tools, which has been described as a hallmark of manipulation knowledge deficit (gesture engrams). However, LBD patients improve significantly their performance with the tool in hand compared to pantomime of tool use tasks (for a review see Baumard et al., 2014). MBA explains this effect by assuming that during the actual use of tools, gesture engrams activation become less critical as the presence of the tool may afford serious advantages (i.e., tactile-kinesthetic cues) and therefore facilitate the position of hand and arm posture (De Renzi, Faglioni, & Sograto, 1982). However, if physical feedback provided by the tool was sufficient to fully compensate impaired manipulation knowledge, thus manipulation knowledge should not be critical for using tools (for a discussion see Osiurak et al., 2010, 2011). In the following sections, we tested the predictions of the two approaches by exploring different contexts of use: pantomiming the use of tools (PTU), the use of the tool in isolation (i.e., single tool use; STU), the use of the tool and the associated object (i.e., real tool use; RTU). We hypothesize that a critical form of representation for using tools may be involved in all object-related actions whatever the context of use.

We also tested additional hypotheses. For MBA, manipulation knowledge is sufficient to explain familiar tool use, and mechanical knowledge may be involved only in unfamiliar tool use. A deficit of manipulation knowledge may be associated with impaired familiar object-related actions and particularly PTU tasks. For RBA, mechanical knowledge supports all object-related actions (familiar and unfamiliar), and manipulation knowledge is not needed in tool use context (see also Goldenberg, 2013).

2. Cognitive organization of conceptual tool knowledge

2.1. Action tool knowledge

2.1.1. Definition

Our ability to use tools is based on action tool knowledge, allowing us to specify the action required to use a tool. Action tool knowledge might contain hand-tool centered information about how to manipulate tools and is "thought to contain the features of gestures which are invariant and critical for distinguishing a given gesture from others" (i.e., MBA; Buxbaum, 2001, 2017). Other authors assume that action tool knowledge might contain tool-object centered information about physical principles (e.g., cutting, lever), which specify the mechanical action that must be performed (i.e., RBA; Osiurak & Badets, 2016; Osiurak, Jarry, & Le Gall, 2010, 2011; Osiurak, Lesourd, Navarro, & Reynaud, 2020). In broad terms, action tool knowledge contains mainly two kinds of representations underlying the use of tools, that is, manipulation knowledge (mainly hand-tool-relationships) and mechanical knowledge (tool-object relationships).

2.1.2. Tasks assessing action tool knowledge

Manipulation knowledge is traditionally assessed with either tool-tool compatibility tasks or hand-tool compatibility tasks[1] (see **Figure 7**). In tool-tool compatibility tasks, participants have to decide if two tools are grasped (i.e., hand posture component; Andres, Pelgrims, & Olivier, 2013) or manipulated in the same way (i.e., kinematic component; Canessa et al., 2008). If participants are explicitly asked to focus either on hand posture or on kinematics, some studies do not distinguish between these two action components, considering manipulation as a whole (e.g., Boronat et al., 2005). In hand-tool compatibility tasks, also called recognition of gesture tasks (e.g., Jarry et al., 2013; Osiurak et al., 2009), participants have to decide if a tool is correctly held in hand among several distractors (Baumard et al., 2016; Decroix & Kalénine, 2019; Jarry et al., 2013; Osiurak et al., 2009). In a variant of this task, participants have to choose among several hand postures the one that is suitable for grasping a target tool (Kleineberg et al., 2018; Pelgrims, Olivier, & Andres, 2011). Hand-tool tasks can also focus on the kinematics component of action by asking participants if the motion of the tool held in hand is correct or not (e.g., Martin et al., 2017). The main difference between tool-tool and hand-tool compatibility tasks, apart from the experimental variations (e.g., number of distractors), is the presence of a hand only for the latter tasks.

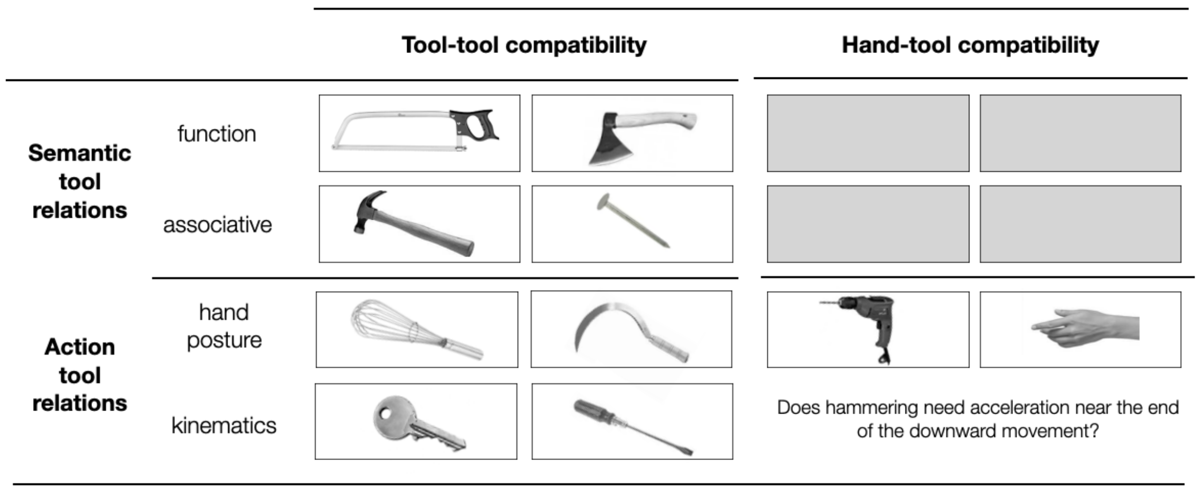

Figure 7. Example of tasks assessing semantic tool and action tool knowledge. Adapted from Lesourd et al. (2021).

Mechanical knowledge is assessed with mechanical problem-solving tasks (Baumard et al., 2016; Goldenberg & Hagmann, 1998; Jarry et al., 2013; Ochipa, Rothi, & Heilman, 1989; Osiurak et al.,

[1] We proposed the terms of tool-tool compatibility and hand-tool compatibility tasks in a recent paper presented in this work to overcome the multilabelling issue (Lesourd et al., 2021). Indeed, it is not uncommon to encounter different terms to qualify the same kind of tasks, leading to important confusions.

2013) (see **Figure 8**). In these tasks, participants are traditionally asked to retrieve a wooden cube from a cylinder by applying the appropriate action with a given tool (e.g., pushing, lifting, etc.). Participants are presented with a metal block with a fixed bendable wire protruding from two sides and are asked to devise tools from the metal block with the bendable wire relative to the cylinders proposed. In the Novel tool test (Goldenberg & Hagmann, 1998), cylinders are proposed to the participants with three different tools. A cylinder is put in a socket and has a part to which only one of the tools fit. Subjects are asked to select the appropriate tool that is best suited for taking up the cylinder, to attach it to the cylinder and to lift the cylinder out of the socket. Two scores are derived from this test: a score of selection and a score of application. As participants do not devise their tools, the selection score assesses the ability to recognize the technical means suitable for performing the task. In the sequential mechanical problem-solving task (Jarry et al., 2013; Osiurak, Jarry, Lesourd, Baumard, & Le Gall, 2013), a choice and a no choice condition are systematically proposed. Thus, the choice condition assesses the ability to select the tool that best fits with the experimental design from an array of several tools. Moreover, the choice condition allows investigating the strategies employed by the participants to solve the problem (e.g., trial-and-error strategies; Lesourd et al., 2016; Osiurak et al., 2013). In non-conventional tool use tasks, participants can be presented with several tools and a given object. Nevertheless, given that none of these tools are usually used with the object, participants have to choose the tool that shares similar mechanical attributes with the conventional tool and to show how to use it with the given object (see for example Osiurak et al., 2009). In the alternative tool selection task, participants are asked to select a correct tool but not perform the action. For instance, Lesourd et al. (2019) showed action verb/phrase (e.g., hammering a nail into a wall) and three pictures of objects (e.g., saw, shoe and brush). The participants were asked to select among the three objects the one that could be used to perform the intended action. As the tool typically used to perform the action was always absent (e.g., hammer), the participants were asked to select the tools which had the physical features required to perform the action (i.e., the heel of the shoe could be used to knock the nail into the wall).

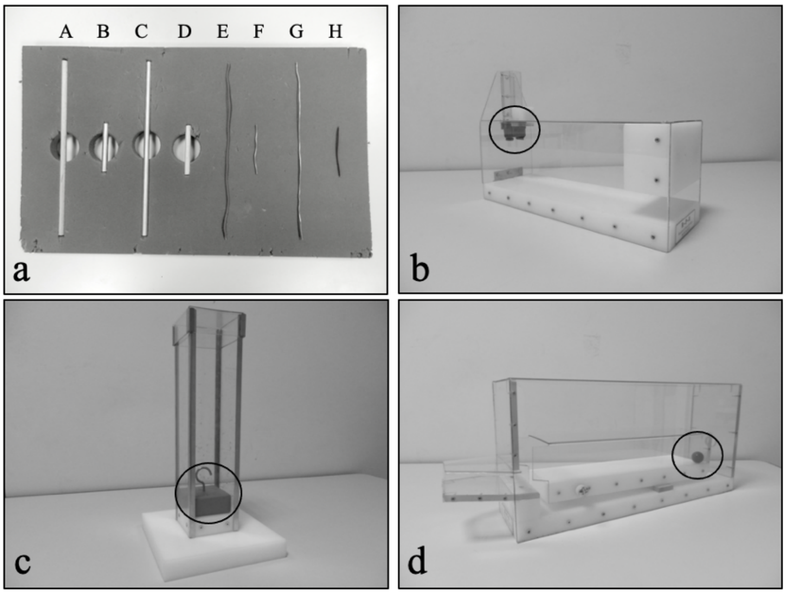

Figure 8. An example of Mechanical Problem-Solving test (MPS) used in several studies from our group. The top left picture (a) represents the 8 rods used in the choice condition. The three other pictures show the 3 transparent boxes (b, c and d) used in the test in both the choice and the no choice condition. Black circles indicate the wooden targets subjects had to extract out from the box. Explanations about the extraction of the targets out from each box are given in the text. Adapted from Lesourd et al. (2016).

2.2. Semantic tool knowledge

2.2.1. Definition

Semantic tool knowledge has received many terms in the field of tool use, namely, semantic knowledge about tool function (Gonzalez Rothi et al., 1991), semantic knowledge about tool use (Baumard et al., 2016; Lesourd et al., 2020), functional knowledge (Bozeat et al., 2002; Goldenberg, 2013), instruction of use (Goldenberg & Hagmann, 1998), conceptual knowledge (Hodges, Bozeat, Lambon Ralph, Patterson, & Spatt, 2000), or semantic memory (Buxbaum et al., 1997). Semantic tool knowledge is tool-centered, as it contains information about the prototypical use of familiar tools. When there are several possible ways of using a tool, they are likely to be weighted as a function of their familiarity and frequency (Goldenberg, 2013). Semantic tool knowledge may inform individuals about where to find tools if not present in the visual field (Osiurak, 2014).

Tool use depends on explicit semantic knowledge about tool-object usual relationships (i.e., associative relations; a hammer goes with a nail) and tool function (i.e., function relations; a hammer and a mallet share the same purpose). Function relations can be seen as taxonomic (Kalénine & Buxbaum, 2016; Mirman, Landrigan, & Britt, 2017), meaning relations based on shared features (e.g., saw – knife). Associative relationships can be seen as thematic, that is, contiguity relations between objects that often belong to distinct semantic categories but have complementary roles (e.g., saw – wood).

2.2.2. Tasks assessing semantic tool knowledge

A classical way to assess semantic tool knowledge is to propose tool-tool compatibility tasks, in which participants have to make a decision/choice based on the characteristics that are shared or not by the stimuli (**Figure 7**).

In function tasks, participants are instructed to choose among several tools, the two that share the same purpose or goal. For instance, in the presence of a knife, a saw and a screwdriver, participants have to choose the knife and the saw, as these two tools share the same function of 'cutting'[2] (Buxbaum & Saffran, 2002; De Bellis et al., 2020; Kalénine & Buxbaum, 2016). In a variant of this task, participants are presented with two tools, and have to decide if they share the same purpose (e.g., knife-saw; Canessa et al., 2008).

Associative tasks consist in choosing among several objects (e.g., nail and screw) or contexts (e.g., kitchen or garage) the one that is usually associated with a target tool (e.g., hammer) in events. Two tools may also be presented, and participants have to decide if they can be found in the same context (e.g., knife-saw; Perini, Caramazza, & Peelen, 2014). Finally, one tool and one object can be presented, and participants have to decide if they are functionally related or not (e.g., hammer-nail).Dissociation between action and semantic tool knowledge.

2.2.3. Dissociation between manipulation and semantic tool knowledge

Semantic tool knowledge differs from action tool knowledge as dissociations have been reported between these two forms of knowledge. Buxbaum and Saffran (2002) found that apraxic patients but not non-apraxic patients were impaired in tasks where patients were asked to select two objects, among three, sharing the same way of being manipulated (i.e., tool-tool compatibility task). No difference was observed between apraxic and non-apraxic patients in tasks where the

[2] We see here that function relations can be confounded with action relations (i.e., hand posture and kinematics), as saw and knife have the same function (i.e., cutting), but both are also grasped and moved in a similar way.

tools had to be selected if they share the same goal (i.e., function relations). Several works reported neuropsychological dissociations between manipulation and function knowledge (Garcea, Dombovy, & Mahon, 2013; Sirigu, Grafman, & Sunderland, 1991). Thus, it appears that semantic tool knowledge (i.e., particularly function relations) and manipulation knowledge are supported by distinct neurocognitive processes (Buxbaum & Saffran, 2002; Chen, Garcea, & Mahon, 2016; Garcea et al., 2013; Garcea & Mahon, 2012, 2019). To refine the previous results, we reviewed the performance of LBD patients in tasks assessing semantic tool knowledge and manipulation knowledge (described previously in section *2.1.2 Tasks assessing action tool knowledge*, page 18; and section *2.2.2 Tasks assessing semantic tool knowledge*, page 21).

Regarding brain-damaged patients, we focused our analysis on behavioral performance. We selected brain-damaged studies according to a series of selection criteria: (1) single case studies were not included; (2) Only patients presenting exclusively LBD were considered; (3) presence of a control group[3]; (4) relevance of the tasks used in relation to the scope of the present study (see above); (5) Tasks using verbal material were not considered because of the potential presence of aphasia (Buxbaum, Kyle, & Menon, 2005; Buxbaum, Sirigu, Schwartz, & Klatzky, 2003). The final selection resulted in 7 studies including 138 LBD patients. The studies considered in the review are displayed in **Table 1.**

[3] A control group can be another group of patients. For instance, a group of LBD patients without apraxia can be considered as a control group for LBD patients with apraxia (see for instance Buxbaum & Saffran, 2002).

Table 1. Overview of the LBD patients' studies considered in Lesourd et al. (2021)

Study	Subjects'age (*n*)	Task name	Instruction	Lesion description
Buxbaum and Saffran (2002)	62.3 ± 11.1 (*n* = 13)	Manipulation	Selecting the two objects that shared the same manipulation among three (e.g., type-writer - piano)	apraxic (*n* = 7) F, P, T
		Function	Selecting the two objects among three that shared the same purpose (e.g., radio - vynil turntable)	non-apraxic (n = 6) T
Buxbaum et al. (2003)	62.6 ± 9.8 (*n* = 14)	Manipulation	Forced choice of two objects among three that shared the same way to be held and used	apraxic (*n* = 9) T, P, F, SubC
		Function	Forced choice of two objects among three that shared the same possible function	non-apraxic (*n* = 5) Cereb, F, T, P
Bartolo et al. (2007)[a]	54.2 ± 9.6 (*n* = 5)	Object-manipulation	Matching two objects that have the same manner of manipulation (e.g., pipe - penny whistle) in the presence of a distractor (e.g., spoon)	F, T, P
		Object-function	Matching two objects that have similar function (e.g., jug - bottle) in the presence of a distractor (e.g., pot)	
		Object-relation	Matching two objects which functionally interact when used (e.g.,teapot - cup) in the presence of a distractor (e.g., glass)	
		Pantomime recognition	Matching the pantomime executed by the examiner with the correct tools in presence of three distractors	
Osiurak et al. (2009)	58.2 ± 16.3 (*n* = 20)	Functional picture matching (associative)	Selecting among 4 objects the one (e.g., screw) which is associated with the target (e.g., screwdriver)	F, T, P, O, SubC
		Functional picture matching (categorical)	Selecting among 4 objects the one (e.g., belt) which is functionally equivalent with the target (e.g., pair of shoulder straps)	
		Gesture recognition	Selecting the photograph depicting the correct use of a tool among three representing the tool incorrectly oriented, inappropriately held or dangerously held	
Jarry et al. (2013; 2016)[b]	2013: 70.2 ± 10.3 (*n* = 16)	Functional association	Selecting from 4 objects, the one (e.g., nail) that is functionally associated with the target (e.g., hammer)	F, T, P, O, SubC
	2016: 68.2 ± 9.5 (*n* = 17)	Categorical association	Selecting among 4 objects the one (e.g., saw) which shares the same purpose as the target (e.g., axe)	
		Gesture recognition	Selecting the photograph depicting the correct use of a tool among four representing the tool incorrectly oriented, inappropriately held or dangerously held	
Kalénine et al. (2016)	57 ± 11 (*n* = 48)	Thematic relationship	Deciding which object of two is semantically related with the target (e.g., saw - wood)	MTG, STS, Pre/PostC, IPL, IFG, MFG
		Taxononmic relationship	Deciding which object of two is semantically related with the target (e.g., saw - drill)	
Lesourd et al. (2019)	65.2 ± 13.9 (*n* = 21)	Manipulation matching	Choosing two objects among three (e.g., slingshot, sword, bow) that required the same manner of manipulation	N/A
		Function matching	Choosing two objects among three (e.g., candle, cigarette, lamp) that could be used for the same purpose	
		Associative matching	Choosing among two objects (e.g., screw and nail), the one that is more likely to be used with the target (e.g., hammer)	

[a] Six patients were initially included in Bartolo et al. (2007) but one patient had right lesion (case 6) and was excluded from the present review
[b] One patient and 17 controls were added between Jarry et al. (2013) and Jarry et al. (2016)
F: frontal; P: parietal; T: temporal; SubC: Sub-Cortical; Cereb: Cerebellum; O: Occipital; MTG: Middle Temporal Gyrus; STS: Superior Temporal Sulcus; Pre/PostC: Pre- and Post-Central gyrus; IPL: Inferior Parietal Lobe; IFG: Inferior Frontal Gyrus; MFG: Middle Frontal Gyrus; N/A: Not Available

The lack of data prevents us from conducting quantitative meta-analysis of behavioral performance. Thus, we used a qualitative meta-analysis methodology developed by our group (Baumard et al., 2014; Lesourd et al., 2013), leading us to enable direct comparisons between distinct studies. First, for each study and condition, mean raw scores obtained by the patients' group were converted to percent by dividing each mean raw score by the maximum score on the task. The same procedure was applied for the matched control groups. Second, we calculated a mean difference score, corresponding to the difference between the percent score of the patient group and that of the matched control group (e.g., patients' mean difference score = 60%, controls' mean difference score = 90%, difference between patients and matched controls = 30%). The greater the difference is between patients and controls the more impaired the patients are. Third, we used a graphical illustration of the results in which each study was represented by a different colored disk, the size of which depended on the number of patients included in the study. When a study documented several conditions or distinct groups of patients, then several disks of the same color appear on the figure.

The results are presented in **Figure 9** and showed the control-patient differences for each condition and each study. In LBD patients, we first found a dissociation between action tool task variants: tool-tool compatibility tasks (difference control-patients = 15-48.1%, excluding non-apraxic patients' performance) were more impaired than hand-tool compatibility tasks (difference control-patients = 3.4-11.4%). Second, we found a gradient in the performance of tool-tool compatibility tasks between action, function, and associative relations: the largest difference between controls and patients was observed in action tool-tool compatibility tasks (range = 2.4%-48.1%), followed by function tool-tool compatibility tasks (range = 2.4%-30.7%), and finally by associative tool-tool compatibility tasks (range = 2%-19.8%). Considering that non-apraxic LBD patients perform in sub-normal range in action tool-tool compatibility tasks (i.e., control-patient difference = 2.4%; Buxbaum et al., 2003), the difference between controls and patients for action tool tasks (range = 15%-48.1%) is even more important than the two other tasks. This gradient was systematically observed for the studies that tested several conditions in the same group of patients (Bartolo, Daumüller, Della Sala, & Goldenberg, 2007; Buxbaum & Saffran, 2002; Buxbaum et al., 2003; Kalénine & Buxbaum, 2016; Lesourd et al., 2019; Osiurak et al., 2009). When trying to control for the difficulty between function and associative conditions (Kalénine & Buxbaum, 2016), the control-patient difference was indeed reduced, but the authors found that both patients and controls identified significantly faster associative relationships compared to function relationships.

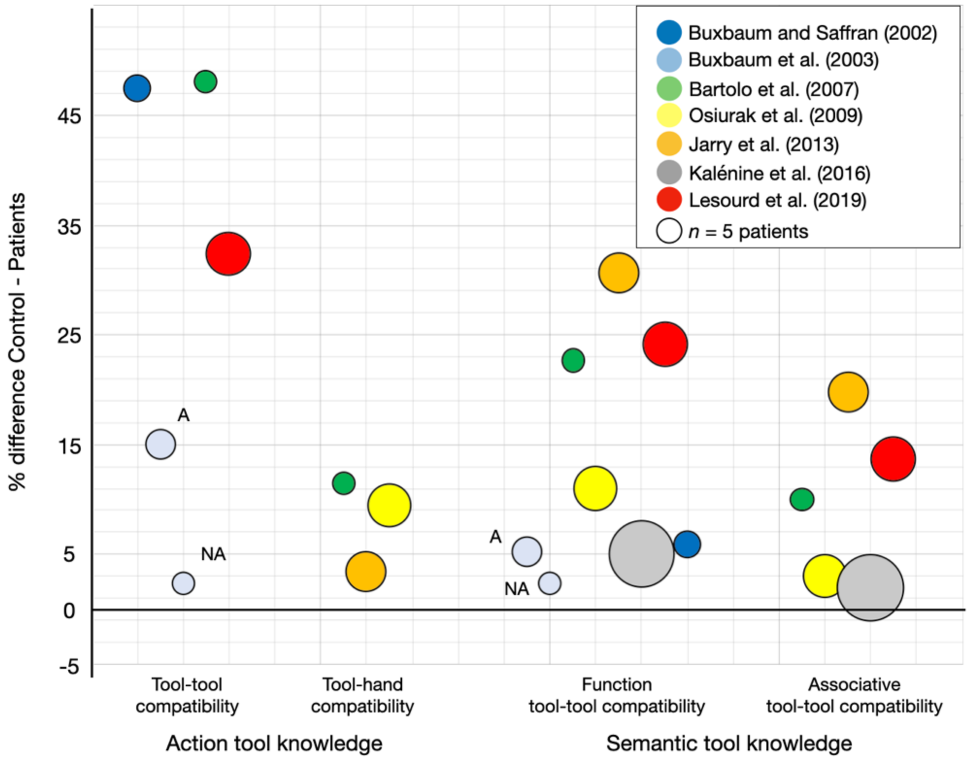

Figure 9. Control-patient differences (%) for each condition and each study. Each circle represents the difference between patients and control's performance, thus the greater the difference is between patients and controls the more impaired the patients are. Each study is represented by a different colored disk, the size of which depended on the number of patients included in the study. Adapted from Lesourd et al. (2021).

We examined the proportion of impaired patients and dissociations between tasks in LBD patients using single case statistics (Crawford & Garthwaite, 2005; Crawford & Garthwaite, 2007). These results are presented in **Table 2**. The proportion of patients showing significant impairments in action and semantic tool tasks confirmed the gradient observed in **Figure 9**. When individual data for both patients and controls were available, we also calculated dissociations between tasks (RSDT; Crawford & Garthwaite, 2005). Dissociations were found among all the tasks investigated in the present review and particularly between function and associative tasks (range = 29-47%), between action hand-tool tasks and function tasks (range = 45-53%), and between action tool-tool tasks and associative tasks (48%).

Table 2. Patients' impairments and dissociations according to Crawford and Garthwaite's (2005, 2007).

	Per cent of patients showing a deficit[a]				Per cent of dissociations[b]					
	Action		Function	Associative	Action TT - Action HT	Action TT - Function	Action TT - Associative	Action HT - Function	Action HT - Associative	Function - Associative
	Tool-tool	Hand-tool	Tool-tool	Tool-tool						
Bartolo et al. (2007)	5/5 (100)	2/5 (40)	5/5 (100)	4/5 (80)	na	na	na	na	na	na
Osiurak et al. (2009)	-	8/20 (40)	12/20 (60)	7/20 (35)	-	-	-	9/20 (45) A>F: 7/9 F>A: 2/9	2/20 (10) A>Ass: 1/2 Ass>A: 1/2	8/20 (40) F>Ass: 1/8 Ass>F: 7/8
Jarry et al. (2016)	-	4/17 (25)	10/17 (59)	9/17 (53)	-	-	-	9/17 (53) A>F: 8/9 F>A: 1/9	6/17 (35) A>Ass: 6/6 Ass>A: 0/6	8/17 (47) F>Ass: 4/8 Ass>F: 4/8
Lesourd et al. (2019)	17/21 (81)	-	12/21 (57)	14/21 (67)	-	5/21 (24) F>A: 5/5 A>F: 0/5	10/21 (48) A>Ass: 6/10 Ass>A: 4/10	-	-	6/21 (29) F>Ass: 5/6 Ass>F: 1/6

Action TT: action tool-tool compatibility tasks; Action HT: action hand-tool compatibility tasks; A: action; F: Function; Ass: associative
na: not available

[a] The presene of a deficit is attested according to the Crawford-Garthwaite Bayesian test for single-case analysis (2007).

[b] The presence of a dissociation is attested according to the Revised Standardised Difference Test (Crawford and Garthwaite, 2005)

To summarize, a lesion within the left hemisphere of the brain significantly affected action tool tasks, more particularly action tool-tool compatibility tasks, and to a lesser extent function and associative tasks. These results generally confirmed the dissociation observed between manipulation knowledge and semantic tool knowledge, but while dissociations were observed in almost all tasks, we did not find any double dissociation between function and action tool-tool tasks, with the available data. Interestingly, we also found that within action tool knowledge, hand-tool tasks are relatively spared compared to tool-tool tasks, suggesting the existence of dissociations between tasks assessing manipulation knowledge. All action compatibility tasks focused on the kinematic component but never in the hand posture component.

2.2.4. Dissociation between mechanical and semantic tool knowledge

Goldenberg reported in LBD patients, the existence of neuropsychological dissociations between functional association and novel tool test (Goldenberg & Spatt, 2009). Moreover, he found that patients with impaired performance in novel tool test and spared performance in functional association presented inferior parietal lesions whereas patients with the opposite profile presented temporal lesions. In a patient with left temporal lesions, Osiurak et al. (2008) found while suffering from a loss of semantic tool knowledge, the patient was able to use tools in a non-conventional way, suggesting that her ability to reason on physical principles about tools and objects was spared. Moreover, several studies pointed out that the ability to solve mechanical problems are relatively spared in patients with semantic dementia while they are impaired in semantic tool tasks (Baumard et al., 2016, 2019; Bozeat et al., 2002; Hodges et al., 2000; Lesourd et al., 2016).

In a recent work, we hypothesized that if mechanical and semantic tool knowledge were distinct, they may be differentially impacted by age-related effects. Thus, we tested the differential effect of aging on mechanical, semantic tool knowledge and actual use of tools[4] (Lesourd, Baumard, Jarry, Le Gall, & Osiurak, 2017). We proposed to 98 healthy participants (36 males, 62 females, mean age = 66.69 years, range = 50-86 years; 88 right-handers, 10 left-handers; mean Mini-Mental-State-Examination score = 28.04; range = 24-30; mean level of education = 12.71 years, range = 5-20 years) to complete a mechanical problem-solving test in choice (MPS-C) and no-choice (MPS-NC) conditions which is assumed to assess mechanical knowledge, and two tool-tool compatibility tasks, namely, functional matching (FM) and contextual matching (CM), known to assess semantic tool knowledge (function and associative relations, respectively). To confirm that MPS-C and MPS-NC were good indicators of mechanical knowledge and, FM and CM of semantic tool knowledge, respectively, we first carried out an exploratory factor analysis with MPS-C, MPS-NC, FM and CM composite scores[5] as variables. Principal axis factoring was used to obtain an initial solution, followed by a Varimax axis rotation to obtain the final one. This procedure was used because the factors were expected to be orthogonal. From this exploratory factor analysis, we calculated participants' factor scores for each factor (i.e., mechanical and semantic factor scores), which were used in the following sections. As can be seen in **Table 3**, MPS-C and MPS-NC load with factor 2 (.91 and .71, respectively) whereas FM and CM load with factor 1 (.88 and .89, respectively). This result confirms that we have a mechanical factor (i.e., factor 2) and a semantic factor (i.e., factor 1).

[4] In this section I will not discuss about the results on actual use of tools. This part will be discussed in depth in Chapter 4. *Conceptual tool knowledge and contexts of use*, page 45.

[5] We used composite scores instead of raw scores because ceiling effects are frequent in tool use tasks, particularly in healthy subjects. The composite scores were obtained using a procedure I developed in a previous paper (Lesourd et al., 2016) and which is presented in details in section 4.1.3 *Overcoming ceiling effects in tool use tasks: a new scoring system approach* (page 40).

Table 3. Factor loading scores from factor analysis of mechanical and semantic tool knowledge tasks after Varimax rotation

Tasks	Factor 1	Factor 2
MPS-C	.06	**.91**
MPS-NC	.41	**.71**
FM	**.88**	.25
CM	**.89**	.13
	Semantic	*Mechanical*
Eigen values	2.28	.88
% Var. explained	.44	.35

Factor loading scores > .70 are in bold
MPS-C: Mechanical Problem-Solving in Choice condition;
MPS-NC: Mechanical Problem-Solving in No-Choice condition;
FM: Functional Matching; CM: Contextual Matching; Var.: Variance

Effect of aging was examined in two ways. First, we examined the amount of variance explained for mechanical and semantic factor scores in all subjects, using linear regressions with chronological age as predictor. When mechanical factor scores were predicted, chronological age (β = -.22, p = .03) was found to be a significant predictor and the model was able to account for 4% of the variance, $F(1,96) = 4.96$, $p = .028$, $R^2_{adj} = .04$. When semantic factor scores were predicted, chronological age (β = -.45, $p < .001$) was found to be a significant predictor and the model was able to account for 20% of the variance, $F(1,96) = 24.76$, $p < .001$, $R^2_{adj} = .20$.

Second, we examined the relationship between chronological age and mechanical and semantic knowledge tasks when controlling for motor speed and cognitive functioning, using partial correlations. If a correlation was found to decrease when controlling for motor speed or cognitive functioning, mediation analyses were performed using the Baron and Kenny (1986) causal-four steps approach; in addition, a bootstrapped confidence interval (CI) for the indirect effect was obtained using procedures described by Preacher and Hayes (2008). We found that only correlations between chronological age and tool use tasks, and mechanical and semantic factor scores seem to decrease when controlling for cognitive functioning but not when controlling for motor speed. This observation leads us to consider the cognitive functioning as a mediator of the effect of aging. Results of these analyses are displayed in **Table 4** and **Figure 10**. The initial causal variable is chronological age, in years; the outcome variables are semantic and mechanical factor scores, successively; and the proposed mediated variable is the cognitive functioning (i.e., BEC).

Table 4. Coefficients for the hypothesized causal chain in which age affects cognitive functioning (i.e., BEC) that in turns, affects mechanical and semantic factor scores, and real tool use tasks.

			direct effect	indirect effect	Sobel test for *ab* product significancy		CI(95%)	
Tasks/Factor scores	*a*	*b*	*c'*	*ab*	z	p	lower	upper
RTU-C	-.271***	1.137***	-.638***	-.307	-3.348	.00081	-.5040	-.1443
RTU-NC	-.271***	1.023**	-.636**	-.276	-2.277	.0057	-.4940	-.0944
Semantic factor scores	-.271***	.096***	-.043**	-.026	-3.424	.0006	-.0422	-.0126
Mechanical factor scores	-.271***	.045	-.022	-.0122	-1.775	.076	-.0258	.0014

RTU-C: Real Tool Use in Choice condition; RTU-NC: Real Tool Use in No-Choice condition; CI: Confident Interval
a: unstandardized regression coefficient that estimated the effect of age on cognitive functioning
b : unstandardized regression coefficient that estimated the effect of cognitive functioning on tool use tasks and factor scores
c' : unstandardized regression coefficient that estimated the direct effect of age on tool use tasks and factor scores
ab: strength of the indirect effect of age on tool use tasks and factor scores through cognitive functioning
* $p < .05$; ** $p < .01$; *** $p < .001$

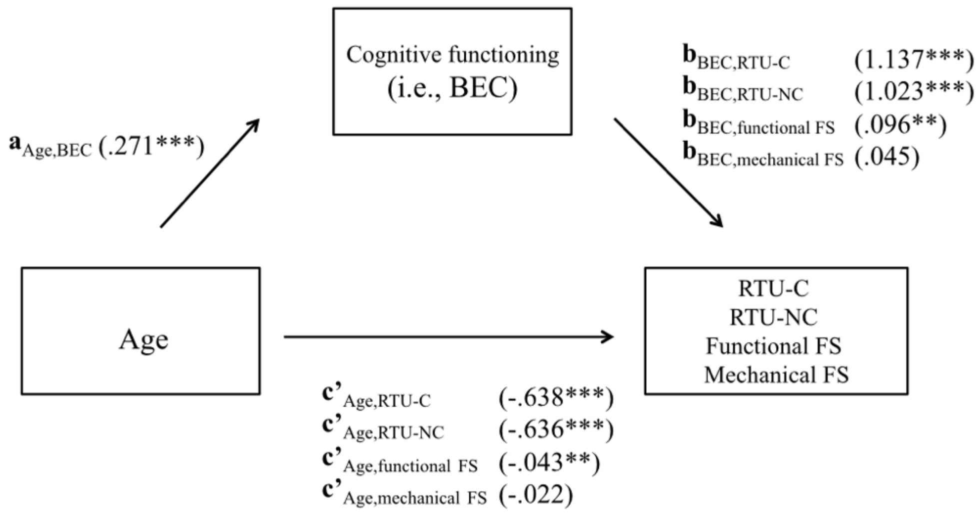

Figure 10. Path diagrams of hypothesized causal chains in which Age affects the cognitive functioning that, in turn, affects semantic factor scores and mechanical factor scores. The path coefficients a, b and c' are estimated by unstandardized regression coefficients. Explanations are given in the text. Semantic FS: Semantic factor scores; Mechanical FS: Mechanical Factor scores. Adapted from Lesourd et al. (2017).

For semantic factor scores, we found that both *a* and *b* coefficients were significant, the Sobel test for the *ab* product was significant and the bootstrapped CI for *ab* did not include zero. By all these criteria, the indirect effect (*ab*) of age on semantic factor scores through BEC was statistically significant. The direct path from age to semantic factor scores (*c'*) was also statistically significant; therefore, the effect of age on semantic factor scores was only partly mediated by BEC. Comparison of the coefficients for the direct versus indirect path (*c'* = -.043 *vs ab* = -.026) suggested that only a part of the effect of age on semantic factor scores was mediated by BEC. For mechanical factor scores, we found that only *a* coefficient was significant, *b* and *ab* coefficients were not statistically significant and the bootstrapped CI for *ab* included zero. All these data suggests that the indirect effect (*ab*) of age on mechanical factor scores through BEC was not significant.

Our results suggest that aging does not affect mechanical and semantic knowledge in the same way. We observed that cognitive functioning is a mediator of aged-related effect on semantic knowledge but not on mechanical knowledge. We assessed cognitive functioning with a French cognitive battery (i.e., BEC) that assesses working memory, spatiotemporal orientation, verbal and visual episodic memory, naming and semantic memory tasks. All these tasks investigate declarative forms of knowledge/skills. Semantic knowledge stores semantic features about tool functions and is assumed to be declarative whereas mechanical knowledge is assumed to be a non-declarative form of knowledge (Osiurak, 2014; Osiurak et al., 2011). In broad terms, aging may impact mechanical and semantic knowledge through different mediators. However, we found that chronological age was a significant predictor but explains only 4% of the amount of the variance of mechanical factors scores whereas it explains 20% of the amount of the variance of semantic factor scores. Thus, it seems that aging has a little impact on mechanical knowledge compared to semantic tool knowledge. Furthermore, as explained before, significant evidence has shown that mechanical knowledge and semantic tool knowledge could be supported by the left inferior parietal lobe and the left temporal lobe, respectively. Moreover, it has been showed that parietal lobes are less affected than temporal lobes with aging (Raz, 2004; Raz et al., 2005). So taken together these findings may suggest that mechanical knowledge could be more spared compared to semantic knowledge with aging.

2.3. Results in a nutshell

- Dissociations between manipulation and function tasks occur less frequently than dissociations between function and associative tasks, ***questioning the real nature of the links between function and manipulation relations***.

- LBD patients are more likely to be impaired in action (kinematic component) tool-tool compatibility tasks compared to hand-tool compatibility tasks, ***suggesting that classical tasks assessing manipulation knowledge are relying upon distinct processes.***

- Mechanical knowledge tasks are less influenced by age-related effect compared to semantic tool knowledge tasks, ***confirming the distinct format of semantic and mechanical representations***.

3. Cerebral correlates of conceptual tool knowledge

3.1. The Tool Processing Network (TPN)

The cognitive representations supporting the use of tools are underpinned by a predominantly left-lateralized brain network (Johnson-Frey 2004; Johnson-Frey et al. 2005; Lewis 2006; Gallivan et al. 2013; Ishibashi, Pobric, Saito, and Lambon Ralph 2016; Reynaud et al. 2016). This large brain network, hereafter called Tool Processing Network (TPN; see Garcea, Chen, Vargas, Narayan, & Mahon, 2018) collectively supports the ability to recognize and use objects and is functionally organized according to the hypothesis of two segregated visuo-motor pathways: a ventral pathway ("what") which mediates semantic aspects of tools (i.e., semantic tool knowledge) and a dorsal pathway ("where") which mediates online control of object-directed actions (Goodale & Milner, 1992; Ungerleider & Mishkin, 1982). In a recent account of the two visuo-motor pathways, Binkofski and Buxbaum (2013) proposed an anatomical and functional subdivision of the dorsal pathway into a ventro-dorsal pathway (visual extrastriate cortex, angular gyrus, supramarginal gyrus, anterior intraparietal sulcus and ventral precentral gyrus) and a dorso-dorsal pathway (visual extrastriate cortex, posterior intraparietal sulcus, superior parietal lobe, and dorsal precentral gyrus). While the dorso-dorsal pathway is mainly involved in online monitoring of action (e.g., reaching/grasping; Rossetti et al., 2005; Tunik, Frey, & Grafton, 2005), the ventral and the ventro-dorsal pathways underpin the main representations about tool use.

3.2. Distinct predictions concerning the organization of action tool knowledge in the TPN

Both the MBA and the RBA assume that the use of tools and the knowledge supporting the use of tools are relying upon the TPN. We examined the predictions derived from MBA and the RBA by conducting a comprehensive meta-analysis on functional neuroimaging data, based on activation likelihood estimation (ALE; Eickhoff, Bzdok, Laird, Kurth, & Fox, 2012). To do so, we used a coordinate-based meta-analysis (CBMA, Turkeltaub, Eden, Jones, & Zeffiro, 2002) with the aim of identifying anatomical locations where an effect can be observed consistently across experiments.

First, we considered the cerebral correlates of hand-tool and tool-object relationships in non-production tasks. Several predictions of the MBA can be tested, taking into account the evolution of the theory: (1) manipulation knowledge is stored in the left IPL (Buxbaum, 2001; van Elk, 2014); (2) manipulation knowledge is distributed across the left IPL and the left pMTG, the former supporting hand posture component and the latter rather supporting kinematic component (Buxbaum, Shapiro, & Coslett, 2014); (3) manipulation knowledge contains both hand-tool and tool-object relationships and is distributed across the left IPL and the left pMTG (Buxbaum, 2017). Moreover, hand posture[6] may emerge from the functional interactions of temporal and parietal areas. Finally, semantic tool knowledge is supported by the temporal lobe and the intraparietal sulcus (IPS) is involved in the production system. Concerning RBA, mechanical knowledge (tool-object relationships) is supported by the left IPL (supramarginal gyrus [SMG]/PF; Goldenberg, 2013; Orban & Caruana, 2014), semantic tool knowledge is supported by the temporal lobes and the IPS is involved in the production system (hand-tool relationships). Moreover, the RBA assumes that only the production system supports hand-tool interaction (i.e., egocentric relationship).

Second, we tested the cerebral correlates of familiar versus unfamiliar tools (production and non-production tasks). The MBA remains silent about the strong link between real tool use and mechanical problem solving. Consequently, it does not predict that familiar and unfamiliar use of tools should involve different cerebral regions (e.g., Buxbaum, 2001; Elk, 2014). At best, it can be expected that both the left IPL (i.e., manipulation knowledge) and the left temporal cortex (i.e.,

[6] The MBA tends to focus now on the hand posture component, which is considered as the most critical part of the tool use action (pantomime of tool use and imitation of meaningless gestures; Metzgar, Stoll, Grafton, Buxbaum, & Garcea, 2022).

function knowledge) are preferentially activated by familiar use as compared to unfamiliar use. By contrast, the RBA suggests that only left temporal lobe regions should be more involved in familiar use than in unfamiliar use (e.g., Goldenberg, 2013; Osiurak, 2014). This rationale is based on the idea that the left temporal lobe contains semantic tool knowledge that is of particular interest for familiar tools. Moreover, the left IPL (particularly the area PF of SMG; see Orban & Caruana, 2014) should be more activated in unfamiliar use than in familiar use, because only mechanical knowledge is involved when people are confronted with unfamiliar use.

Candidates for inclusion were initially identified using a search through the following databases: PubMedand and PsycInfo. We restricted our search to studies published between January 2000 and February 2014. To narrow our search, we used the logical conjunction of keywords: (“brain mapping” OR “functional magnetic resonance imaging” OR “fMRI” OR “positron emission tomography” OR “PET”) AND (“tool use” OR “object use” OR “tool manipulation” OR “object manipulation” OR “praxis” OR “tool recognition”). This search returned 302 studies at the date of 03/03/2014. We evaluated candidate papers for inclusion; according to a series of selection criteria: (1) Theoretical papers and reviews were excluded; (2) Papers must use functional magnetic resonance imaging or positron emission tomography as imaging modality; (3) They were comprised of neurologically healthy and adults’ participants; (4) Relevance of the tasks used in relation to our goal. As explained above, both use and non-use tasks were considered. Moreover, only studies using visual stimuli were included with the exception of two studies using words; (5) Neuroimaging results must be based on whole-brain scanning. Regions of interest analyses were therefore excluded from our selection; (6) The complete list of activation peaks (i.e., foci) with their coordinates must be reported in a stereotactic space; (7) We selected only reported results corrected for multiple comparisons with a statistical significance threshold of $p < 0.05$ or, for a small part of the selected results uncorrected data thresholded at $p < 0.005$. We did require that the same threshold be applied uniformly across the whole brain. Results derived from ROI (Region of Interest) or SVC (Small Volume Correction) analyses were excluded even if spatial coordinates were provided. Because our meta-analytic statistical tests assumed that foci were spatially randomly distributed across the whole brain under the H0 assumption, it was important to avoid experimenter-induced bias in the locations at which effects could be identified. The search resulted in 35 studies and 60 experiments fulfilling our criteria, involving a total of 916 participants (all right-handed) and 642 peaks of activation (participants that took part in more than one experiment were only counted once).

3.2.1. Hand-tool versus Tool-object relationships

For tool-object tasks, the subjects had to focus on the understanding of the action made by the tool with the object (allocentric relationships; e.g., is it correct to use this pair of scissors to cut this sheet of paper?; Bach, Peelen, & Tipper, 2010). Here, no judgment has to be made on the appropriateness of the manipulation. For hand-tool tasks, the subjects had to determine whether the manipulation is correct or not (egocentric relationship), without considering the action made by the tool with the object (e.g., Does this hand posture – for instance a pinch posture – matches the action goal – for instance, throwing a dart?; Vingerhoets, Nys, Honoré, Vandekerckhove, & Vandemaele, 2013). In the Tool-centered tasks, the subjects had to determine with which object or in which context a given tool can be used (allocentric relationship; e.g., Can these two tools – poultry shears and hand spiral beater – be used in the same context?; Canessa et al., 2008).

The results of the meta-analyses conducted separately for each condition are illustrated in **Figure 11**. For tool-object relationships (**Figure 11A**), activation occurred only in the left hemisphere, in the IPL (PF), the ventral premotor cortex (vPMC) and the middle frontal cortex (BA46). The left IPS (phAIP, DIPSA, DIPSM), the left posterior inferior temporal cortex (pITC), and the left occipital cortex (BA19) were more robustly activated for Hand-tool relationships (**Figure 11B**). Finally, the left occipital cortex (LOC, BA19) and the left frontal cortex (BA46, BA11) were more activated by tool-centered conditions (**Figure 11C**).

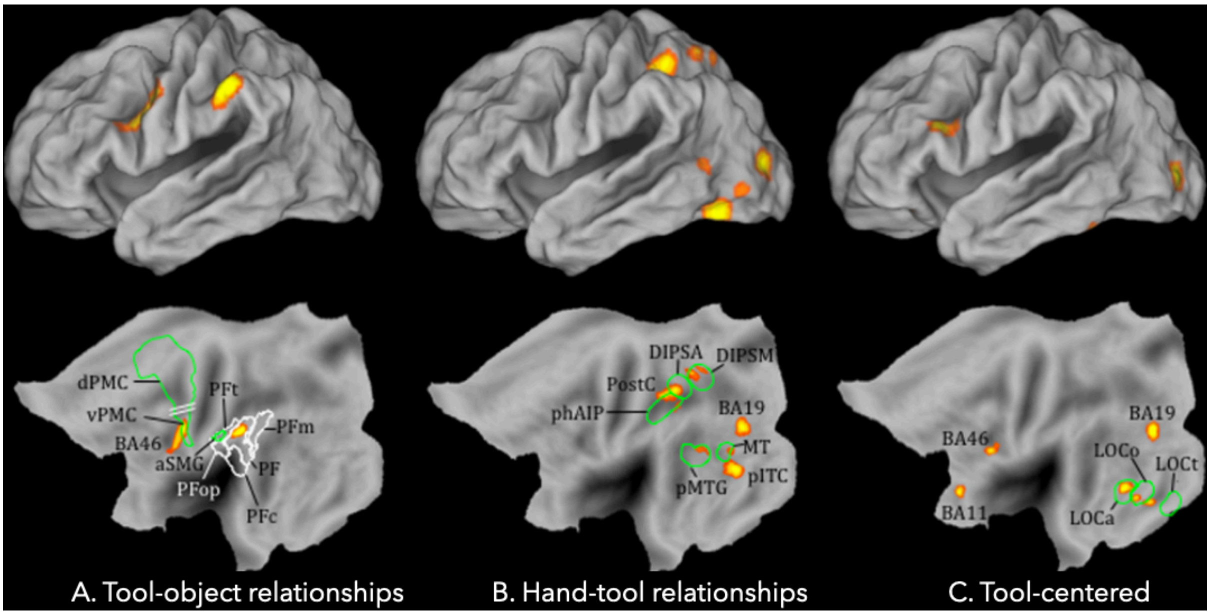

Figure 11. Tool-object, Hand-tool and Tool-centered relationships. Panels A, B, and C show the ALE maps resulting from all the studies included in the three conditions and mapped on two PALS-B12 left hemisphere atlas surface configurations (Van Essen, 2005): lateral fiducial surfaces (Top) and flat maps (Bottom). Adapted from Reynaud et al. (2016).

Concerning the predictions made by the MBA, we did not find any activation of the left IPL in hand-tool relationships therefore invalidating the first assumption. Indeed, it suggests that the left IPL does not store manipulation knowledge. We found activations in the left IPS and the left LOTC (pMTG and pITC). Thus, manipulation knowledge may be supported by the left IPS and in the LOTC. Thus, if the second assumption was true, manipulation knowledge should be supported by the left IPS and the left pMTG. However, the left IPS is devoted to online motor control and does not contain stored representations *per se*. Concerning the third assumption, we found specific activations for tool-object relationships and for hand-tool relationships, suggesting that these representations are dissociable, but we also found that these representations were not both supported by temporal and parietal areas. Thus, our results pointed out the limits of the third assumption derived from the MBA. By contrast, in line with the predictions of the RBA, tool-object relationships are encoded in the left IPL (SMG/PF) and the hand-tool relationships are processed in the left IPS. However, our results indicate that hand-tool relationships were supported by the left pMTG, which is at odds with the predictions of the RBA. Finally, both approaches correctly hypothesized that tool-centered representations are processed in the temporal lobe.

3.2.2. Familiar versus unfamiliar tool use

The familiar task focused on the conventional use of familiar tools (e.g., pantomiming the use of a pair of scissors; Vingerhoets, Vandekerckhove, Honoré, Vandemaele, & Achten, 2011) and the unfamiliar tasks included novel tools or familiar tools used in a non-conventional way (e.g., pantomiming the use of screwdriver-like tool; Vingerhoets et al., 2011).

The results of the meta-analyses conducted separately for each type of stimulus are displayed in **Figure 12A-B**. A left-lateralized brain network was recruited for familiar (**Figure 12A**). A smaller, left-lateralized network was found for unfamiliar, including the IPL (PF, PFm, PFt/aSMG), the IPS (phAIP, DIPSA), the premotor cortex (vPMC and dPMC) and the precentral gyrus (**Figure 12B**). Statistical comparisons were conducted to identify brain regions responding more reliably to one type of stimulus relative to the other (**Figure 12C-D**). Specifically, we found that the left temporal cortex (pMTG, posterior superior temporal gyrus [pSTG]), the left superior parietal lobe (SPL), the left occipital cortex (MT cluster), and the left cingular gyrus (BA24) were more likely to be activated by familiar as compared to unfamiliar (**Figure 12C**). A left-lateralized network, including the IPL (PF, PFm, PFt/aSMG, BA39), the IPS (particularly phAIP), the premotor cortex (vPMC and dPMC) and the PreC was more reliably activated by unfamiliar than familiar (**Figure 12D**).

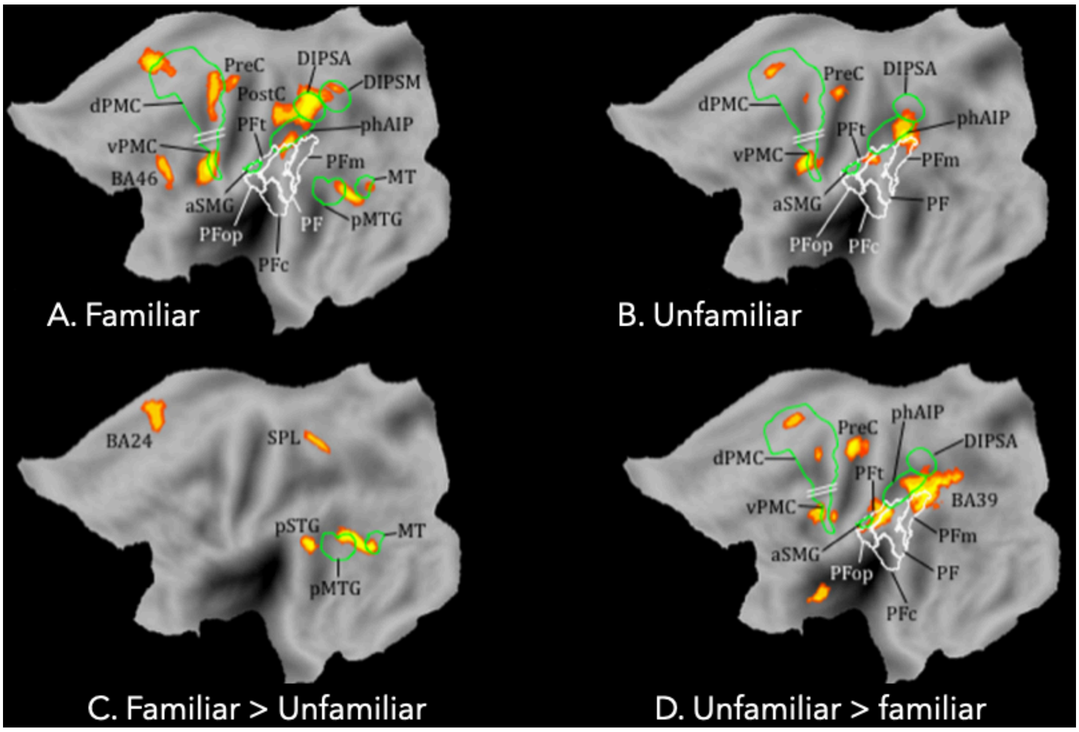

Figure 12. Familiar and unfamiliar use of tools. Panels A and B show the ALE maps resulting from all the studies included in the two conditions, and viewed on the PALS-B12 left hemisphere flat surface. Brain regions more robustly activated by one condition compared to the other are displayed in Panels C (familiar > unfamiliar) and D (unfamiliar > familiar), and viewed on the PALS-B12 left hemisphere flat surface (Van Essen, 2005). Adapted from Reynaud et al. (2016).

MBA considers that both manipulation knowledge and semantic tool knowledge are useful for determining how familiar tools have to be used. It has even been suggested that manipulation knowledge might be activated automatically (i.e., without any intention) from the mere observation of a familiar tool (e.g., Buxbaum & Kalénine, 2010). Therefore, it should be expected that the cerebral regions underlying both manipulation knowledge and semantic tool knowledge (i.e., the left IPL and the left temporal cortex, respectively) are preferentially activated by the visual observation of familiar use as compared to unfamiliar use. Our findings are partially at odds with these predictions given that we observed that only the pMTG and the pSTG are activated for familiar (see familiar > unfamiliar). In addition, we found that the left IPL (PF, PFm, PFt/aSMG) is more reliably involved in unfamiliar (see unfamiliar > familiar). One way of interpreting this finding is that unfamiliar tool use is based on manipulation knowledge, but not on function knowledge. However, manipulation knowledge is thought to contain information about how to manipulate familiar tools in a conventional way, but not on how to use unfamiliar tools or familiar tools in a non-conventional way. In sum, the MBA fails to explain the pattern of results obtained for these conditions. For the RBA, mechanical knowledge located within the left IPL (PF; Orban

& Caruana, 2014) is useful for using tools whatever they are familiar or unfamiliar. Nevertheless, unfamiliar tool use might require a stronger activation of mechanical knowledge (Osiurak, 2014). This prediction is confirmed by our results, showing a specific involvement of the left IPL (PF, PFm, PFt/aSMG) for unfamiliar (see also unfamiliar > familiar). In addition, the specific activation of the left pMTG for familiar (see familiar > unfamiliar) is consistent with the idea that function knowledge is involved only when tools are familiar.

3.3. Action tool knowledge and semantic tool knowledge: common and distinct networks

In the chapter 2, we highlighted the neuropsychological dissociations existing between action tool and semantic tool knowledge. In this part, we are going to explore the cerebral correlates of action tool and semantic tool knowledge by examining specifically the tool-tool compatibility and hand-tool compatibility tasks. Few studies have reported the dissociations between mechanical and semantic tool knowledge (e.g., Goldenberg & Spatt, 2009), thus we will focus only on manipulation knowledge and semantic tool knowledge (function and associative relations). To better understand the neural underpinnings of manipulation and semantic tool knowledge, we performed a systematic comparison of neural networks engaged in manipulation tasks versus function and associative tasks. This review deals with explicit retrieving of action and semantic tool knowledge. To be considered in the present analysis, a study must include one of the following tasks: action tool-tool compatibility tasks (tools held and moved in the same manner), action hand-tool compatibility task (i.e., recognition of gesture tasks; e.g., choosing the correct hand posture associated with a tool), function (tools used for the same purpose) or associative (tools/objects found in the same context or typically used together).

We selected neuroimaging studies according to a series of selection criteria: (1) reviews were excluded; (2) studies had to use functional magnetic resonance imaging (fMRI) or positron emission tomography (PET) as imaging modality; (3) studies had to include only neurologically intact participants; (4) relevance of the tasks used in relation to the scope of the present study (see above); (5) the complete list of activation peaks of main effects (e.g., action tool > control; Kellenbach, Brett, & Patterson, 2003), contrasts (e.g., action tool > function; Canessa et al., 2008), or region of interest (ROI) analyses with their coordinates had to be reported in a stereotaxic space; and (7) only the results corrected for multiple comparisons (e.g., FWE or FDR) with a statistical threshold of $p < .05$ were considered. The final selection resulted in 6 studies including 97 healthy subjects and 61 peaks of activation. These studies are described in **Table 5**. Based on these criteria, a quantitative meta-analysis of neuroimaging studies could not be performed (e.g., Activation Likelihood Estimation method), thus, only cortical activation sites (i.e., peak maxima coordinates) were reported for the different conditions, that is, action tool, function and association (for a similar methodology see Lesourd et al., 2018; Niessen, Fink, & Weiss, 2014; Osiurak, Reynaud, et al., 2021).

Table 5. Overview of the neuroimaging studies considered in Lesourd et al. (2021).

Study	Subjects' age (*n*)	Method	Task name	Instruction	Stimuli
Kellenbach et al. (2003)	27 (*n* = 9)	fMRI	Action knowledge Functional knowledge	Does using the object involve a twisting or turning action? Is this object used to attach or hold objects together?	Color photographs of manipulable and non manipulable tools One stimulus
Boronat et al. (2005)	23.1 (*n* =15)	fMRI	Manipulation Function	Are items related by manipulation? Are items related by function?	Words and line-drawing of manipulable and non-manipulable objects Pair of stimuli
Ebisch et al. (2007)	21.7 (*n* =14)	fMRI	Functional decision	Do the two items are functionally related?	Words and line-drawing of objects Pair of stimuli
Canessa et al. (2008)	24.6 (*n* =15)	fMRI	Action knowledge Function knowledge	Are these objects used with the same manipulation pattern? Are these objects used in the same context of use?	Photographs of manipulable objects Pair of stimuli
Perini et al. (2014)	27.7 (*n* = 24)	fMRI	Action task Location task	Dectecting repetition of same action (1-back task) (i.e., rotate or squeeze) Dectecting repetition of same location (1-back task) (i.e., kitchen or garage)	Picture of manipulable tools One item at a time
Kleineberg et al. (2018)	25.3 (*n* = 20)	fMRI	Manipulation knowledge Function knowledge task	Judging which hand posture best fit with the tool target Judging which recipient was functionally related with the target tool	Pictures of tools and recipients/hand postures One target and two items

The cortical activation sites (i.e., peak maxima coordinates) corresponding to the different conditions and contrasts considered in the present work are represented in **Figure 13**. Distinct patterns emerged when contrasting both conditions. Semantic tool>action tool contrasts were associated with scattered activations in the left hemisphere, comprising lateral temporal cortex and ventral stream of the visual cortex (TE1a/TGd), AG (PGi and PGs), but also medial prefrontal cortex (mPFC; 10d/10v) and in posterior cingulate cortex (7m/31pd). Action tool>semantic tool contrasts were associated with changes in neural activity in inferior premotor cortex (6r) and superior premotor cortex (i6-8/6a) gyrus, in visual association areas of the lateral occipital and posterior temporal cortex (PH), in temporo-parietal occipital junction (TPOJ2) and mostly in parietal regions, that is, in SMG (PFt), IPS (AIP, IP2, LIPd and IP1) and in AG (PGi). We found that a similar brain region in the AG (PGi) could be engaged in both action>semantic and semantic>action contrasts. This apparent discrepancy can be explained easily by the nature of the tasks included in these contrasts. In Kleineberg et al. (2018), the semantic tool task focused on associative relations (e.g., hammer-nail), whereas in Boronat et al. (2005), the semantic tool task focused on function relations (e.g., lighter – match). Thus, function relations elicit less changes in neural activity than action relations in AG (PGi/PGs), whereas the opposite pattern of activation is observed for associative relations. Finally, action tool studies focusing on either hand posture or kinematic components invoked the same posterior brain regions, that is, SMG (PFt), IPS (AIP and IP2) and LOTC (TPOJ2 and PH).

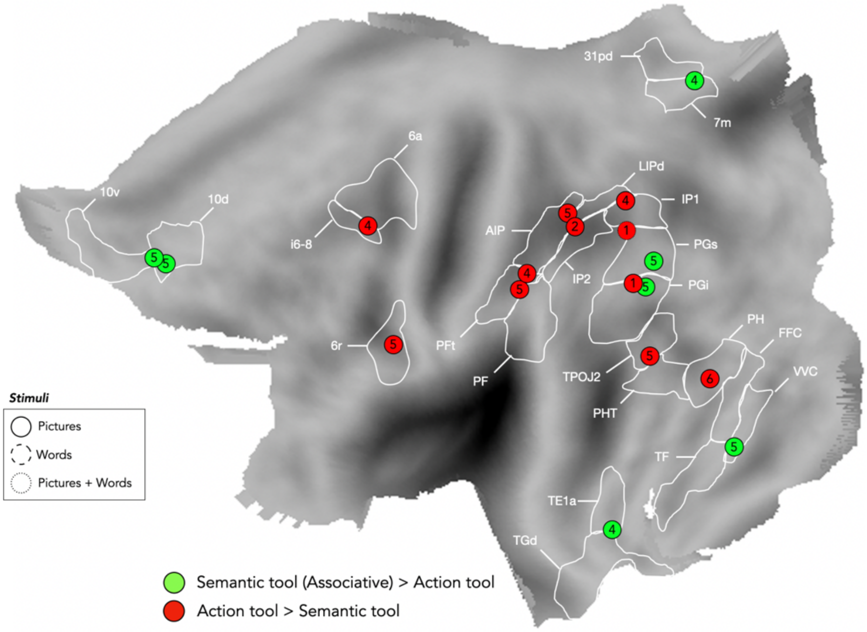

Figure 13. Activation sites reported in the present review are represented on a PALS-B12 left hemisphere (PALS-B12: Population Average, Surface- and Landmark-based human cortical atlas; Van Essen, 2005), using Caret, version 5.65 (http://brainmap.wustl.edu/caret.html; Van Essen et al., 2001). The parcellation is based on Glasser et al. (2016). For abbreviations and explanation, see the main text. Each circle represents an activation site (non-continuous line: words, solid line: pictures, dashed line: words + pictures). Semantic tool>action tool contrasts are depicted in green and Action tool>semantic tool contrasts are represented in red. Each number refers to a specific study: (1) Boronat et al. (2005); (2) Kellenbach et al. (2003); (3) Ebisch et al. (2007); (4) Canessa et al. (2008); (5) Kleineberg et al. (2018); (6) Perini et al. (2014). Adapted from Lesourd et al. (2021).

We selected stimulation studies according to a series of selection criteria: (1) studies had to employ stimulation parameters known to interfere with brain activity; (2) studies had to include only neurologically intact participants; (3) relevance of the tasks used in relation to the scope of the present study (see above); (4) stimulation coordinates had to be reported in a stereotaxic plane (i.e., MNI or Talairach). The final selection resulted in 6 studies including 114 healthy subjects and 9 stimulation sites. These studies are described in **Table 6**.

Table 6. Overview of the stimulation studies considered in Lesourd et al. (2021).

Study	Subjects'age (*n*)	Method	Task name	Instruction	MNI coordinates of stimulation sites
Ishibashi et al. (2011)	27.08 ± 7.02 *n* = 13	rTMS	Manipulation matching	Choosing among 3, the target that had the same way of manipulation as the probe	Left ATL: x = -51, y = 9, z = -21 Left IPL: x = -38, y = -44, z = 48
			Function matching	Choosing among 3, the target that had the same function as the probe	
Pelgrims et al. (2011)	26.1 ± 5.4 *n* = 16	rTMS	Hand confitguration task	Deciding whether the same hand posture is normally adopted to use the two objects displayed on the screen	Left SMG: x = -59, y = -32, z = 46 Right SMG: x = 60, y = -28, z = 47
			Object-hand task	Deciding if a hand posture was compatible or not to use a tool	
			Contextual task	Deciding whether the two objects displayed on the screen are normally used in the same context	
			Functional task	Deciding whether two objects are used together to achieve a common goal	
Andres et al. (2013)	27.6 *n* = 16	rTMS	Hand confitguration task	Deciding whether the same hand posture is normally adopted to use the two objects displayed on the screen	Left SMG: x = -60, y = -34, z = 46 Left pMTG: x = -60, y = -50, z = -1
			Contextual task	Deciding whether the two objects displayed on the screen are normally used in the same context	
Perini et al. (2014)	27.7	rTMS	Action task	Detecting repetitions of the manipulation dimension (e.g., rotate or squeeze)	Left LOTC: x = -47, y = -68, z = -9
	n = 24		Location task	Detecting repetitions of the location dimension (e.g., kitchen or garage)	
De Bellis et al. (2018)	24.0 ± 1.7 *n* = 27	rTMS	Taxonomic matching task	Identifying, among 3 objects, the 2 related objects (taxonomic relations) among 3 objects after functional, structural or pointing prime	Left SMG: x = -59, y = -36, z = 40 Left pMTG: x = -65, y = -49, z = -8
			Thematic matching task	Identifying, among 3 objects, the 2 related objects (thematic relations) among 3 objects after functional, structural or pointing prime	
Ishibashi et al. (2018)	22.3	tDCS	Manipulation matching	Choosing among 3, the target that had the same way of manipulation as the probe	Left ATL°
	n = 18		Function matching	Choosing among 3, the target that had the function as the probe	Left IPL°

rTMS: repetitive transcranial magnetic stimulation; tDCS: transcranial direct current stimulation; ATL: anterior temporal lobe; IPL: inferior parietal lobe; SMG: supramarginal gyrus; pMTG: posterior medial temporal gyrus
° Precise coordinates are not provided in Ishibashi et al. (2018), but as the same author conducted the studies in 2011 and 2018, we considered that the stimulation sites are identical in 2011 and 2018

The location of stimulation sites and their impact on behavioral performance in manipulation, function and associative tasks are represented in **Figure 14**. We found that manipulation tasks were systematically impaired following virtual lesions in IPS and IPL (Andres et al., 2013; Pelgrims et al., 2011). However, Pelgrims et al. (2011) did not find any effect of a stimulation in left IPL (SMG/PF) in a hand-tool compatibility task, in which participants had to judge if a hand posture was compatible with a given tool (i.e., both hand and tool were presented on the screen). In the other conditions/studies where a negative impact of IPL (SMG/PF) stimulation was found (Andres et al., 2013; Pelgrims et al., 2011), the participants had to judge if two tools were manipulated in the same way, but no hand was present on the screen. These data may suggest that manipulation tasks are not systematically impacted following lesions in IPL. We found that function tasks could be affected following virtual lesions in IPL/SMG and pMTG (PHT/TE1p; De Bellis et al., 2020). Moreover, virtual lesions made in IPS (AIP/IP2) did not impact function tasks at all whereas lesions in anterior temporal lobe (ATL) systematically did (Ishibashi, Lambon Ralph, Saito, & Pobric, 2011; Ishibashi, Mima, Fukuyama, & Pobric, 2018). Concerning associative tasks, few data were available and stimulation sites were only found in IPL and LOTC. The most robust result was that no impact on associative tasks was found following stimulation in IPL.

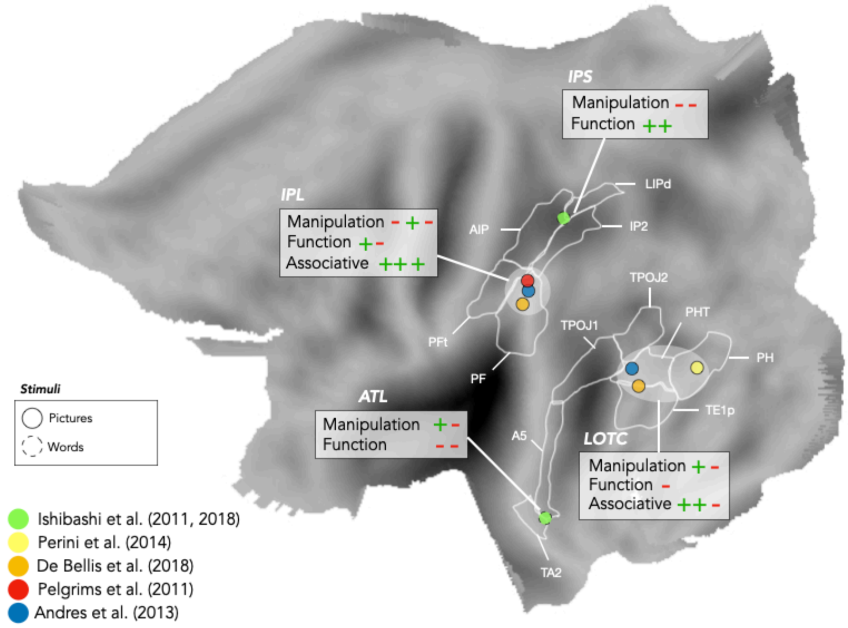

Figure 14. Stimulation sites are represented on a PALS-B12 left hemisphere (flat-map) atlas surface configuration (Van Essen, 2005). The parcellation is based on Glasser et al. (2016). For abbreviations and explanation, see the main text. Each circle represents a stimulation site (non-continuous line: words, solid line: pictures). Stimulations were found mainly in inferior parietal lobe (IPL), in lateral occipito-temporal cortex (LOTC), intraparietal sulcus (IPS), and anterior temporal lobe (ATL). A sign "+" indicates that a brain stimulation at a given location (i.e., LOTC, IPL, IPS, ATL) and in a given task (i.e., manipulation, function, associative) did not affect the behavioral performance, whereas the sign "-" indicates that the stimulation impaired the behavioral performance. Adapted from Lesourd et al. (2021).

Manipulation knowledge appears to rely upon a large brain network including temporal (LOTC and ATL) and parietal regions (IPL and IPS). Semantic tool network is supported mainly by the temporal lobe, with brain areas distributed along the ventral and lateral visual stream, from visual associative regions (VVC) to more anterior parts of the temporal lobe (TE1a/TGd). We found that associative and function relations may rely upon distinct brain regions, that is, AG for associative relations and IPL/SMG for function relations.

In the present review, we found that function tasks and manipulation tasks can be impacted following the same virtual brain lesions in pMTG and IPL (SMG). In a priming experiment, De Bellis et al. (2020) asked participants to perform a function or an associative judgment task, while the pMTG or the SMG were stimulated during the prime (hand posture compatibility or not). The authors found that virtual lesions in pMTG, and to a lesser extent in SMG during the priming of a hand posture, impacted function judgment but not associative judgment. Second, in LBD patients, while we found double dissociations between action tool-tool tasks and associative tasks and between function and associative tasks, our analysis did not reveal any double dissociation between action tool-tool tasks and function tasks (see section 2.2.3 *Dissociation between manipulation and semantic* *tool knowledge*, page 21). This result has to be taken carefully as few neuropsychological data were reported here. One explanation is that judging function relations about tools may engage parietal regions only if a manipulation component is strongly associated with the function to be judged. In a fMRI-adaptation paradigm, Yee et al. (2010) found that adaptation in left IPS was predicted by the degree of function similarity between word pairs and was also predicted by the degree of manipulation similarity. However, as manipulation and function similarity were highly correlated together and function condition did not elicit any activation in this region in whole brain analysis, the authors argued that manipulation was more likely to account for this relationship. Moreover, there is strong evidence in the literature that semantic tool knowledge (i.e., function relations) and manipulation knowledge are supported by distinct neurocognitive processes (Buxbaum & Saffran, 2002; Chen et al., 2016; Garcea et al., 2013; Garcea & Mahon, 2012, 2019). For instance, neuropsychological dissociations have been reported between manipulation and function knowledge (Garcea et al., 2013; Sirigu, Duhamel, & Poncet, 1991). In a fMRI study using MVPA, Chen et al. (2016) found greater action decoding compared to function in the left IPS, left vPMC, and right IFG while greater function decoding compared to action was found in the left parahippocampal gyrus. Further studies are needed to disentangle the role of parietal structures in function relations.

We also examined the brain networks of two components of manipulation knowledge, that is, hand posture and kinematics. First, fMRI studies showed that hand posture and kinematics could indifferently engage IPL/IPS or pMTG. However, stimulation studies showed that hand posture was impaired following virtual lesions in IPL (SMG) only for tool-tool compatibility but not for tool-hand compatibility tasks (Andres et al., 2013; Pelgrims et al., 2011), and kinematics-related knowledge was impaired following virtual lesions of inferior LOTC (Perini et al., 2014). These results suggest that kinematics is preferentially processed in the inferior LOTC, whereas hand posture is preferentially processed in the IPL (SMG). However, in LBD patients, Voxel-Lesion Symptom-Mapping studies of brain correlates of hand posture and kinematics errors have shown inconsistent results. Martin et al. (2017) reported a dependency of hand posture and kinematics components on IPL and pMTG respectively, while Buxbaum et al. (2014) found the opposite pattern. Further studies are required to elucidate the neural correlates of hand-posture and kinematics in object-related actions.

In this review, we reported that brain stimulation occurring in SMG/PF may impair manipulation knowledge (i.e., hand-tool relationships). However, this result is at odds with the results we presented in the section 3.2.1 *Hand-tool versus Tool-object relationships* (page 35), where we found that SMG/PF was specifically involved in tool-object relationships. We propose two hypotheses to explain this contradictory finding: (1) SMG/PF supports both hand-tool and tool-object relationships; or (2) SMG includes several functionally distinct brain areas, and a brain stimulation in SMG/PF may have impacted close brain regions, responsible of this impairment. Concerning the first hypothesis, we found that SMG/PF was involved specifically in tool-object relationships (Reynaud et al., 2016; see also Orban & Caruana, 2014), whereas hand-tool relationships were preferentially processed in the left IPS and the left LOTC. Moreover, we also found that brain stimulations in left SMG/PF impacted differentially manipulation knowledge, that is, tool-tool compatibility tasks but not hand-tool compatibility tasks (Andres et al., 2013; Pelgrims et al., 2011; see **Figure 15**). The second hypothesis is in favor of a spread-out effect due to magnetic field associated with rTMS. In broad terms, brain stimulation may have impacted anatomically close areas and disrupted their associated functions (**Figure 15**; for discussion see Lesourd, Osiurak, Navarro, & Reynaud, 2017). The left SMG is a complex area made of distinct functionally areas (Oberhuber et al., 2016), it is therefore possible that the effect observed here is not directly associated with the disruption of SMG/PF. Moreover, fMRI activations associated with manipulation knowledge were observed in SMG/PFt, an integrative area bordering SMG/PF on its dorsal part and involved in planning and execution of object-related actions (Reynaud et al., 2016; Ishibashi et al., 2016; Orban & Caruana, 2014; see also Potok, Maskiewicz, Króliczak, & Marangon, 2019).

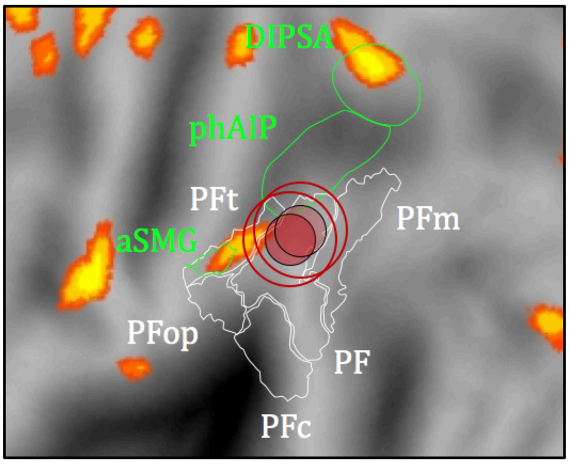

Figure 15. Flat-map representation of the left IPL/SMG (PALS-B12: Population-Average, Surface- and Landmark-based human cortical atlas; Van Essen, 2005), using Caret, version 5.65 (http://brainmap.wustl.edu/caret.html; Van Essen et al., 2001). On the center, are represented, after conversion from MNI to Talairach coordinates (Lacadie, Fulbright, Constable, & Papademetris, 2008), virtual lesions made during a hand-tool compatibility and a tool compatibility task (Andres et al., 2013; x = -59, y = -32, z = 43; Pelgrims et al., 2011; x = -58, y = -30, z = 43; red circles). Automatic Likelihood Estimation (ALE) map, obtained by Reynaud et al. (2016) and representing Planing/Execution of object-related actions is overlaid. The virtual lesions obtained in compatibility tasks are also depicted with a little red circle and a larger one which takes into account the spatial resolution intrinsic to the TMS (~0.5-1cm;

Thielscher & Kammer, 2002; Toschi et al., 2008). Depicted regions represent (1) IPL: aSMG, anterior portion of SMG, which largely overlaps with the cytoarchitectonic area PFt of SMG; PF, PFm, PFop, PFt and PFc, five cytoarchitectonic areas located in the left IPL, approximately at the position of BA 40 on the SMG; and (2) IPS: phAIP, putative human homologue of anterior intraparietal area; DIPSA, anterior dorsal intraparietal sulcus (Orban & Caruana, 2014; see also Peeters, Rizzolatti, & Orban, 2013). Adapted from Lesourd et al. (2017).

3.4. Results in a nutshell

- Action tool knowledge is supported mainly by the ventro-dorsal and the lateral part of the ventral pathway, whereas semantic tool knowledge is mainly supported by the ventral pathway:
  - Manipulation knowledge (hand-tool relationships) are supported by the left IPS and the left LOTC, whereas mechanical knowledge (tool-object relationships) is rather relying upon the left IPL (SMG/PF)
  - Function relations are associated with left IPL and left pMTG whereas associative relations are associated with left pMTG and left AG

- The unfamiliar use of tools is associated with greater brain activity in the ventro-dorsal pathway (IPL) compared to familiar use of tools, whereas familiar use of tools is associated with more brain activity in the left pMTG compared to unfamiliar use of tools.

These results are in general agreement with the predictions of the RBA concerning the role of the IPL, but the MBA better accounts for the involvement of the left pMTG in hand-tool relationships

4. Conceptual tool knowledge and contexts of use

4.1. Tasks assessing the actual use of tools

4.1.1. Pantomime of tool use

PTU is a classical task in the assessment of apraxia and is used in a wide range of neurological population (for reviews see Baumard, Osiurak, Lesourd, & Le Gall, 2014; Lesourd et al., 2013; Zadikoff & Lang, 2005). In this task, participants have to show how they would use a tool without holding it in hand. Pantomimes can be produced on verbal command, on imitation, or at the sight of the tool. Other procedures can be employed, as in the Florida Action Recall Test (Schwartz et al., 2000), wherein participants are presented with pictures depicting an unachieved action (e.g., a piece of butter that has to be spread on bread). In this case, participants have to demonstrate by pantomime the tool commonly used to complete the action. It is traditionally assumed that the ability to produce pantomime of tool use is supported by the activation of gesture engrams (Buxbaum, Kyle, Grossman, & Coslett, 2007; Buxbaum, Sirigu, Schwartz, & Klatzky, 2003; Lesourd, Budriesi, Osiurak, Nichelli, & Bartolo, 2019; Niessen, Fink, & Weiss, 2014). Other processes are known to be involved in PTU task, as semantic knowledge about tool use (i.e., instruction of use; Goldenberg & Hagmann, 1998), working memory (Bartolo et al., 2003), and recently communicative skills (Finkel, Hogrefe, Frey, Goldenberg, & Randerath, 2018; for a discussion see Goldenberg, 2017).

4.1.2. Single and real tool use

Unlike pantomime, familiar tool use involves the achievement of an action with the tool in hand. A first condition, hereafter referred as to STU, is to present participants with a tool in isolation and to ask them to produce the associated gesture. In other conditions, hereafter called real tool use, the tool and the associated object (e.g., a hammer and a nail) are both provided, and participants have to complete the action (i.e., real tool use in no-choice condition, RTU-NC; e.g., driving a nail with the hammer). Sometimes, in tool selection tasks, an object is shown to participants and they have to choose, among several tools, the associated tool to execute the action (i.e., Real tool use in choice condition, RTU-C; e.g., Baumard et al., 2016; Jarry et al., 2013). Several processes are assumed to support our ability to use tools, as semantic knowledge about tool use (Goldenberg, 2013; Goldenberg & Hagmann, 1998), manipulation knowledge (Buxbaum et al., 2007; Buxbaum, 2001; Elk, 2014), and mechanical knowledge (Jarry et al., 2013; Osiurak, 2014; Osiurak & Badets, 2016; Osiurak, Jarry, & Le Gall, 2010, 2011; Osiurak & Badets, 2017; Osiurak & Lesourd, 2014). In multiple-object tasks, the action to be carried out requires the use of several tools and objects in a sequence. For example, when asked to make a cup of coffee, participants can be presented with a cup, a kettle, a piece of sugar, a spoon, and instant coffee. Note that multiple-object tasks as they are commonly used in the domain of apraxia are very close to naturalistic action tasks (Giovannetti et al., 2006; Jarry et al., 2021) and require a higher degree of executive control.

4.1.3. Overcoming ceiling effects in tool use tasks: a new scoring system approach

When assessing the use of tools, ceiling effects are very frequent in controls and even in patients with neurological disorders such as vascular brain damage (e.g., De Renzi & Lucchelli, 1988; Goldenberg & Hagmann, 1998). Thus, the differences observed between controls and patients have to be interpreted with caution, particularly in tasks such as single and real tool use where controls performed generally higher above 97% (for a review see Lesourd et al., 2013). These ceiling effects can minimize the differences between patients and controls in that these differences might be greater if only the task was a little bit more difficult. To avoid this bias here, we proposed an original methodology described below (see Lesourd et al., 2016). The principle is very similar to the one used in the Weschler Adult Intelligence Scale (see for example Wechsler, 1997). The aim of our methodology was to create a composite score that takes into account the *time* spent by the participants to achieve the task. Indeed, an accuracy-based scoring system does not give enough information about the nature (i.e., integrity or deficit) of a cognitive process involved in a task of interest. For example, solving a problem in 10 seconds may not be interpreted in the same way as an achievement occurring in about 2 minutes. Nevertheless, in an accuracy-based scoring system, the same score represents those two kinds of achievement.

To validate our method, 72 control participants took part in a real tool use task and in a mechanical problem-solving task[7]. The distribution of scores of Real Tool Use task is displayed in **Figure 16**. Here, we also present the data from 31 additional control participants (not part of the 72 control participants) that were matched with patients with Alzheimer's disease and described in Lesourd et al. (2016). An accuracy-based scoring system (Jarry et al., 2013) gave strong ceiling effects for both control groups and the scores were obviously not normally distributed, whether for the 72 control participants or for the 31 control participants ($W = .20$, $p < .01$ and $W = .34$, $p < .01$, respectively). After transformation of the data (see below for a detailed explanation), the distributions of scores were normally distributed in both control groups ($W = .97$, $p = .11$ and $W = .96$, $p = .38$, respectively). Moreover, a Kolmogorov-Smirnov test showed that these two samples were not different from each other, suggesting that they came from the same distribution ($D = .14$, $p = .82$).

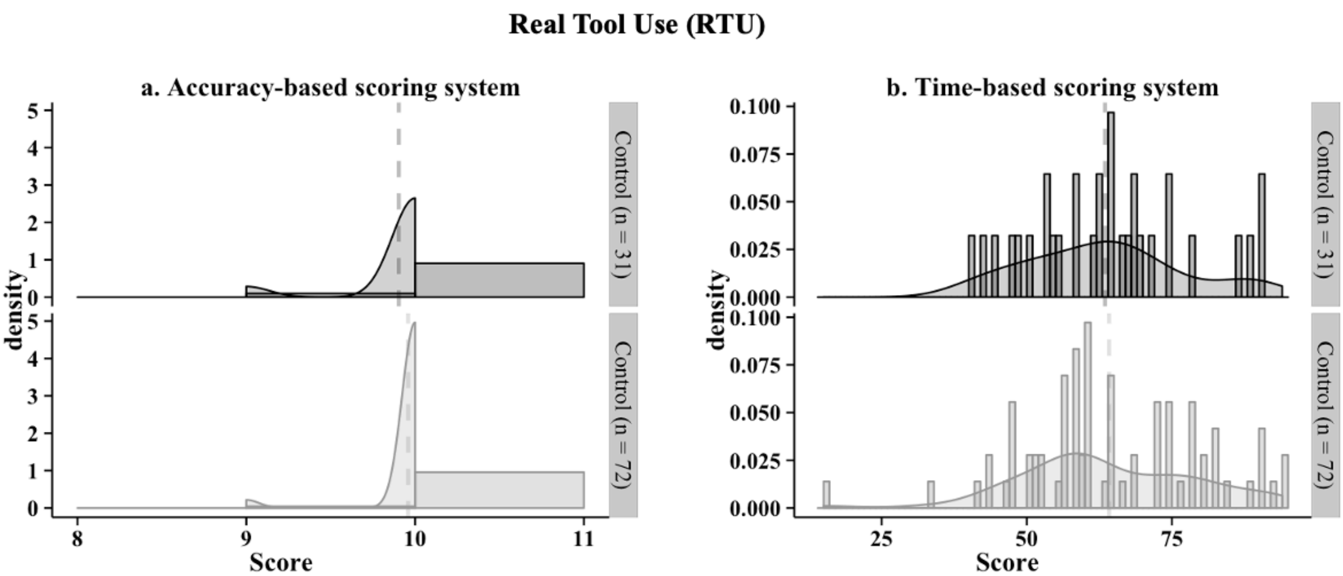

Figure 16. Frequency distribution of scores for Real Tool Use (RTU) obtained using two different scoring systems. a) Accuracy-based scoring (see Jarry et al., 2013). b) Time-based scoring system. Explanations are given in the text.

[7] Here, we illustrate our scoring system only with the performance of controls obtained in the Real Tool Use task, please see Lesourd et al. (2016) for the data obtained on the Mechanical Problem-Solving task.

First, we computed 4 centiles on the whole distribution of achievement times of control subjects (i.e., C_5, C_{25}, C_{75} and C_{95}) (see **Table 7**). Then a score was attributed for each interval delimited by the centiles. The faster the time of completion, the greater the composite score. In the RTU task, each item was scored on a 10 point-scale relative to the completion time of the item[8]. The maximum score for the RTU task was 100. If the time to carry out the accurate action was less than C5, 10 points were accorded, if the completion time was comprised between C5 and C25, 8 points were accorded, if the completion time was comprised between C25 and C75, 6 points were accorded and if the completion time was comprised between C75 and C95, 4 points were accorded. For incomplete actions in the given time or actions correctly carried out but after the allowed time of 30 seconds, no point was attributed. By summing the 10 scores obtained for each item, the maximum score was 100. For example, a control subject successfully pounded the nail with the hammer in 4 seconds. As it can be seen in **Table 7**, this participant obtained a performance comprised between C_{25} and C_{75}, so he obtained a score corresponding to this interval (i.e., 8 points).

Table 7. The 4 centiles computed for each tool of the RTU task of the control group (*n* = 31)

	C_5	C_{25}	C_{75}	C_{95}
Bottle opener	4	5	7	9.5
Saw	5	7	9.5	12.5
Match	2.5	4.3	7	10.1
Hammer	3	3.5	6	9
Jug	3	4	6	8
Key	5	6	9.8	13.6
Scissors	4	6	8	10
Screw driver	4.5	6	8	9.5
Bulb	4.5	6	8	9.5
Plug	3	4	6	9.5

Values in the table are expressed in seconds

Finally, the new scores obtained for each item for a participant were summed and gave a global composite score of completion of the task. The global composite scores of patients were computed relative to the centiles obtained from the distribution of control participants, so that the distributions of scores obtained in patient's groups and in the control group can be compared together. This transformation can easily be made also in the clinical assessment of tool use, as it is usually done with the block design test of the WAIS. Concerning the completion time of a patient,

[8] For RTU task, the completion time consists in the time needed to correctly carry out the action typically associated with the presented tools and objects. For example, the completion time for the pair bulb-bulb socket was recorded only when the bulb was totally screwed inside the bulb socket.

the neuropsychologist can attribute the corresponding score to the patient relative to the controls' performance as it is described above.

4.2. Explaining pantomime of tool use and single tool use with conceptual tool knowledge: neuropsychological data

4.2.1. Neurodegenerative diseases

In another study, we investigated the cognitive predictors of the PTU task in two neurodegenerative diseases, that is, Alzheimer's disease and semantic dementia. We explored the ability of function, manipulation and mechanical knowledge to predict not only the global performance but also the nature of errors in pantomime of tool use task, in Alzheimer's disease (AD) and semantic dementia (SD). More specifically, we shall examine the error profiles in AD and SD. In AD, both production and conception errors should be relatively frequent (Derouesné, Lagha-Pierucci, Thibault, Baudouin-Madec, & Lacomblez, 2000). In SD, given the semantic impairment, only conception errors should be over-represented. Then, we shall try to find the best predictors of conception and production errors in AD and SD patients. We hypothesize that conception errors will be explained by an impairment of semantic tool knowledge while production errors will be explained by an impairment of manipulation knowledge (Buxbaum, 2001; Rothi et al., 1991). Indeed, according to the MBA, a deficit of manipulation knowledge should be the primary cause of a deficit in pantomiming the use of tools, thus manipulation knowledge task should be the main predictor of PTU scores and error production.

Thirty patients with AD and thirteen patients with SD were recruited for this study, as well as 30 control subjects. Neuropsychological data were collected and are presented in **Table 8**.

Table 8. Demographical data and neuropsychological assessment

Test	Control (n = 30)	AD (n = 30)	SD (n = 13)	AD *versus* SD *p-level*
Gender (women/men)	20/10	20/10	6/7	ns
Handedness (left/right)	1/29	0/30	0/13	ns
Age (years)	75.2 (6.0)	76.6 (7.1)	**67.4 (8.2)**	**
Education (years)	12.4 (4.8)	**9.1 (4.4)**	12.5 (2.9)[b]	*
FAB (/18)	-	12.8 (2.3)[c]	13.3 (2.3)[c]	ns
MMSE (/30)	27.3 (1.7)	**20.2 (2.8)**	**23.3 (4.6)**[b]	*
BEC 96 (/96)[a]	87.8 (5.3)	**67.6 (9.3)**	**63.7 (14.8)**[b]	ns
Verbal learning	10.7 (1.5)	**6.8 (2.7)**	**6.4 (2.8)**[b]	ns
Visual recognition	10.8 (0.9)	**5.4 (2.2)**	**8.8 (2.7)**[b]	***
Orientation	11.5 (1.0)	**5.8 (3.9)**	10.0 (2.7)[b]	**
Visuo-constructive skills	10.9 (1.5)	9.8 (2.8)	10.8 (2.2)[b]	ns
General reasoning	9.1 (1.9)	8.2 (2.1)	**6.4 (2.8)**[b]	*
Verbal fluency	11.6 (1.1)	**9.8 (2.6)**	**5.4 (2.9)**[b]	***
Naming	11.5 (0.7)	**10.4 (1.8)**	**4.8 (2.9)**[b]	***
Mental manipulation	11.7 (1.6)	11.5 (2.2)	11.3 (2.6)[b]	ns

AD: Alzheimer's Disease; SD: Semantic Dementia; FAB: Frontal Assessment Battery at bedside;
MMSE: Mini-Mental State Examination; BEC: Batterie d'Evaluation Cognitive.
[a] Every item of the BEC 96 was rated on a 12 points-scale; [b] Data not available for n = 1 participant; [c] Data not available for n = 2 participants
Between-groups comparisons were performed with Mann-Whitney U-tests, except for "Gender" and "Handedness" (Chi-2 analysis)
Values in bold reveal pathological scores for patients relative to control; Values in brackets are standard deviations.
* $p < .05$; ** $p < .01$; *** $p < .001$

All participants were asked to complete four tasks. In the PTU task, ten familiar tools were presented one at a time on a vertical panel. Participants were asked to demonstrate the typical use of the tools without holding them in hand (i.e., pantomime on visual presentation of the tool). The errors made during this task were categorized as either conception or production errors. Conception errors are of two kinds: (1) content errors, in which actions are performed skillfully but out of context; (2) perplexity, in which no action is carried out with unmistakable sign of not knowing what to do. Production errors are also of two kinds: (1) spatiotemporal errors, the action performed is appropriate but poorly executed in the spatial dimension (e.g., incorrect plane of execution or mishandling of the tool if it were in hand) or in the temporal dimension (e.g., poor timing of execution); (2) body-part-object errors, the participant uses a part of his body to simulate the presence of the tool. In the mechanical problem-solving task (Lesourd et al., 2016), three different transparent boxes were presented at a time. A little red wooden cube or a little red wooden bead (i.e., the targets) was stuck inside each box. Participants were asked to extract the target out from the box using a given rod. In the function matching task (Baumard et al., 2016; Lesourd, Baumard, Jarry, Le Gall, & Osiurak, 2017), four images with different objects were presented below the picture of a tool (i.e., target stimulus). Participants were asked to select one out of the four pictures that best matched the target stimulus. The matching criterion was the function of the tool (e.g., jug/bottle). In the recognition of tool manipulation task (RTM; Jarry et al., 2013), participants had to choose among four photographs the one that corresponded to the best way to hold a tool in order to use it with an object (i.e., hand-tool compatibility task; e.g., saw/piece of wood). Each photograph depicted a one-handed manipulation of the tool; the hold differed across photographs, but the relative position of the tools and objects did not vary.

In tool use tasks, ceiling effects are often observed in controls' performance (e.g., Lesourd et al., 2013). To avoid this effect, the methodology described in the section 4.1.3 *Overcoming ceiling effects in tool use tasks: a new scoring system approach* (page 47) and we applied it to the four tasks of the present study. The principle was very similar to the one used in the Wechsler Adult Intelligence Scale (see for example Wechsler, 1997), by creating a composite score that takes into account the *time* spent by the participants to achieve the task, as well as the *performance* in the task. Results of group composite scores and correlation matrix between predictors are displayed in **Table 9** and **Table 10**, respectively.

Table 9. Means and standard deviations of composite scores of the experimental tasks

	PTU	MPS	FM	RTM
Control	51.1	17.1	58.5	59.0
	(14.34)	*(4.9)*	*(14.5)*	*(14.6)*
AD	27.5	10.3	41.5	26.5
	(16.3)	*(3.5)*	*(22.0)*	*(22.4)*
SD	26.0	16.5	26.2	34.4
	(12.6)	*(4.6)*	*(15.7)*	*(19.2)*

PTU: Pantomime of Tool Use; MPS: Mechanical Problem-Solving;
FM: Functional Matching; RTM: Recognition of Tool Manipulation;
AD: Alzheimers' Disease; SD: Semantic dementia
Values in brackets are standard deviations

Table 10. Correlation matrix between predictors in control group, AD, and SD patients

Control (n = 30)				AD (n = 30)				SD (n = 13)			
Tasks	MPS	FM	RTM	Tasks	MPS	FM	RTM	Tasks	MPS	FM	RTM
MPS		.11	.38*	MPS		.67***	.57***	MPS		.23	.06
FM			.32	FM			.57***	FM			.43
RTM				RTM				RTM			

MPS: Mechanical Problem-Solving; FM: Functional Matching; RTM: Recognition of Tool Manipulation; AD: Alzheimer's disease; SD: Semantic Dementia
*** $p < .001$; ** $p < .01$; * $p < .05$

Multiple backward regressions were carried out for each group in order to assess the involvement of each experimental task in PTU scores and in conception and production errors (i.e., raw scores) (**Table 11**).

Table 11. Multiple regressions with PTU, conception and production errors as dependent variables, and MPS, RTM, FM as predictors for the three groups

		β	t	p	R^2_{adj}
Predictors of Pantomime of Tool Use					
Control	MPS	.35	2.0	◆	.09
AD	MPS	.41	2.6	*	.52
	RTM	.43	2.7	*	
SD	-	-	-	-	-
Predictors of conception errors					
Control	-	-	-	-	-
AD	FM	-.36	-2.0	◆	.10
SD	FM	-.70	-3.2	**	.45
	MPS	.42	1.9	◆	
Predictors of production errors					
Control	RTM	-.37	-2.1	*	.11
AD	-	-	-	-	-
SD	FM	.80	4.2	**	.58
	MPS	-.38	-2.0	◆	

MPS: Mechanical Problem-Solving; RTM: Recognition of Tool Manipulation; FM: Functional Matching; AD: Alzheimer's Disease; SD: Semantic Dementia
◆ $p < .08$, * $p < .05$, ** $p < .01$

For AD patients, when PTU was predicted, MPS and RTM were significant predictors and the model accounted for 52% of the variance, $F(2,27) = 16.45$, $p < .001$, $R^2 = .52$. When production errors were predicted, no significant predictors were found. When conception errors were predicted, a trend toward significance was found for FM as predictor and the model accounted for 10% of the variance, $F(1,28) = 4.09$, $p = .053$, $R^2 = .10$.

For SD patients, when PTU was predicted, no significant predictor was found. When production errors were predicted, FM was a significant predictor. MPS was also selected and the model accounted for 58% of the variance, $F(2,10) = 9.41$, $p < .01$, $R^2 = .58$. When conception errors were predicted, FM was a significant predictor. MPS was also selected and the model accounted for 45% of the variance, $F(2,10) = 5.88$, $p < .05$, $R^2 = .45$.

When global performance of pantomime of tool use was predicted, we found that mechanical problem solving was a good predictor in AD patients and control participants whereas recognition of tool manipulation was a significant predictor only in AD patients. In the long standing tradition of study of apraxia, a prerequisite for pantomiming object use is the activation of the motor schema (i.e., manipulation knowledge; Niessen et al., 2014), so manipulation knowledge should be activated since we need to pantomime the use of a tool. However, this is not the case in this study because mechanical problem solving was found to be a more robust predictor of pantomime of tool use. Obviously, we cannot exclude that mechanical problem solving and pantomime of tool use are both production tasks while recognition of tool manipulation is not a production task. It could explain why mechanical problem-solving task was found to be a good predictor of pantomime of tool use task while recognition of tool manipulation was not. We tested this hypothesis in section 4.2.2 *Left brain-damaged patients* (page 55).

Concerning the prediction of errors during the pantomime of tool use task, we found that functional matching was a robust predictor of conception errors for both AD and SD patients. Indeed, we found that functional matching composite scores were linked by a negative regression coefficient to the amount of conception errors in SD and to a lesser extent in AD. Thus, an increasing of conception errors is explained by a decrease in functional matching composite scores. In other words, impairment of semantic tool knowledge is involved in conception errors in AD (Adlam, Bozeat, Arnold, Watson, & Hodges, 2006) and SD patients (Hodges et al., 2000). Concerning production errors, we observed different results among the three groups: recognition of tool manipulation was a good predictor of production errors in control participants, functional matching and mechanical problem solving were good predictors in SD patients and there was no significant predictor in AD patients. This result is quite surprising; given that recognition of tool manipulation is supposed to assess manipulation knowledge, production errors should be a hallmark of impaired manipulation knowledge (Rothi et al., 1991). Thus, one may assume that recognition of tool manipulation task does not assess manipulation knowledge; so, it would not be surprising that production errors are not consistently explained by recognition of tool manipulation. However, this task is basically linked to the study of manipulation knowledge (Buxbaum & Saffran, 2002; Buxbaum, 2001; Buxbaum, Sirigu, Schwartz, & Klatzky, 2003; Rothi et al., 1991). Another explanation is that manipulation knowledge is not mandatory to produce pantomime of tool use, so production errors could be explained by many other impaired cognitive processes (e.g., working memory; Bartolo, Cubelli, Della Sala, & Drei, 2003). Indeed, pantomiming the use of tools is now assumed to be a multifaceted task (Goldenberg, 2017) and these findings, among others, question the role of manipulation knowledge in the pantomime of tool use task.

4.2.2. Left brain-damaged patients

In this work, we proposed to test two hypotheses. First, we hypothesized that mechanical knowledge may explain the performance in several tool use tasks whereas manipulation knowledge may explain the performance in pantomime of tool use tasks only. In broad terms, mechanical knowledge should be involved in all contexts of use, whereas the involvement of manipulation knowledge should be relatively limited.

Second, we tested the idea that mechanical knowledge could explain the performance in familiar tool use not only because these two activities share the production of a motor action (see previous section), but because, mechanical knowledge plays a major role in our ability to use tools. Indeed, in LBD patients, studies on tool use have found a strong association between familiar use of tools and mechanical knowledge (Goldenberg & Hagmann, 1998; Jarry et al., 2013; for a review see Baumard et al., 2014). However, in these studies, mechanical knowledge is usually assessed with production tasks, as mechanical problem solving tests or alternative use of tools (Osiurak et al., 2009). Thus, a possible interpretation of the strong association existing between tool use and mechanical knowledge tasks is that both tasks require the production of a motor action. Thus, familiar tool use would not be subsumed by mechanical skills *per se* but would simply be associated with mechanical problem-solving tasks because of their common motor nature. One way to challenge the notion that mechanical knowledge and tool use are associated only because they both require the production of a motor action is to demonstrate that familiar tool use depends on an alternative tool selection task. Indeed, in this task, subjects are asked to guess alternative uses of tools based on their physical properties, but the actual use of tools is not needed. If familiar tool use depends on mechanical knowledge, an alternative tool selection task would be the best predictor to explain the amount of variance between familiar tool use tasks. To assess familiar tool use, we used a single tool use task and a pantomime of tool use task (e.g., Jarry et al., 2013).

However, the alternative tool selection task could be claimed not to be purely mechanical as semantic features are made available through the tools presented in it. To circumvent this objection, we used several semantic tasks (i.e., function, associative, manipulation and identity matching) in an attempt to establish that the alternative tool selection task, although not a pure mechanical task (e.g., Mechanical Problem-Solving task; Lesourd, Baumard, Jarry, Etcharry-Bouyx, et al., 2016), is the best predictor among all the semantic tasks. Some examples of the predictors used in the experiment are displayed in **Figure 17**.

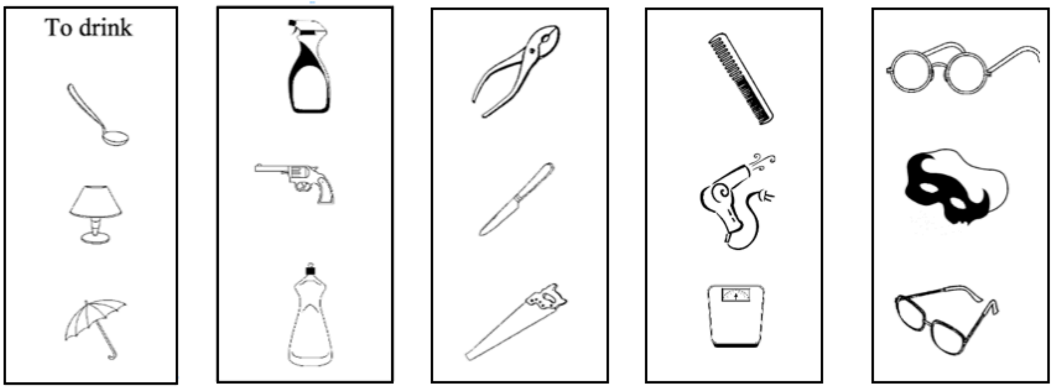

Figure 17. The five tasks used as predictors for PTU and STU tasks. From the left to the right: alternative tool selection, manipulation, function, associative, and identity matching tasks. Adapted from Lesourd et al. (2019).

Performance of experimental tasks for controls and LBD patients are displayed in **Table 12**. LBD patients scored significantly lower than controls on all experimental tasks (all *ps* $< .001$). Moreover, controls and LBD patients significantly improved their performance between PTU and STU tasks ($p = .012$ and $p < .001$, respectively). Correlation matrices between tasks are shown in **Table 13** for LBD patients. We found significant correlations between tool use tasks (i.e., STU and PTU) and all the other tasks (all $r > .45$, all *ps* $< .05$). Moreover, Alternative tool selection scores were significantly associated with all the tasks assessing semantic knowledge (i.e., Function, Associative and Identity matching, all $r > .73$, all *ps* $< .001$).

Table 12. Results of experimental tasks in controls and LBD patients

	STU	PTU	Alter.	Manip.	Func.	Assoc.	Ident.	Lesion site
Controls								
Mean	15	14.38	14.29	14.29	14.38	14.86	14.81	
Standard deviation	-	.86	.85	.85	.86	.36	.40	
Range	15	13-15	12-15	12-15	12-15	14-15	14-15	
Cut-off[a]	13	11	10	10	10	12	12	
LBD patients								
P1	14	15	11	15	13	15	14	T, F, I
P2	15	15	15	12	14	15	15	F, BG
P3	**9**	**8**	**8**	**9**	**9**	12	**11**	n/a
P4	15	15	15	15	15	15	15	F, T, P, I
P5	**5**	**0**	**7**	**4**	**6**	**8**	**11**	T, BG
P6	15	14	13	**9**	11	13	13	F, P
P7	14	11	12	**6**	10	13	14	T, I
P8	**11**	**6**	**9**	**6**	**8**	**9**	**8**	n/a
P9	14	**8**	13	**8**	**9**	**11**	**11**	F, I, T, P, BG
P10	14	**3**	**9**	**8**	**6**	14	**9**	F, T, I
P11	13	14	14	13	14	14	14	F, P
P12	13	**7**	12	11	14	12	15	T, P, BG
P13	15	13	15	12	13	15	15	BG
P14	15	14	15	13	15	15	15	F, P
P15	13	**5**	**9**	**4**	**4**	**10**	**11**	F, T, I, BG
P16	14	**8**	10	10	**9**	12	14	F, I, BG
P17	15	15	13	**8**	12	14	12	F, I, BG
P18	14	**7**	12	**8**	**9**	**11**	**11**	T, BG
P19	13	11	**9**	**9**	**7**	**11**	**8**	F, I
P20	14	14	14	12	15	15	14	BG
P21	15	**5**	12	**6**	13	15	14	BG
Mean	13.33	9.90	11.76	9.43	10.76	12.81	13.93	
Standard deviation	2.42	4.58	2.53	3.26	3.37	2.18	1.22	

STU: Single Tool Use; PTU: Pantomime of Tool Use; Alter.: Alternative selection; Manip.: Manipulation; Func.: Function; Assoc.: Associative; Ident.: Identity

F: Frontal; T: Temporal; P: Parietal; I: Insulae; BG: Basal Ganglia; n/a: not available

[a] Cut-off scores were determined as the worst score achieved by the controls minus two points (Bartolo et al., 2003)

Values in bold reveal pathological scores for patients relative to controls

Table 13. Correlations between test results in LBD patients (*n* = 21)

Tasks	STU	PTU	Alter.	Manip.	Func.	Assoc.	Ident.
STU		.61**	.73***	.45*	.50*	.71***	.43*
PTU			.76***	.76***	.73***	.70***	.54*
Alter.				.64**	.84***	.73***	.73***
Manip.					.78***	.71***	.60**
Func.						.78***	.81***
Assoc.							.68***
Ident.							

*** $p < .001$; ** $p < .01$; * $p < .05$

To further explore the structural properties of the correlation matrix in LBD patients, it was subjected to multidimensional scaling which yields a graphical representation of the correlational structure (Young, 1987) (see **Figure 18**). Higher correlations are represented by smaller distances between the respective data points. The distances correspond to the rank order of the correlations but not necessarily to their absolute values. There was a separation between STU task and all the other experimental tasks which may be explained by the presence/absence of tool. Indeed, STU was the only task requiring the actual manipulation of a tool compared to the other tasks. We found that Alternative tool selection and Associative matching were strongly associated and occupied an intermediate position almost equidistant from the other tasks. Manipulation matching and PTU were also strongly associated. Finally, Function matching and more particularly Identity matching were isolated from the other tasks.

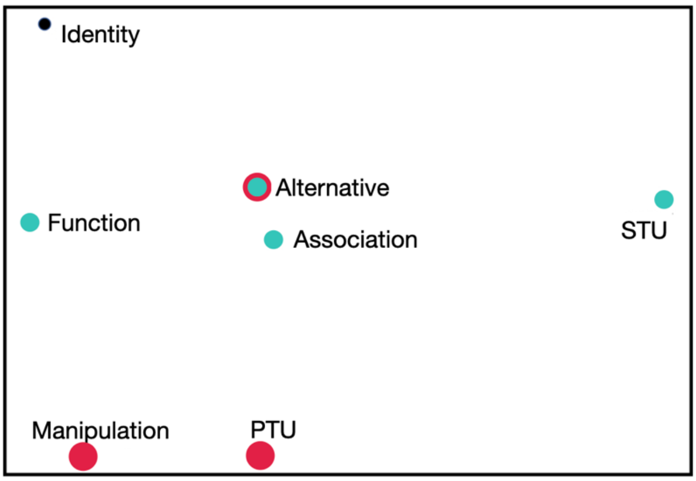

Figure 18. Multidimensional scaling of correlations between experimental tasks in LBD patients. Shorter distances between points represent higher correlations between tasks. STU: Single Tool Use; PTU:

Pantomime of Tool Use. Red circles indicate the significant predictors for the PTU task whereas blue circle indicate the significant predictors for the STU task. Adapted from Lesourd et al. (2019).

To investigate which of the correlated variables explained a significant amount of variance in STU and PTU tasks, we carried out multiple stepwise regression analyses. Results of the multiple regressions are shown in **Table 14.** When STU scores were predicted, Alternative tool selection, Associative and Function matching were found to be significant predictors and the model was able to account for 72% of the variance. When PTU scores were predicted, Alternative tool selection and Manipulation were found to be significant predictors and the model was able to account for 70% of the variance.

Table 14. Multiple regressions with single tool use and Pantomime of tool use as criterion and Alternative tool selection, Associative matching, Function matching and Manipulation matching as predictors.

Criterion	Predictors	β	t	p
Single Tool Use				
	Alter.	.85	3.53	**
	Assoc.	.65	3.10	**
	Func.	-.72	-2.75	*
	$F(3,17) = 14.75$, $p < .001$, $R^2 = .72$, $R^2_{adj} = .67$			
Pantomime of Tool Use				
	Alter.	.46	2.73	*
	Manip.	.46	2.74	*
	$F(2,18) = 20.95$, $p < .001$, $R^2 = .70$, $R^2_{adj} = .67$			

Alter.: Alternative tool selection; Assoc.: Associative; Func.: Function; Manip.: Manipulation
* $p < .05$, ** $p < .01$, *** $p < .001$

Here, we found that the Alternative tool selection task was a significant predictor and accounted for a large amount of variance in the STU and PTU tasks. Moreover, LBD patients were impaired in the Alternative tool selection task compared to controls, as already observed with classical tasks assessing mechanical knowledge (e.g., Sequential Mechanical Problem Solving; Jarry et al., 2013; Osiurak, Jarry, Lesourd, Baumard, & Le Gall, 2013). This result corroborates the idea that mechanical knowledge is of primary importance when we use tools (Osiurak et al., 2010), even if tasks assessing mechanical knowledge do not require the production of any motor action.

The Alternative tool selection task was selected in the regression model as the better predictor with two other semantic tasks (i.e., Function and Associative matching), suggesting that subjects may reason about the physical properties of tools even in the STU task (Baumard et al., 2014). Interestingly, the Manipulation matching task was not selected in the model to explain the amount of variance in the STU task, suggesting that mechanical and semantic knowledge (Associative and Function) may replace manipulation knowledge when we use familiar tools, as recently proposed by Goldenberg (2013). In line with this hypothesis, multidimensional scaling analysis showed that the Alternative tool selection and the Associative matching tasks were strongly associated and occupy a central position almost equidistant to the other tasks, which was not the case for the Manipulation matching task. These findings question the idea that people directly activate the gesture engram associated with the usual use of tools (see Osiurak et al., 2011 for a discussion). Moreover, individual results examined with a conservative criterion revealed the presence of 7 patients (P1, P2, P4, P11, P13, P14 and P20) with spared abilities in all the tasks administered and 3 severe patients (P3, P5 and P8) with deficits in all the tasks (only P3 was at the cut-off in the Associative task). Intriguingly, the profiles of these 3 patients show that tool use is always impaired in association with deficits in all the semantic and mechanical tasks. This suggests that a combination of deficits in the semantic system and in mechanical problem-solving skills favors the emergence of this defective behavior, as already reported (Goldenberg & Hagmann, 1998).

Concerning the PTU task, the group results are less straightforward than for the STU task. Indeed, the Alternative tool selection and Manipulation matching tasks were both selected as significant predictors and explained the same amount of variation as obtained in the PTU task. At first glance, this seems quite logical given that (1) the activation of manipulation knowledge is considered to be a prerequisite to pantomime the use of tools (e.g., Niessen, Fink, & Weiss, 2014); and that (2) it has recently been shown that mechanical knowledge is involved in pantomiming the use of tools (Baumard et al., 2014; Lesourd, Baumard, Jarry, Etcharry-Bouyx, et al., 2017). However, regarding individual results in the pantomime production task, P12 and P19 had intriguing profiles. P12 had preserved semantic and mechanical skills coupled with deficits in the production of pantomimes while P19 had exactly the opposite profile, i.e. spared ability to produce pantomimes and difficulties in all the semantic and mechanical tasks. The results of these two patients point to a double dissociation between a production and a receptive system and suggest that the integrity of the semantic system and preserved mechanical problem-solving skills are neither necessary nor sufficient to produce pantomimes (Negri et al., 2007). This is also confirmed by the profiles of P9, P16, P18 and P21 who showed preserved ability to perform the mechanical task yet failed in the production of pantomimes. With regard to manipulation knowledge, P6, P7 and P17 were able to produce pantomimes, regardless of deficits in Manipulation matching. Thus, PTU is a complex motor activity which is subsumed by several cognitive abilities (i.e., communicative skills; Finkel et al., 2018; Goldenberg, 2017; for a review see Osiurak et al., 2021).

To sum up, we found that an Alternative tool selection task assessing mechanical knowledge, and which did not need the production of a motor action was the best predictor of a familiar tool use task (i.e., STU task). This result confirms the major role of mechanical knowledge in tool use (Goldenberg & Hagmann, 1998; Osiurak et al., 2009, 2010) by demonstrating that our abilities to reason about the physical properties of tools and objects may sustain our ability to use familiar tools. We also show that manipulation and mechanical knowledge are both predictors of the PTU task, however, the individual results suggest that pantomime production does not depend on any semantic or mechanical knowledge.

4.3. Do we need manipulation knowledge to use tools: the case VF

The previous section pointed out in group studies that manipulation knowledge could explain, at least in part, the performance in pantomime of tool use task. However, several case studies have reported that manipulation knowledge and pantomime of tool use could be doubly dissociated. For instance, Valério et al., (2021) reported the case of FP who presented problems in pantomiming the use of tools in a context of spared ability to perform judgment about an object's manipulation and the case of LS who showed the reverse pattern. We also showed that manipulation knowledge was a poor predictor of single tool use task (Lesourd et al., 2019) questioning the role of manipulation knowledge also for actual use of tools. Recently, we reported a rare observation of VF, a left-handed patient, left-lateralized for language, who developed a severe apraxia following a right brain lesion (Lesourd, Naëgelé, Jaillard, Detante, & Osiurak, 2020). Interestingly the patient showed a significant number of hand posture errors, while she perfectly demonstrated the actual use of tools (**Figure 19**).

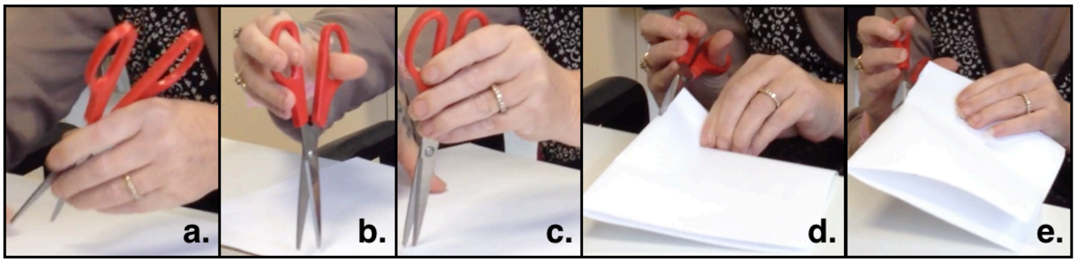

Figure 19. Manual prehension of a pair of scissors by VF who was asked to cut the piece of paper with the scissors (real tool use). The first three frames (a.-d.) show the behavior of VF during attempts at manipulating the tool and making interact the tool with the object. In the last two frames (d. and e.), VF correctly achieved the action (i.e., cutting the piece of paper) using an incorrect hand posture (i.e., hand posture error). Adapted from Lesourd et al. (2020).

This case of apraxia questions the predictions made by the current theories of tool use. According to the MBA, the presence of hand posture errors in VF in pantomime and real tool use tasks should be well explained by a severe damage or impaired access to manipulation knowledge. For instance, the patient LL (Sirigu et al., 1995) who presented the same hand posture deficit as VF, showed hand posture errors in both pantomime and real tool use tasks in association with defective manipulation knowledge. However, VF and LL are rare cases reported in the literature with this kind of impairment (see also Hayakawa, Fuji, Yamadori, Meguro, & Suzuki, 2015). Indeed, while hand posture errors are commonly reported in pantomime of tool use in apraxic patients (e.g., Buxbaum et al., 2007), they are rarely observed in real tool use tasks (Osiurak, Aubin, Allain, Jarry, Etcharry-Bouyx, et al., 2008; Randerath, Goldenberg, Spijkers, Li, & Hermsdörfer, 2010; Randerath et al., 2009). Thus, in apraxic patients, if defective manipulation knowledge is a good predictor of hand posture errors in pantomime of tool use task, this is less obvious in real tool use task, where both the tools and the corresponding objects are available. Additionally, if hand posture errors are rare in real tool use tasks, they are nevertheless systematically followed by action errors (Randerath et al., 2010). However, VF produces few action errors following hand posture errors, suggesting the existence of a dissociation between hand-tool and tool-object representations. MBA can hardly explain why a severe damage of manipulation knowledge is not associated with a deficit for using tools, unless assuming either that manipulation knowledge is not necessary for the actual use of tools (Osiurak & Badets, 2016; Osiurak et al., 2009, 2010; Osiurak, Jarry, & Le Gall, 2011) or invoking additional compensatory processes (i.e., production system). In contrast, the RBA assumes that the ability to use tools largely depends on mechanical knowledge (i.e., tool-object representations). In broad terms, RBA assumes that using tools relies firstly upon the integrity of tool-object representations. As VF commit few action errors, the preservation of mechanical knowledge should explain why she can properly use familiar tools, despite high frequency of hand posture errors.

4.3.1. The case history

VF, a 47 years-old woman with 8 years of education was working as a florist for 10 years when she underwent, in August 2014, an ischemic stroke affecting the right hemisphere (**Figure 20**).

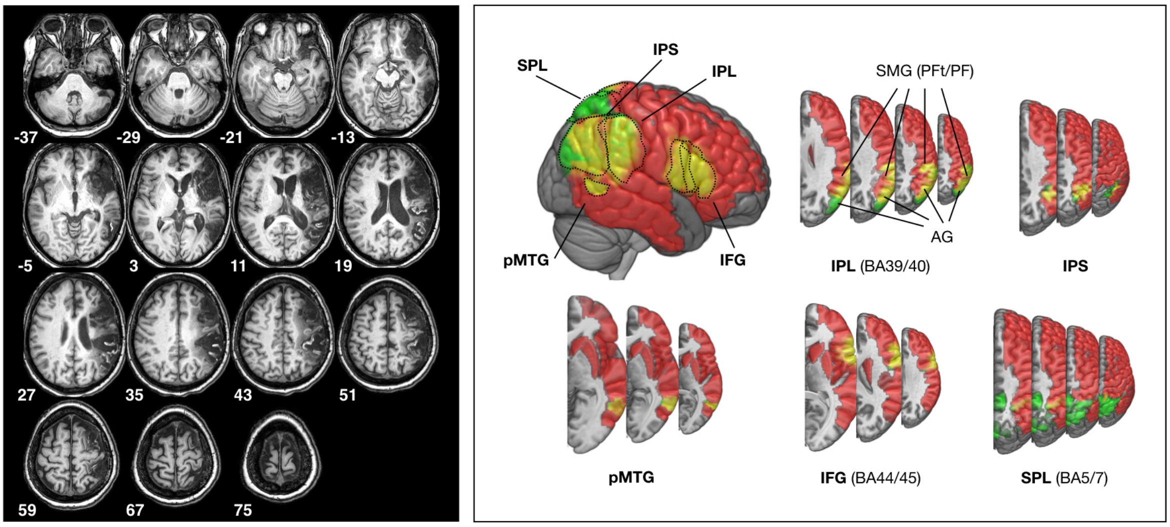

Figure 20. On the left panel: T1-weighted axial slices of VF brain performed at the chronic stage of stroke (6 months after the stroke). On the right panel: Lesion extension (red color) was determined on the basis of a T1-weighted sequence and projected on a MNI template. Spared brain areas are colored in green whereas damaged brain areas are colored in yellow. SPL: Superior Parietal Lobe; IPS: Intraparietal Sulcus; AG: Angular Gyrus; SMG: Supramarginal Gyrus; IFG: Inferior Frontal Gyrus; pMTG: posterior Middle Temporal Gyrus. Adapted from Lesourd et al. (2020).

Table 15 summarizes the results obtained with the preliminary praxis evaluation (TLA; Anicet, Calais, Lefeuvre, & Rousseaux, 2007). VF was largely impaired when she was asked to produce transitive and intransitive gestures whatever the modality (i.e., imitation or verbal command). However, the ability to name and discriminate gestures according to their meaning were preserved, as well as functional knowledge. During pantomime of tool use, VF made characteristic errors observed in apraxia, that is, recognizable gestures containing spatiotemporal errors (e.g., stereotypic movement, body part object, etc.). Moreover, when asked to use tools in isolation (i.e., single tool use), VF grasped the tools in an awkward way, as it has been previously observed with the case LL (Sirigu et al., 1995). Interestingly, the hand posture deficit seemt to persist in real tool use situation (i.e., using a tool with an object), for instance, when VF was asked to cut a piece of paper with a scissor, despite a very uncomfortable hand posture, VF successfully cut the piece of paper.

Table 15. Preliminary praxis testing: TLA (Anicet et al., 2007)

	Raw score	Significance
Intransitive and meaningless gestures		
Imitation of meaningless gestures		
Hand postures	**6/10**	***
Finger postures	**9/10**	*
Symbolic gestures		
Naming	20/20	
Production on verbal command	**12/20**	***
Imitation	**12/20**	***
Discrimination of gestures according to their meaning	15/20	n.s.
Transitive gestures		
Semantic knowledge about tool use		
Functional matching	10/10	
Pantomime of tool use		
Production on verbal command	**9/20**	***
Imitation	**9/20**	***
Object use	**11/20**	***

Pathological scores are in bold
TLA: Test Lillois d'Apraxie gestuelle (french battery for apraxia screening)
* $p < .05$, ** $p < .01$, *** $p < .001$

4.3.2. Hand posture and use of familiar tools

We investigated the use of familiar tools with three classical tasks, namely, pantomime of tool use, single tool use and real tool use tasks. In these tasks, the performance of VF was compared with three groups of brain-damaged patients: LBD apraxic (LBD-A; n = 8), LBD non-apraxic (LBD-NA; n = 7) and RBD (n = 5). We found that VF and LBD-A patients were equally impaired in PTU task for hand posture compared to LBD-NA and RBD patients, suggesting that apraxia specifically impairs hand-tool relationships (Buxbaum et al., 2007; Buxbaum et al., 2003). However, whereas LBD-A patients improved significantly their hand posture with the tool in hand, which is commonly observed with apraxia (for a review see Baumard et al., 2014), this was not the case for VF neither in the STU task (**Figure 21**), nor in the RTU task (**Figure 22**).

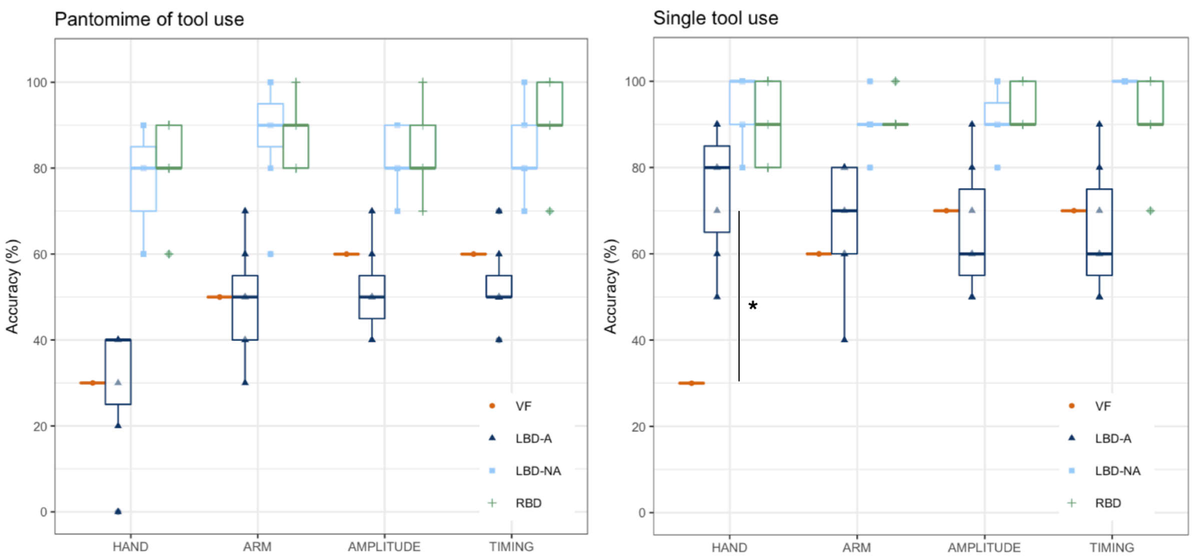

Figure 21. Scores of VF, LBD-A, LBD-NA and RBD patients on the hand posture, arm posture, amplitude and timing components during pantomime of tool use task (left panel) and single tool use task (right panel). The boxplots display the interquartile range (first quartile, median, third quartile). * $p < .05$. Adapted from Lesourd et al. (2020).

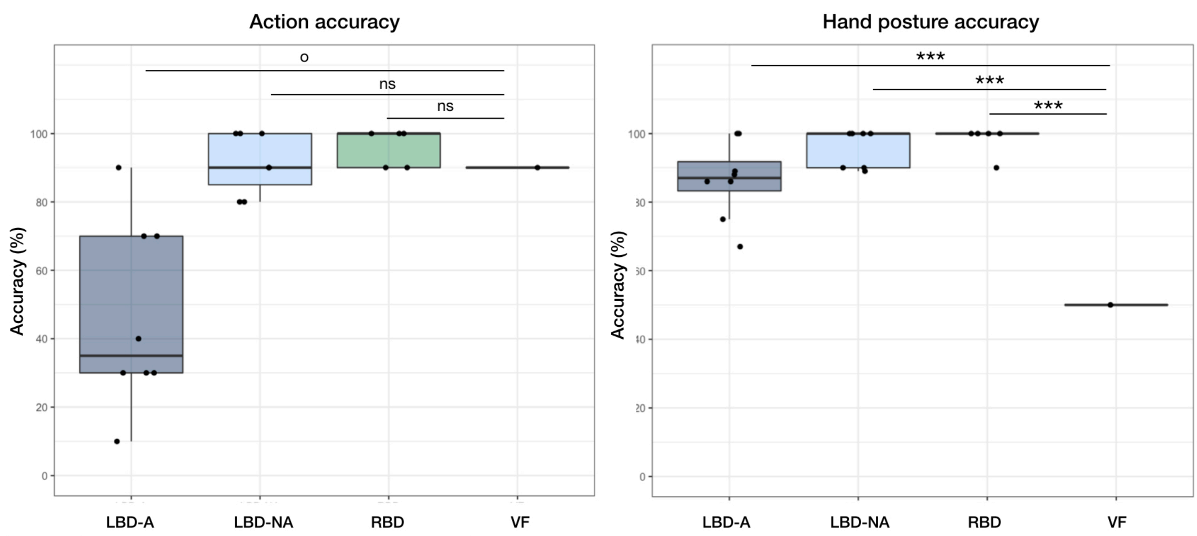

Figure 22. Scores of VF, LBD-A, LBD-NA and RBD patients for action accuracy (left panel) and hand posture accuracy (right panel) in the real tool use task in choice condition (RTU-C). The boxplots display the interquartile range (first quartile, median, third quartile). ns: non-significant, *** $p < .001$, ° $p = .08$. Adapted from Lesourd et al. (2020).

We also found a significant association between hand posture errors and action errors in LBD-A in the RTU task. Consistent with our findings, Randerath et al., (2010) reported in a grasping to use task (i.e., single tool use task), that hand posture errors were strongly associated with action errors in LBD patients. However, if hand posture errors (also called non-functional grips) are more frequent in LBD than in RBD patients, this behavior remains rare in LBD patients

(Osiurak et al., 2008; Randerath et al., 2009). Surprisingly, VF produced more hand posture errors than LBD-A patients, without impacting the correct achievement of tool use actions.

We further investigated the grasping components of action in VF, namely, grasping to transport and grasping to use (see Osiurak et al., 2008 for a similar task). These tasks will test the specificity of the hand posture impairment (i.e., familiar tool use *vs* novel tool use) and should confirm the lack of association observed between action errors and grip errors.

4.3.3. Grasping components of action: transport and use

In the grasping to transport condition, VF sat at a table upon which was fastened a cradle that included two supports (see **Figure 23A**). A red-and-blue wooden dowel (length 32cm, diameter 2cm) laid on supports with the blue end on the left support. To each side of the dowel laid a red and a blue disk (diameter 3cm). VF began each trial with the hand resting in a neutral orientation (thumb pointing to 12 o'clock). When the examiner pointed to a red (blue) disk, VF was required to pick up the dowel and place the red (blue) end squarely on the red (blue) disk. Each disk was pointed 6 times, totaling 24 trials. VF performed the grasping-to-transport condition with the left hand (24 trials) and the right hand (24 trials). VF was told to use a power grip and not to twirl the dowel. To prevent the patient from seeing appropriate grips, the examiner moved the dowel by holding it between the index and the middle finger of each hand, with the palms facing each other. Two final postures were distinguished at the time the dowel was placed on the disk, that is, a comfortable final posture corresponded to the thumb pointing up, and an uncomfortable final posture to the thumb pointing down. Two initial grips were distinguished at the time the dowel was grasped: an overhand or an underhand grip (Rosenbaum et al., 1990). In the grasping to transport condition, VF performed only one uncomfortable final posture (n = 47/48) made with the left hand (left hand: n = 23/24, right hand: n = 24/24). Moreover, the distribution of overhand (left hand: n = 13/24, right hand: n = 12/24) and underhand (left hand: n = 11/24, right hand: n = 12/24) grips did not differ significantly between both hands (χ^2 = .17, df = 3, p = .98).

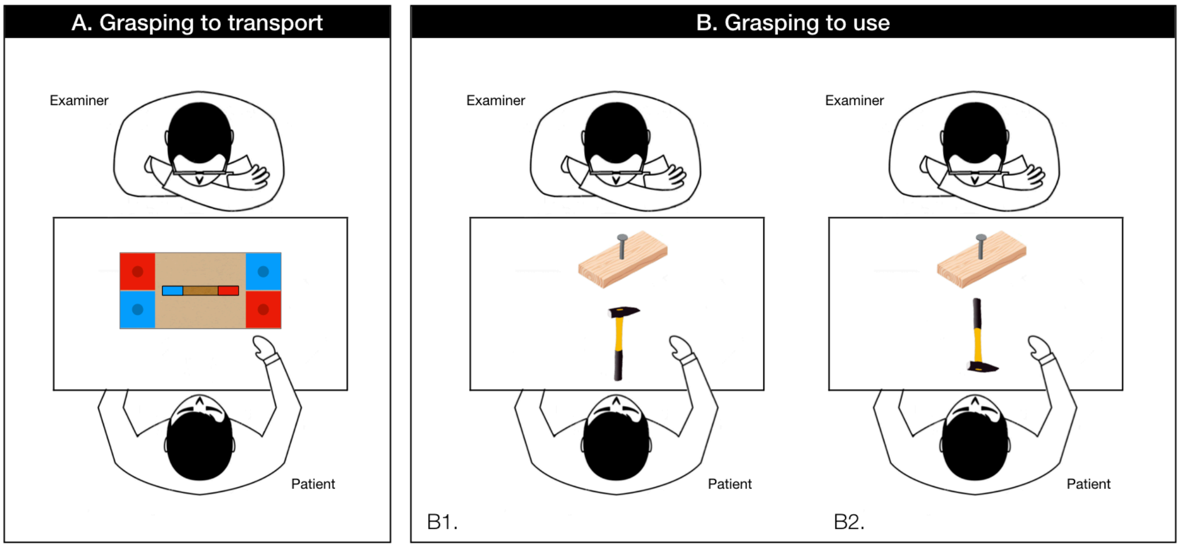

Figure 23. Apparatus used in the grasping to transport (A.) and in the grasping to use task (B.). Left hand and right hands were assessed in both tasks (only initial position of the right hand is showed here). In the gasping to use task, the handle of the tool can be presented either toward (B1.) or away (B2.) from the patient. In this example, if VF can grasp the hammer either with the thumb away from the active part of the tool (non-functional grip) or with the thumb toward the active part (functional grip). Adapted from Lesourd et al. (2020).

In the grasping to use condition, VF sat at a table upon which were placed a familiar object and the corresponding recipient (see **Figure 23B**). VF began each trial with the hand resting on the desk in a palm down position. VF completed the task with her left hand first and then with her right hand. Her thumb pointed to either the 3 o'clock position (left hand) or the 9 o'clock position (right hand). VF was instructed to pick up the tool and to demonstrate how she uses it with the recipient. It was stressed that the grip should remain unchanged once VF picked up the tool. Tool orientation was manipulated: the handle toward (**Figure 23B1**) versus away from VF (**Figure 23B2**). To prevent VF from seeing appropriate grips, the examiner moved the tools by holding them between the index and the middle finger of each hand, with the palms facing each other. Each tool was presented 4 times in each orientation totaling 112 trials (7 tools/recipients x 2 orientations x 4 trials x 2 hands). Two handgrips were identified: a functional grip occurred if the handle was grasped with the thumb toward the active part of the tool and a non-functional grip, if the handle was grasped with the thumb away from the active part. An ANOVA for single case studies (*Q'* test; Michael, 2007) were carried out on percentage of functional grips (i.e., number of functional grips/total of grips x 100) relative to the orientation of the tool (handle forward *vs* handle away) and of the hand (left *vs* right). In the grasping to use task, VF produced a significant number of non-functional grips when the tool was presented with the handle away from her. Indeed, the analysis of variance carried out on percentage of functional grips revealed a main effect of the orientation of the tool, $Q'(1) = 13.76$, $p < .001$), VF produced more error grips when the tool was presented with the handle away (37.5%) from her than with the handle toward her (76.8%). Although this deficit seems to be a hallmark of left brain-damage (Sunderland, Wilkins, Dineen, & Dawson, 2013), this behavior tends to be rare and quite mild in LBD patients (2/16 LBD patients produced only 1 uncomfortable posture in Osiurak et al., 2008) and in apraxic LBD patients (3/10 patients produced more than one non-functional grasp in Randerath et al., 2009). Interestingly, in Randerath et al. (2009), only 1 apraxic LBD patient (Patient IL) produced less functional grips than VF when the handle of the tool was presented away (IL: 25% and VF: 37.5%). Moreover, we did not find any association between grip errors and action errors neither for the left hand (*phi* = -.09, *Chi-2* < 1, df = 1, $p = .94$) nor for the right hand (*phi* = -.14, Chi-2 < 1, df = 1, $p = .79$), instead of what we found in our LBD-A group and what it has been previously reported (Randerath et al., 2009).

VF showed a striking dissociation between grasping to transport versus grasping to use conditions. Whereas she perfectly completed the grasping to transport task, she met severe difficulties in the grasping to use task, which suggests that VF suffers from a specific grasping impairment for familiar tools.

4.3.4. Knowledge supporting tool use

To stress the association between manipulation knowledge and the presence of the grasping deficit for familiar tools observed in VF, we tested in a last part, different kinds of representations known to support tool use.

The use of tools may rely on semantic memory about their function and context of use (Hodges, Bozeat, Lambon Ralph, Patterson, & Spatt, 2000; Osiurak, 2014; Roy & Square, 1985). VF was asked to select among an array of four pictures the one that best matched the picture of a tool (hammer, jug, electrical plug, match, bottle opener, saw, scissors, screwdriver, key, bulb). In the functional condition, the matching criterion was the function of the tool (e.g., target = match; choice = lighter, pen, coffee maker, colander) and in the contextual condition, the criterion was the usual context of use (e.g., target = match; choice = anniversary, wedding, Christmas day, baptism). VF performed in the normal range for both functional (score = 8/10; cut-off = 7/10) and contextual matching (score = 9/10; cut-off = 6/10) tasks. Consistent with these findings, we found in the preliminary praxis evaluation that VF obtained 10/10 in the functional association task of the TLA (Anicet et al., 2007) which assesses specifically functional knowledge and we also found in the RTU-C task, that VF made as many selection errors as non apraxic patients, which let us suppose that VF does not suffer from a deficit of selection of tools. Taken together, these results suggest that semantic tool knowledge is relatively spared for this patient.

Using familiar tools may rely upon manipulation knowledge (Buxbaum, 2001; Gonzalez Rothi, Ochipa, & Heilman, 1991). Manipulation knowledge informs individuals about how to manipulate tools (e.g., knowing how to use a hammer is associated with oscillations of the elbow). We assessed manipulation knowledge by asking to recognize the best way to hold a tool in order to use it with an object (e.g., saw/piece of wood). The same ten tools as in the semantic about tools task were used. We proposed two versions of this test, that is, the 4-choice Recognition of tool-gesture manipulation (4C-RTM) and the forced-choice Recognition of tool-gesture manipulation (FC-RTM). In the 4C-RTM, VF made 3 errors (7/10), but her performance was in normal range (cut off score = 6). She failed 3 items (i.e., plug, hammer, bottle opener) that were not the same as those failed in the semantic matching tasks. VF performed in normal range for the 4C-RTM task, suggesting, at first glance, that manipulation knowledge is spared. An account of the gestural deficit of VF (i.e., accurate discrimination of hand postures while impaired execution of hand postures) would be explained by an impaired access to manipulation knowledge (Gonzalez Rothi, Ochipa, & Heilman, 1991; Heilman, Rothi, & Valenstein, 1982). In the FC-RTM task, the accuracy of VF to distinguish correct from incorrect postures was 78% (31/40), high above from chance level (binomial $z = 3.32, p < .001$). Furthermore, we found a significant difference between each type of posture accuracy, $Q(3) = 9.32, p < .05$, indicating that the errors made by VF were not distributed uniformly across all the conditions. Whereas VF categorized accurately the Target and Impossible conditions (10/10 and 9/10, respectively), she encountered more difficulties for the Active part condition (7/10) and furthermore for the Uncomfortable hand posture condition (5/10). In the case of familiar objects, most apraxic patients are impaired in gesture recognition as well as in gesture production, indicating damage to the representation underlying knowledge of appropriate hand postures for functional object interactions (Buxbaum et al., 2003).

The interaction between the tool and the object may depend on mechanical knowledge (Goldenberg & Hagmann, 1998; Jarry et al., 2013; Osiurak, Jarry, & Le Gall, 2010). Mechanical knowledge can be assessed using mechanical problem-solving tasks in which patients have to select and use tools for which there is no pre-existing usage (e.g., choosing a tool to lever a cylinder; Goldenberg & Hagmann, 1998). For both MPS-C and MPS-NC, VF performed in normal range (MPS-C: 7/9, cut-off score: 7/9 and MPS-NC: 8/9, cut-off score: 7/9). Moreover, in the MPS-C, we found the same pattern of time spent in each condition between VF and Controls: Tool-box

(VF: M = 54%, Controls: M = 43%, SD = 11; modified-t = .91, p = .21), Tool (VF: M = 26%, Controls: M = 24%, SD = 13; modified-t = .14, p = .45), Box (VF: M = 12%, Controls: M = 21%, SD = 13; modified-t = -.63, p = .28) and No action (VF: M = 9%, Controls: M = 11%, SD = 7; modified-t = -.26, p = .40). Moreover, the mean completion time did not differ between VF and controls (VF: M = 96s, Controls: M = 49s, SD = 47, modified-t = .91, p = .21). Finally, VF grasped a similar number of tools compared to Controls during the task (VF: M = 2.67, Controls: M = 2, SD = 1.21, modified-t = .51, p = .32), importantly, she did not grasp more irrelevant tools compared to controls (VF: M = 0, Controls: M = .25, SD = .45, modified-t = -.51, p = .32). VF performed normally in both MPS-C and MPS-NC tasks, which suggests that VF understood the mechanical interactions needed to solve the task. Moreover, she showed the same pattern of strategy compared to controls (i.e., more time spent in the Tool-box condition), which is interesting given that previous studies found that apraxic patients failed this kind of task (Goldenberg & Hagmann, 1998; Jarry et al., 2013) and showed a particular pattern of strategy (i.e., same amount of time spent in each condition; Osiurak et al., 2013). Mechanical knowledge, a crucial form of representation supporting tool use, seems to be spared in VF.

4.3.5. Summary

Here we found that VF produced a significant number of hand posture errors even with the tool in hand, instead of LBD apraxic patients who significantly improved their performance with the tool in hand (i.e., single tool use and real tool use tasks). Thus, the predictions of the MBA seem to be limited to the pantomime of tool use task, as the presence of hand posture errors are atypical once the tool has been grasped (Osiurak, Aubin, Allain, Jarry, Etcharry-Bouyx, et al., 2008; Randerath et al., 2009), except for some rare cases described in the literature (e.g., patient LL; Sirigu et al., 1995). Regarding the status of manipulation knowledge in VF, if we assume that the presence of hand posture errors is the hallmark of impaired manipulation knowledge according to the MBA, we found that VF was still able to use familiar tools with their corresponding objects. This is another limit for this approach as it questions the role and the importance of manipulation knowledge to explain tool use situations and particularly real tool use situations which are the most frequent in everyday life.

As mentioned above, another finding of the present study was the presence of a dissociation between high frequency of hand posture errors and few action errors in VF. In line with the RBA that hypothesizes that mechanical knowledge is essential to use familiar and novel tools (Osiurak & Badets, 2016; Osiurak et al., 2010, 2011), we found that VF had spared mechanical knowledge.

Additionally, the RBA posits that in a situation where a tool has to be used with an object, the technical reasoning process generates a mental simulation of how the tool has to be used with an object (i.e., expected perceptual effect) and is followed by a simulation of the potential motor actions (i.e., motor simulation) which evaluate the costs associated with the intended tool-use actions. It is therefore possible that VF cannot adapt the mental simulation via motor simulation to the situation of tool use and would explain why VF produced a significant number of hand posture errors in absence of action errors. Thus, a dissociation between the mental simulation originating from technical reasoning process and motor simulation is a good candidate to explain the deficit observed here but further studies are needed to test this hypothesis.

4.4. The two-knowledge hypothesis

4.4.1. Explaining actual use of tools with mechanical and semantic tool knowledge

Goldenberg, (2013) criticized the idea that using tools could be supported by manipulation knowledge, which is in line with the results presented in the previous sections of this chapter. According to Goldenberg, mechanical knowledge could replace manipulation knowledge, as it is more flexible and efficient. Finally, using tools may be supported mainly by mechanical knowledge and semantic tool knowledge. Thus, we tested three hypotheses within the perspective of building a cognitive-based model of familiar tool use in normal aging (Lesourd et al., 2017). According to the "semantic knowledge only" hypothesis, the ability to use familiar tools may depend solely on semantic knowledge, but not on mechanical knowledge. Alternatively, in line with the "mechanical knowledge only" hypothesis, the ability to use familiar tools may depend exclusively on mechanical knowledge. Finally, according to the "semantic and mechanical knowledge" hypothesis, mechanical and semantic knowledge may be complementary processes, which would be involved together in the ability to use familiar tools. Thus, mechanical and semantic knowledge may play a significant role in the context of familiar tool use. In order to assess familiar tool use, we used two classical tool use tasks, that is, real tool use in choice condition and real tool use in no-choice condition (e.g., Jarry et al., 2013; see **Figure 22**). The participants included in this experiment were the same as those presented in the section *2.2.4 Dissociation between mechanical and semantic tool knowledge* (page 26).

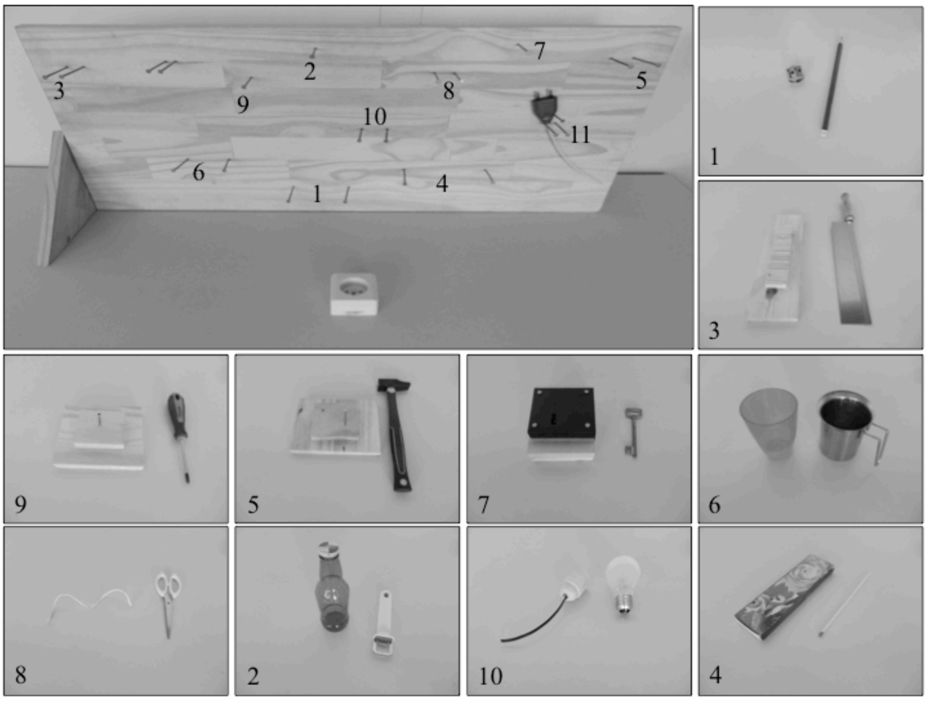

Figure 24. The Real Tool Use (RTU) tasks. The top left picture represents the vertical "tool panel" used for the presentation of tools. In the RTU in Choice Condition (RTU-C), all the tools were presented simultaneously on the vertical tool panel and one object at a time was placed on the table. In the RTU in No-Choice condition (RTU-NC), only the tool associated with the object was presented on the "vertical tool panel" and the object was presented in front of the participants. Each number represents the place of the tool on the panel in RTU-C and RTU-NC (e.g., the hammer was located on the top right of the panel whatever the tool use task). The pair pencil-pencil sharpener was used as first trial for both RTU tasks.

Multiple regression analyses were used to choose the best model among those proposed from the theoretical frameworks for predicting participants' tool use abilities (i.e., RTU-C, RTU-NC). In order to predict the scores in RTU-C and RTU-NC tasks, we used the semantic and mechanical factor scores obtained from the factorial analysis described in section *2.2.4 Dissociation between mechanical and semantic tool knowledge* (page 26). The model with the highest adjusted R^2 was selected as the one that best accounting for tool use tasks performance in normal aging. We showed that cognitive functioning (i.e., BEC) was a mediator of aging on tool use performances; thus, this variable was entered, as a predictor, in the regressions. As aging did not influence tool use tasks and knowledge supporting tools through motor speed, this factor was not entered in the regressions. Regression coefficients are shown in **Table 16.**

Table 16. Multiple regressions with tool use tasks as criterion and Age, cognitive functioning (BEC), semantic and mechanical factor scores, according to the three hypotheses.

RTU-C				RTU-NC			
	β	t	p		β	t	p
"Semantic knowledge only"				*"Semantic knowledge only"*			
Semantic	.25	2.61	*	Semantic	.40	4.14	***
Age	-.39	-4.00	***	Age	-.24	-2.47	*
R^2_{adj} = .28, $F(2,95)$ = 20.31, p < .001				R^2_{adj} = .29, $F(2,95)$ = 20.42, p < .001			
Semantic	.22	2.21	*	Semantic	.39	3.90	***
Age	-.33	-3.19	**	Age	-.22	-2.12	*
BEC	.14	1.43		BEC	.04	.43	
R^2_{adj} = .29, $F(3,94)$ = 14.36, p < .001				R^2_{adj} = .28, $F(3,94)$ = 13.56, p < .001			
"Mechanical knowledge only"				*"Mechanical knowledge only"*			
Mechanical	.28	3.30	**	Mechanical	.28	3.04	**
Age	-.44	-5.05	***	Age	-.36	-3.91	***
R^2_{adj} = .31, $F(2,95)$ = 23.03, p < .001				R^2_{adj} = .23, $F(2,95)$ = 15.66, p < .001			
Mechanical	.27	3.15	**	Mechanical	.27	2.93	**
Age	-.36	-3.69	***	Age	-.30	-2.95	**
BEC	.17	1.75		BEC	.11	1.06	
R^2_{adj} = .33, $F(3,94)$ = 16.7, p < .001				R^2_{adj} = .23, $F(3,94)$ = 10.83, p < .001			
"Semantic and mechanical knowledge"				*"Semantic and mechanical knowledge"*			
Semantic	.29	3.21	**	Semantic	.44	4.86	***
Mechanical	.32	3.81	***	Mechanical	.32	3.92	***
Age	-.30	-3.20	**	Age	-.15	-1.59	
R^2_{adj} = .37, $F(3,94)$ = 20.29, p < .001				R^2_{adj} = .38, $F(3,94)$ = 20.8, p < .001			
Semantic	.27	2.85	**	Semantic	.44	4.69	***
Mechanical	.30	3.64	***	Mechanical	.32	3.87	***
Age	-.26	-2.65	**	Age	-.15	-1.50	
BEC	.10	1.04		BEC	-.00	-.04	
R^2_{adj} = .37, $F(4,93)$ = 15.5, p < .001				R^2_{adj} = .37, $F(4,93)$ = 15.43, p < .001			

RTU-C: Real Tool Use in Choice condition; BEC: Batterie d'Evaluation Cognitive; RTU-NC: Real Tool Use in No-Choice condition
*** p < .001, ** p < .01, * p < .05

The cognitive functioning (i.e., BEC) was not found to be a significant predictor of RTU-C whatever the hypothesis (i.e., “semantic knowledge only”, “mechanical knowledge only” and “semantic and mechanical knowledge”). Thus, we did not consider this factor for selecting the best model of tool use tasks. For both tasks, a three-predictor model including Age, semantic and mechanical factor scores was obtained. Our results are in accordance with the predictions of the “semantic and mechanical knowledge” hypothesis, which assumes that both semantic and mechanical knowledge are needed to use tools. Moreover our findings confirm that semantic knowledge and mechanical knowledge do not support on their own the ability to use familiar tools (for a discussion see Goldenberg, 2013; see also Osiurak, 2014). It is widely accepted that mechanical knowledge supports novel tool use as well as non-conventional tool use (Goldenberg & Hagmann, 1998; Osiurak et al., 2009) whereas semantic knowledge is involved only in familiar tool use (De Renzi & Lucchelli, 1988). However, in the literature on apraxia of tool use, a growing body of evidence shows that mechanical knowledge is also linked with the ability to use familiar tools, notably in LBD patients (for a review see Baumard et al., 2014). In normal aging, we clearly demonstrate that, like semantic knowledge, mechanical knowledge supports the ability to use familiar tools. To resume, the real tool use task in choice condition needs to correctly select among several tools (e.g., hammer, screwdriver, scissors) the one that is usually associated with an object (e.g., a nail) and the real tool use task in no-choice condition needs to correctly use a tool (e.g., hammer) with a given object (e.g., a nail). Therefore, the completion of these familiar tool use tasks needs two components: (1) retrieval of information about the purpose and the usual recipient of tools (i.e., semantic knowledge); (2) the understanding of oppositions existing between physical properties of tools and objects (i.e., mechanical knowledge).

4.4.2. Use of tools when semantic tool knowledge is impaired: example of semantic dementia

Patients with semantic dementia presented a pronounced deficit in semantic knowledge, but several data showed that these patients have preserved mechanical knowledge (Bozeat et al., 2002; Hodges et al., 2000). In a recent work from our group (Baumard et al., 2016), we confirmed these results by showing that SD patients are impaired in semantic tool knowledge tasks and tool use tasks (STU and RTU) but have preserved mechanical skills (**Figure 25**).

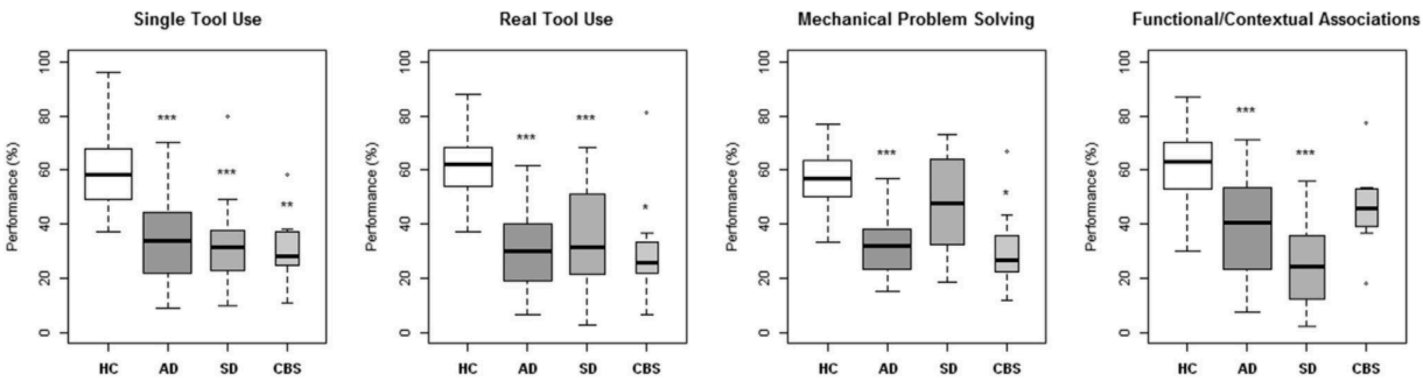

Figure 25. Boxplots displaying the interquartile range (minimum, first quartile, median, third quartile, and maximum). Cases with values more than 1.5 box lengths from the upper or lower edge of the box are displayed as outliers. The width of boxplots is proportional to the sample size. Results in the choice and no-choice conditions were averaged for Real Tool Use and Mechanical Problem Solving. HC: Healthy controls; AD: Alzheimer's disease; SD: Semantic dementia; CBS: Corticobasal syndrome. Comparisons with healthy controls are significant with * $p < .05$; ** $p < .01$; *** $p < .001$.

One of the main arguments of the RBA is that mechanical knowledge is of first importance when we use tools, thus, one may ask why SD patients with impaired semantic tool knowledge and spared mechanical knowledge are impaired when they use tools. Another way to investigate mechanical knowledge is to look at the strategies employed by the patients to solve mechanical problems. Recently, Osiurak et al. (2013) explored the different strategies employed by LBD patients and control subjects to solve mechanical problems in a choice condition. To assess the strategies used by the patients, they recorded the time spent in carrying out four types of action (no manipulation, tool manipulation, box manipulation, and tool-box manipulation) as well as the number of relevant and irrelevant tools grasped. Results indicated that LBD patients grasped a higher number of irrelevant tools and spent less time performing tool-box manipulation than controls. Globally, these findings suggest that LBD patients tend to be perplexed and cannot engage in trial-and-error strategies because of the inability to reason about the objects' physical properties. To test whether SD patients may have difficulties to engage trial-and-error strategies, we recorded their strategies when solving mechanical problems. The patients were the same as those described in section 4.2.1 *Neurodegenerative diseases* (page 50).

We found a significant effect of the factor "Action", $F(3,222) = 82.1$, $p < .01$, $\eta^2_p = .53$. Tool-box manipulation ($M = 40\%$) was more applied than tool manipulation ($M = 25\%$), followed by box manipulation ($M = 21\%$), and no manipulation ($M = 15\%$, all $ps < .013$). There was no significant interaction between the factors "Group" and "Action", $F(6,222) = 1.8$, $p = .09$, $\eta^2_p = .05$. Thus, AD and SD patients exhibited the same profiles as controls but were distinct compared to LBD patients that spent more time in tool, box and no manipulation conditions (**Figure 26**).

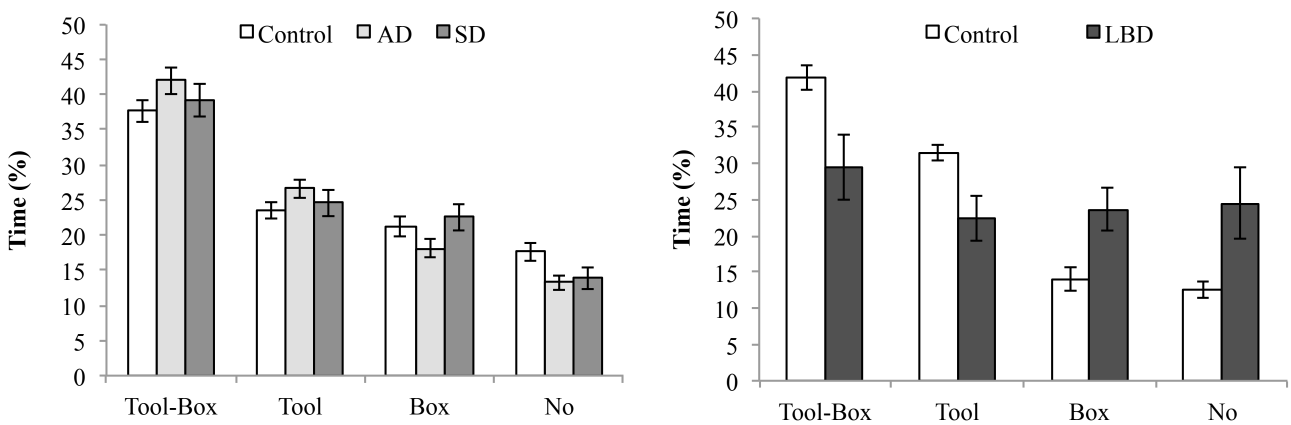

Figure 26. Time (in %) spent performing each kind of actions in the choice condition of the Mechanical Problem-Solving task (MPS-C). Results of AD and SD patients (i.e., present study) are displayed in the left panel and results of LBD patients (Osiurak et al., 2013) are displayed in the right panel. Error bars represent standard errors. Adapted from Lesourd et al. (2016).

Moreover, there were no interaction between the factor Tool (relevant necessary tool, relevant non-necessary tool, and irrelevant tool) and the factor Group, $F(4, 148) = 1.9$, $p = .11$, indicating that there were no differences between the number of irrelevant grasped tools according to each group (**Figure 27**).

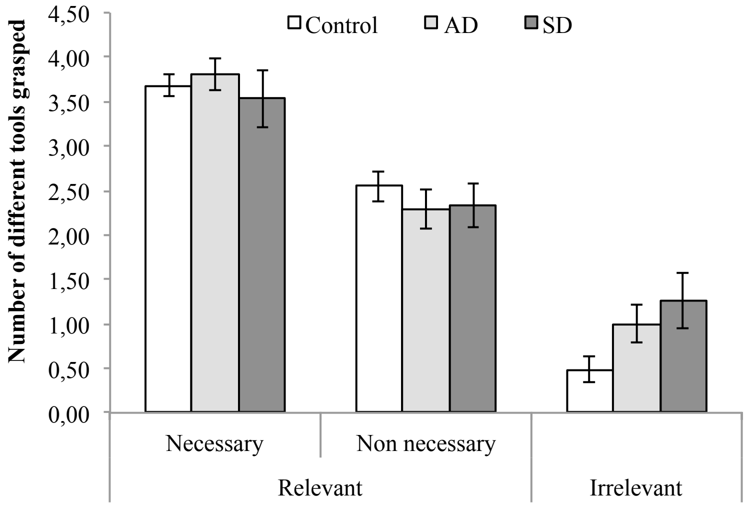

Figure 27. Number and nature of the different tools grasped in the choice condition of the Mechanical Problem-Solving task (MPS-C). Error bars represent standard errors. Adapted from Lesourd et al. (2016).

To sum up, we did not find any difference in the time spent between the four actions (i.e., tool-box, tool, box and no manipulation) between SD and control group. Furthermore, the nature and the number of tools grasped by SD patients during the choice condition were equivalent to those grasped by control participants. Taken together, these results suggest that the strategy employed by SD patients was similar to the one used by control participants. Nevertheless, the strategy profile exhibited by SD patients was qualitatively distinct from the one used by LBD patients. Thus, we replicated previous results (Bozeat et al., 2002; Hodges et al., 2000) and extended them, by demonstrating that SD patients employed the same strategies as healthy controls. It seems pretty clear that SD patients do not have mechanical knowledge impairment as both quantitative scores and strategy profiles are similar to that of controls.

Without semantic tool knowledge, but with spared mechanical knowledge, why SD patients could not normally use tools? In fact, we can suppose that SD patients have tool selection deficit because they suffer from a loss of semantic tool knowledge, but they are still able to produce tool-related actions that are compatible with the tool's physical properties (Hodges et al., 2000; Osiurak et al., 2008). Thus, SD patients may engage trial-and-error strategies based on spared mechanical knowledge, but semantic tool knowledge cannot inform them anymore on the prototypical associations between tools and recipients. Thus, in choice condition of tool use tasks, SD patients have to consider an important number of potential combinations between tools and recipients, which can be time consuming and ineffective, particularly in time limited tasks. In no-choice condition, as only a tool and the associated recipient are given, the combinatorial possibilities are largely reduced, which could explain why SD patients significantly improved their performance between choice and no-choice in RTU tasks (Baumard et al., 2016).

To illustrate this last point, I will briefly present the behavior of one patient (FD) in the RTU-C and the RTU-NC tasks (**Figure 28**). This patient was part of the SD group which was described in several papers (Baumard et al., 2016, 2018, 2019; Lesourd et al., 2016; Lesourd, Baumard, Jarry, Etcharry-Bouyx, et al., 2017). FD was drastically impaired in semantic tool knowledge while performing normally in the problem-solving task. In the RTU-C task, FD was perplexed in front of the ten tools (**Figure 28.A)** and grasped several irrelevant tools (**Figure 28.B**, the bottle opener with the screwdriver). In the RTU-NC task, FD grasped the screwdriver and tried to use it as a lever by introducing the screw in the hole of the screwdriver handle (**Figure 28.C**). Then, after exploring the tool and the screw, she realized that they can be combined together, and she finally carried the expected action (**Figure 28.D**).

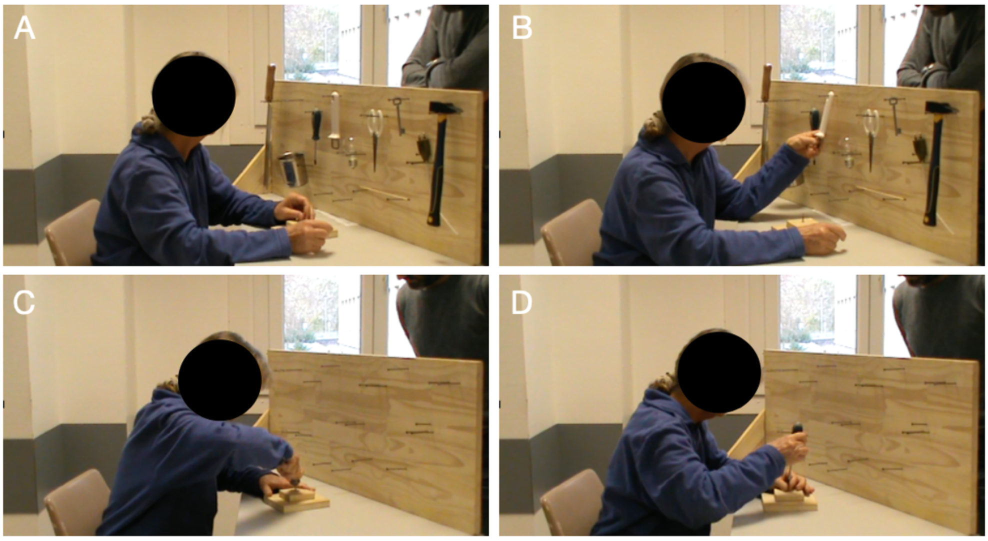

Figure 28. Behavior of FD, a SD patient in RTU-C (A and B) and RTU-NC (C and D) tasks. Explanations are given in the text.

Observing the behavior of this patient leads us to consider that she perfectly understands the physical constraints of the world and she acts in consequence, by employing suitable trial-and-error strategies based on spared mechanical skills. However, this strategy is time consuming, and all the potential combinations cannot be reasonably tried (i.e., important degree of freedom in the RTU-

C task). This hypothesis can explain why even with spared mechanical knowledge, SD patients do not totally compensate the loss of semantic tool knowledge, to correctly use familiar tools. However, we can suppose that with enough time and with tool situations based on transparency of mechanical relationships[9], SD patients could retrieve the use of familiar tools.

4.5. Results in a nutshell

- Mechanical knowledge tasks predict successfully all familiar tool use tasks (pantomime of tool use, single and real tool use tasks) whereas manipulation tasks predict only (but inconsistently) pantomime of tool use tasks, ***which is in line with the predictions of the RBA which assumes that mechanical knowledge is involved in all tool use contexts.***

- Preserved mechanical and semantic tool knowledge with defective hand posture in a rare case of apraxic patient who is still able to use tools, suggests that using tools is relying mainly upon mechanical and semantic representations, ***questioning the role of manipulation knowledge in familiar use of tools***.

- Using familiar tools may be well explained by a two-knowledge hypothesis (mechanical and semantic tool knowledge) in healthy subjects; and patients with semantic impairment may improve their performance with trial-and-error strategies based on preserved mechanical knowledge, only if (1) they have enough time/reasonable degree of freedom; and (2) the mechanical relation between the tool and the object is relatively transparent.

[9] Previous studies found that some tool use tasks call for semantic memory whereas other call for problem solving skills depending on transparency of mechanical relationships between tools and objects or between different elements of the same device (Hartmann, Goldenberg, Daumüller, & Hermsdörfer, 2005). In broad terms, some modern technological tools as automatic coffee machine may be harder to use, as its functioning principle is relatively hidden from the user.

5. Perspectives

5.1. Synthesis

The aim of this work was to better understand the neurocognitive organization of semantic tool and action tool knowledge (i.e., mechanical and manipulation knowledge) and how these representations could support the actual use of tools. We also examined the predictions from two theories of tool use, namely, the MBA and the RBA.

5.1.1. Where action and semantic tool knowledge meet and differ

We confirmed that semantic tool and action tool knowledge are distinct. We found double dissociations between associative tasks and manipulation tasks in LBD patients, and we reported brain regions involved specifically in action tool knowledge (IPS; Ishibashi et al., 2011, 2018) and other involved specifically in semantic tool knowledge (ventral visual cortex and angular gyrus; Kleineberg et al., 2018). We also found that aging has a differential effect on semantic and mechanical knowledge, the former being more impacted than the latter (Lesourd, Baumard, Jarry, Le Gall, et al., 2017). We also found that the left pMTG was sensitive to both action tool (hand-tool relationships) and semantic tool knowledge (for reviews see Lingnau & Downing, 2015; Wurm & Caramazza, 2022). However, we also found that manipulation and function tasks may have particular relations, i.e., double dissociations were not found between function and manipulation relations, and we also pointed out that IPL/SMG and pMTG are both sensitive to manipulation and function relations (for a review see Lesourd et al., 2021). These results are at odds with what is traditionally reported in the literature and need further investigations (Garcea et al., 2013; Garcea & Mahon, 2012). I also found that the tasks investigating manipulation knowledge leads to controversial results. For instance, manipulation tool-tool compatibility tasks but not manipulation tool-hand compatibility tasks were impaired following stimulation in left SMG (PF) (Andres et al., 2013; Pelgrims et al., 2011). Moreover, LBD patients showed subnormal performance in tool-hand compatibility tasks compared to tool-tool compatibility tasks. Taken together, these data indicate that manipulation knowledge needs to be more specified.

5.1.2. The 4-pathway model of understanding and producing object-related actions

We also examined several predictions from the RBA and MBA, two theories of tool use. We found that RBA offered an interesting theoretical framework to better understand our interactions with tools and objects. Indeed, mechanical knowledge was involved in all situations of tool use whereas manipulation knowledge was only involved in pantomime of tool use tasks. Moreover, in VF, an apraxic patient, that defective hand posture was not associated with a deficit in using tools. By considering hand-tool, tool-object and tool-centered relationships, we revealed an interesting organization in the posterior TPN (see **Figure 29**). We found that the left IPL (SMG/PF) was representing tool-object relationships and was more involved in unfamiliar tool use than in familiar tool use (Federico et al., 2022; Reynaud et al., 2016; Reynaud, Navarro, Lesourd, & Osiurak, 2019). All these points raised the limits of the MBA. However, if hand-tool relationships were found in IPS (i.e., production system; see also aIPS for abstract manipulation representations (Chen, Garcea, Jacobs, & Mahon, 2018), the RBA does not predict that hand-tool relationships may be supported by the left pMTG. Indeed, RBA assumes that the temporal lobe stores only tool-centered knowledge.

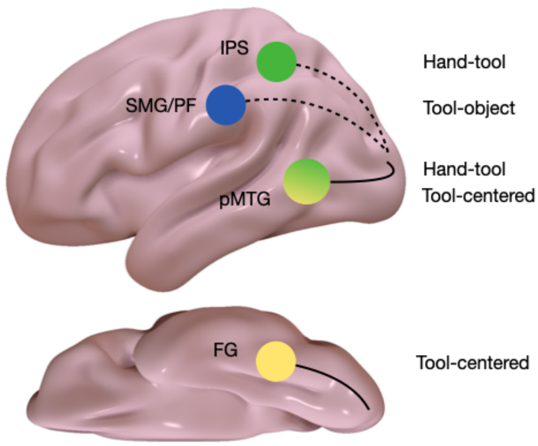

Figure 29. Schematic illustration of the distribution of hand-tool, tool-object and tool-centered relationships within the posterior TPN.

If we admit that manipulation and mechanical knowledge co-exist in the brain, one may accept that these representations are not equipotential in their relations with actual use of tools, as it has been demonstrated in this work. The understanding and the production of object-related actions are relying upon mechanical knowledge (i.e., tool-object relationships; Reynaud et al., 2016, 2019). In the temporal dynamics of representations activation, the technical reasoning comes first (Osiurak, Federico, Brandimonte, Reynaud, & Lesourd, 2020) and may be followed by the activation of other sources of stored representations (i.e., manipulation and semantic tool knowledge), which are neither required nor sufficient for using tools (Buxbaum et al., 1997; Lesourd et al., 2020; Negri et al., 2007; Valério et al., 2021). Manipulation and semantic tool knowledge may afford an economic advantage (e.g., in terms of time and motor effort; see Osiurak, 2014) in the use of familiar tools. It exists behavioral and neural evidence that tool-object relationships are processed earlier than hand-tool relationships. Studies using gaze data showed that in tool use situations, the visual exploration started with the functional part of the tool followed by the manipulable part (Federico & Brandimonte, 2019; Federico, Osiurak, Reynaud, & Brandimonte, 2021). Behavioral studies showed that action goal[10] representations are first activated compared to hand posture representations (Decroix & Kalénine, 2018; Van Elk, Van Schie, & Bekkering, 2008). In electrophysiological studies, using event related potentials, an earlier modulation of the P300 for object-goal violations (i.e., tool-object relationships; e.g., using a nail on a hammer) in comparison to object-grip violations has been found (i.e., hand-tool relationships; e.g., grasping the hammer by its head instead of its handle) (van Elk, Bousardt, Bekkering, & van Schie, 2012; see also Decroix, Roger, & Kalénine, 2020 for N300).

Accepting that manipulation and mechanical knowledge can neurocognitively coexist in a hierarchical framework is not sufficient and calls for further elaboration.

5.2. Current and future projects

Several perspectives are developed in the final part of this manuscript. They are displayed in **Figure 30** and detailed below.

[10] Action goal may be interpreted as tool-object relationships, and therefore to mechanical knowledge (see section 5.2.1 *What are the temporal dynamics of activation of mechanical and manipulation* representations? page79).

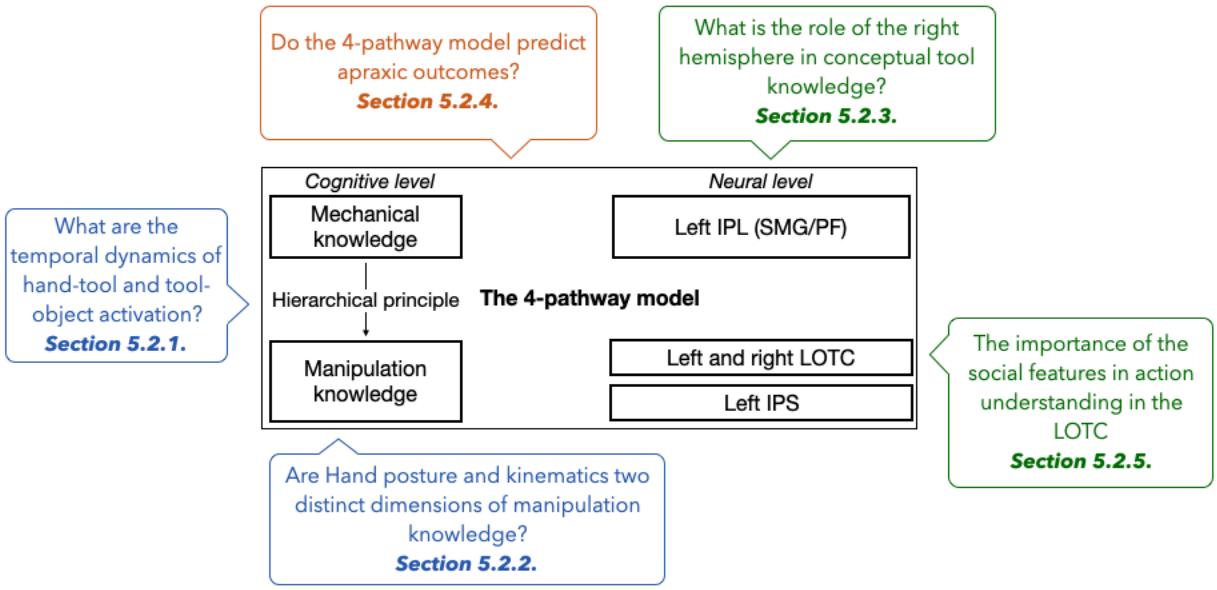

Figure 30. Graphical representation of the future perspectives of research. At the center is represented the 4-pathway model with the possible cognitive organization on the left and the brain correlates on the right. Semantic tool knwoledge is not represented in the model is included in the 4-pathway model. Each question is detailed in a specific part of the last chapter and is related to the cognitive organization (colored in blue), the cerebral correlates (colored in green), or to the general application of the model (colored in orange).

- What are the temporal dynamics of activation of mechanical and manipulation knowledge?
- Are we chasing a chimera by trying to dissociate hand posture and kinematics components?
- What is the role of left and right hemispheres in conceptual tool knowledge?
- Back to apraxia of tool use: Are action tool and semantic tool representations able to predict apraxic outcomes in brain damaged patients?
- Do the LOTC potentiate action understanding through social features?

5.2.1. What are the temporal dynamics of activation of mechanical and manipulation representations?

In the present work, we found that hand-tool and tool-object relationships are supported by distinct cerebral regions. The left IPL (SMG/PF) supports mechanical knowledge (Federico et al., 2022; Orban & Caruana, 2014; Reynaud et al., 2016, 2019; Stoll et al., 2022), whereas LOTC and IPS support hand-tool relationships (i.e., manipulation knowledge). According to the hierarchical hypothesis, mechanical knowledge may be activated first, followed by manipulation knowledge (Federico & Brandimonte, 2019, 2020; Osiurak, Federico, et al., 2020).

We can test this hypothesis with the same kind of priming paradigm used in Decroix and Kalénine (2018), by manipulating hand-tool and tool-object relationships (**Figure 31**). Hand-tool relationships could be either correct or incorrect (e.g., a hand grasping correctly or not a scissor) and tool-object relationships could be possible or not (e.g., a scissor presented with a piece of paper or with a piece of wood). Participants will judge the correctness of target actions according to the typical use of tools. Target will be primed by actions sharing the same hand-tool or same tool-object relationships, both hand-tool and same tool-object relationships, or none. Primes will be presented for 66 or 300ms (see Decroix & Kalénine, 2018). We expect to find a priming effect for tool-object relationships (66ms) before the integration of tool-object and hand-tool relationships (300ms), according to the hierarchical hypothesis.

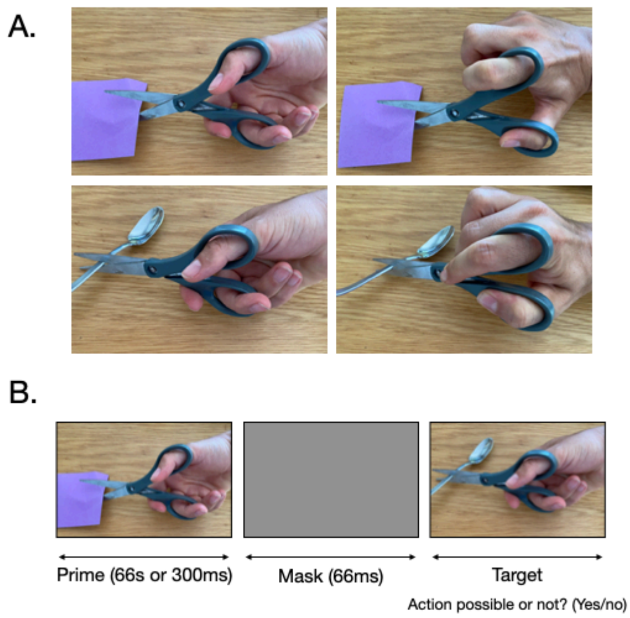

Figure 31. Example of the priminig paradigm inspired from Decroix and Kalénine (2018). A: 4 stimuli represented typical hand posture with possible mechanical action, atypical hand posture with possible mechanical action, typical hand posture with impossible mechanical action, and atypical hand posture with impossible mechanical action. B: a trial where a typical hand posture and possible mechanical action is priming a typical hand posture and impossible mechanical action.

5.2.2. Are we chasing a chimera by trying to dissociate hand posture and kinematics components?

Are there some regions specialized for processing hand posture components and other regions specialized for processing kinematics components (Martin et al., 2017)? Are hand posture component emerge from the functional interactions of temporal and parietal areas (Garcea et al., 2018; Metzgar, Stoll, Grafton, Buxbaum, & Garcea, 2022)? These questions remain unresolved as contradictory findings has been observed in LBD patients (Buxbaum et al., 2014; Martin et al., 2017) and as hand posture and kinematics are both associated with parietal and lateral temporal brain activations in fMRI studies (for a review see Lesourd et al., 2021). Another issue is that hand posture and kinematics are generally not manipulated orthogonally in action tool compatibility tasks, i.e., two objects may have the same hand posture, but have also the same kinematics (e.g., Garcea & Mahon, 2012). Therefore, we developed a set of stimuli whose hand posture and kinematics are orthogonal to each other (see **Figure 32**). These stimuli will be used in future experiments, that we will conduct on hand posture and kinematics.

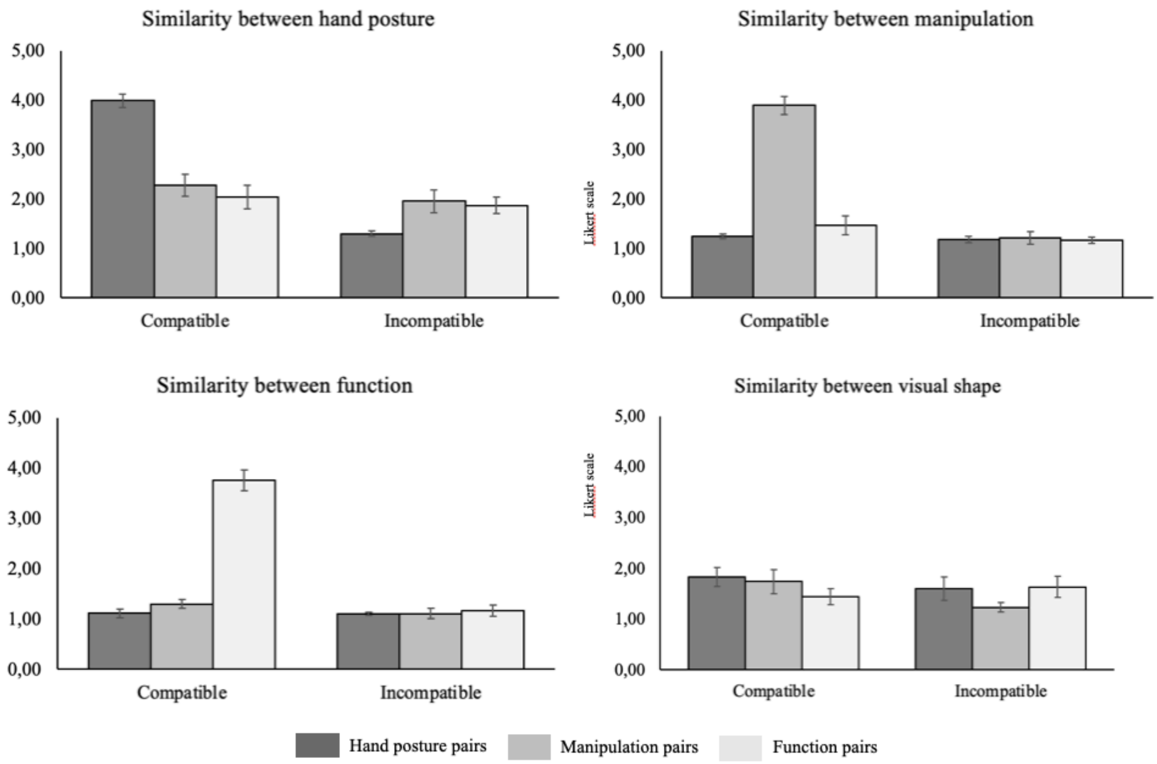

Figure 32. Charcateristics of familiar pair of objects, which are distinct in one dimension (e.g., hand posture) but are similar in the others (e.g., kinematics, function and visual shape). Adapted from Lesourd & Osiurak (in prep.).

We will also use multivariate pattern analyzes (MVPA) in a fMRI study, in which we hypothesize that if hand posture and kinematics are indissociable components, posterior brain regions of the TPN should present similar decoding accuracies in pMTG and IPL, whereas if hand posture and kinematics components are independent neural dimensions, specific regions should encode particular feature of manipulation knowledge, and we should observe greater decoding accuracies for hand posture compared to kinematics in a particular brain region, and *vice versa*.

Pantomime of tool use task is usually used in fMRI paradigm, as this task is assumed to target specifically the hand posture component (Garcea & Buxbaum, 2019; Garcea et al., 2018; Metzgar et al., 2022). Thus, healthy participants will pantomime the use of tools inside the scanner. Each tool will be selected along two dimensions of hand posture (e.g., precision grip/power grip) and kinematics (e.g., rotating/cutting) (see **Figure 33A**). Mass-univariate analyzes may inform us whether a voxel is sensitive to some kind of information by fitting a GLM on the BOLD activity of this voxel, but multivariate pattern analyses (MVPA) will tell use more precisely which kind of information is represented in a given region by taking into account several voxels (Gilron, Rosenblatt, Koyejo, Poldrack, & Mukamel, 2017; Haxby, Connolly, & Guntupalli, 2014; Norman, Polyn, Detre, & Haxby, 2006).

We will conduct a within and an across category decoding separately (**Figure 33B**). While the presence of significant within-category decoding allows to affirm whether a brain region contains information about action categories at a low level of abstraction, the presence of significant across-category decoding indicates that a brain region represents information about action categories at a higher level of abstraction. We will train on a subset of data, a linear support vector machine (SVM) classification algorithm, to distinguish patterns of parameter estimates associated with each condition. We will test the classifier ability to decode the conditions associated with patterns of parameter estimates on the remaining data. For within category decoding, to decode along kinematics, the SVM classifier will be trained to discriminate between precision grip/rotating vs power grip/rotating and tested on precision grip/rotating vs power grip/rotating. In another step, the SVM classifier will be trained to discriminate between precision grip/cutting vs power grip/cutting and tested on precision grip/cutting vs power grip/cutting, then mean accuracies will be averaged. For the across category decoding, to decode along kinematics, the SVM classifier will be trained, to discriminate between precision grip/rotating vs power grip/rotating and tested precision grip/cutting vs power grip/cutting. Classification accuracies will be averaged across the 2 generalization directions (e.g., Rotating to Cutting, and vice versa). The same decoding scheme will be used for Hand posture.

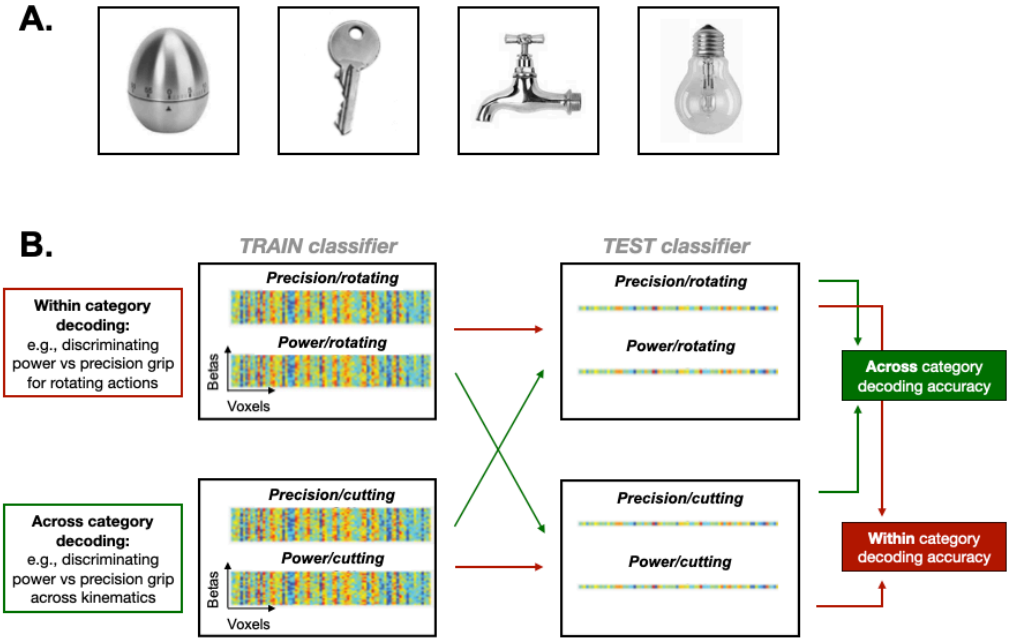

Figure 33. Schematic representation of the MVPA. A, Exmaples of the objects that will be used in the pantomime of tool use task; B. Presentation of the within and across decoding scheme. Explanations are given in the text.

We will conduct analyses on region of interest (ROI) as it is traditionally used in MVPA studies, by selecting ROIs based either on localizer (e.g., Chen et al., 2016) or on brain regions from previous metanalysis of our group (i.e., IPL, IPS, pMTG; Reynaud et al., 2016; Reynaud, Navarro, Lesourd, & Osiurak, 2019). We will also carry out searchlight whole-brain analyses for seeking for additional putative brain regions (Allefeld & Haynes, 2014). An additional rTMS study will be conducted and will target one or several ROIs revealed in the fMRI study (see for a similar procedure Perini et al., 2014), to confirm our results.

5.2.3. What is the role of left and right hemispheres in conceptual tool knowledge?

The aim of this project is twofold. First, we will study the impact of RBD and LBD in conceptual tool knowledge. An intriguing question is the role of the right hemisphere in manipulation knowledge and semantic tool knowledge, as this hemisphere is generally neglected in neuropsychological literature on conceptual tool knowledge (e.g., Buxbaum et al., 2014; Goldenberg & Spatt, 2009; Kalénine et al., 2010; Martin et al., 2017; Tarhan et al., 2015). Second, I will explore the dissociation between tasks (e.g., hand posture vs kinematics and kinematics vs function) using single case methodology and neuroimaging techniques. This project focuses only on conceptual tool knowledge but not on the link between conceptual tool knowledge and actual use of tools (see section 5.2.4 *Back to apraxia of tool use: predicting apraxic outcomes from action tool and semantic tool knowledge*, page 89).

For this project, I started a collaboration in March 2022 with the Neurovascular Unit of the CHU of Besançon (Pr. Thierry Moulin). The project was funded by the Region Bourgogne Franche-Comté and was approved by the local ethic committee of the University of Bourgogne Franche-Comté (CERUBFC-2022-02-15-006). We plan to include 120 post stroke patients (*n* = 60 LBD and *n* = 60 RBD) over the next two years. Currently, 38 control participants and 40 patients have been included at the date of 15/07/2022 (*n* = 20 LBD and *n* = 20 RBD, days post-stroke: *M* = 115.5, *SD* = 48.8). I supervised a master's degree student (Margaux de Bergen, 2021-2022) who participated in the inclusion and the analysis of the preliminary data. All the participants will undergo three action compatibility tasks (kinematics, hand posture, and hand-tool conditions) and one semantic compatibility task (function) (see **Figure 34**).

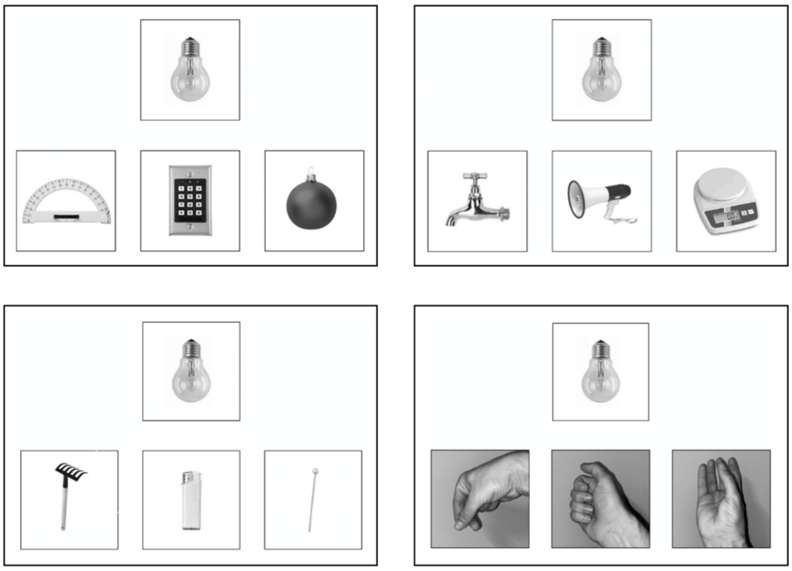

Figure 34. Action and semantic tool tasks proposed in LBD and RBD patients. The same target items are proposed in all conditions. Top left: hand posture matching task, Top right: kinematics matching tasks, Bottom left: function matching task, Bottom right: hand-tool matching task.

Several behavioral and neuroimaging analyzes will be carried out. Group comparisons (LBD vs RBD vs Controls), correlational analyzes, and analysis of individual cases based on the single case statistics will be carried out (deficit and dissociation; Crawford & Garthwaite, 2002, 2005; Crawford & Garthwaite, 2007). Preliminary results showing group comparisons are displayed on **Figure 35**.

These first analyses show that RBD patients are impaired, as LBD patients, in both action and semantic tool tasks, suggesting that action and semantic tool knowledge may be impacted following RBD.

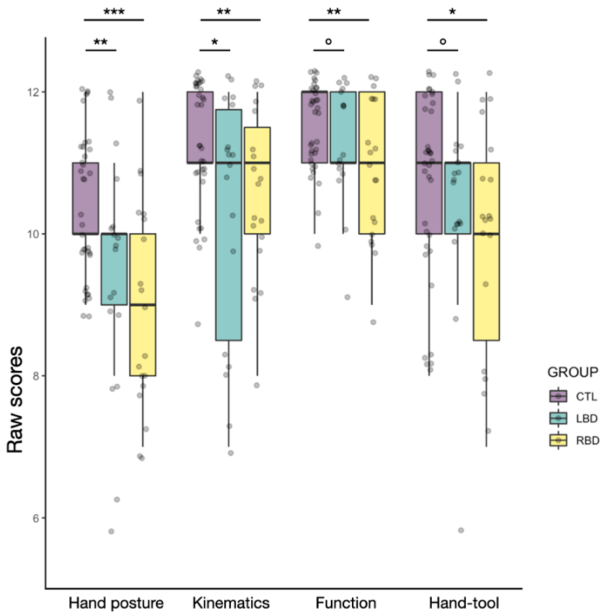

Figure 35. Group comparisons between Controls, LBD and RBD patients for the the action and semantic tool tasks. ° $p < .1$, * $p < .05$, ** $p < .01$, *** $p < .001$ (Mann-Whitney tests).

Another objective of this work is to apply Voxel-Lesion Symptom Mapping analyses (VLSM; de Haan & Karnath, 2018; Karnath, Sperber, Wiesen, & de Haan, 2019) to better understand the association between brain regions and the dimensions tested here[11]. I will compare lesion maps for patients presenting preserved hand posture and impaired kinematics and the opposite pattern in LBD and RBD patients (e.g., Martin et al., 2017). However, the fundamental limitation of VLSM approaches is that they are constrained to voxels within a lesion mask, and therefore are blinds to the cascade of changes occurring remotely. Behavioral deficits in stroke reflect both structural damage at the site of injury, and widespread network dysfunction caused by structural and functional disconnections (Pini et al., 2021; Salvalaggio, de Filippo De Grazia, Zorzi, de Schotten, & Corbetta, 2020; Thiebaut de Schotten, Foulon, & Nachev, 2020). Thus, I will test whether a behavioral deficit observed in our study could be associated with the disconnection of particular white matter fibers (e.g., left superior longitudinal fasciculus in tool use and semantic tool concept;

[11] Multivariate lesion-symptom methods (SVR-LSM) can be used instead of VLSM, as they are superior to univariate methods, as they account for non-independence between voxels and map the impact on wider brain networks (e.g., Garcea, Stoll, & Buxbaum, 2019).

Bi et al., 2015). For instance, I hypothesis that function relations, particularly those containing manipulation features (e.g., “cutting”), may be retrieved by mutual interactions between temporal and parietal areas. In a recent unpublished fMRI study from our group (see **Figure 36**), we found that function relations were associated with significant pattern of functional connectivity between SMG and inferior LOTC, although univariate analyses showed brain activations in LOTC, but not in SMG (see also Yee et al., 2010). Thus, we may observe impaired performance in the function matching task caused by the interruption of white matter fibers between IPL and LOTC.

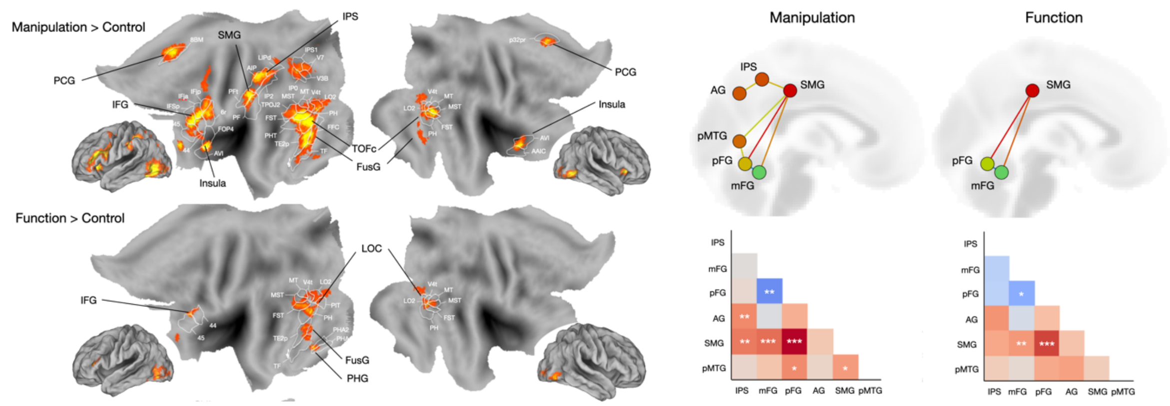

Figure 36. Left panel: Statistical maps for the contrasts Manipulation>Control and Function>Control obtained in tool-tool compatibility tasks, where participants have to judge whether two tools are manipulated similarly (i.e., kinematics) or whether two tools have the same function. Right panel: Functional connectivity within 6 seed ROIs for Manipulation *vs* Control and Function *vs* Control (top); and Sagittal view of the ROI-to-ROI functional connectivity (*p*-FDR seed-level corrected < .05) with pairwise correlation matrices (Z-Fisher transformed) used to visualize both significant and non-significant correlations at *p*-FDR seed-level corrected < .05 (bottom). Adapted from Lesourd, Reynaud, Navarro et al. (under review in *Cerebral Cortex*).

5.2.4. Back to apraxia of tool use: predicting apraxic outcomes from action tool and semantic tool knowledge

Apraxia is a cognitive disorder of motor control which cannot be explained by elemental motor deficits nor by general cognitive impairment (De Renzi & Lucchelli, 1988). Apraxic symptoms may occur following stroke and can either spontaneously disappear in the first months post-stroke (Goldenberg, Daumüller, & Hagmann, 2001); or impact durably the functional autonomy of brain damaged patients. If therapies focusing on compensatory mechanisms exist (for a review see Dovern, Fink, & Weiss, 2012), the possibility of recovery in apraxic patients are relatively limited. For instance, a follow-up study of 5 years post-stroke in 532 patients, showed that the autonomy of patients was similar at 2 months post stroke and at 5 years post stroke. Several factors may explain this effect: the presence of aphasia (Lemmetyinen, Hokkanen, & Klippi, 2019), and/or anosognosia (Buchmann, Finkel, Dangel, Erz, & Maren, 2019), the use of rehabilitation therapies that are not based on theoretical models of apraxia (for a discussion see Worthington, 2016).

To date, the predictors of functional recovery in brain damaged patients are still unknown. Studies focusing on long-term recovery of apraxic patients are rare and focused on production tasks, and showed that the presence of a lesion within the left TPN is a not a good predictor of apraxic outcome, and that production errors persist in imitation of meaningless gestures and pantomime of tool use tasks (Dressing et al., 2021; Kusch et al., 2018). The aim of this project is to reveal the cognitive factors that underlie the functional recovery in brain damaged patients. We showed that several representations are supporting our abilities to use tools in different contexts (e.g., pantomime of tool use and actual use of tools), that is, manipulation, mechanical and semantic tool knowledge; Lesourd, Baumard, Jarry, Etcharry-Bouyx, et al., 2017; Lesourd, Baumard, Jarry, Le Gall, et al., 2017; Lesourd et al., 2019). Moreover, a recent study reported encouraging results when using action semantics in the rehabilitation of stroke patients (Stoll, de Wit, Middleton, & Buxbaum, 2020). Thus, studying the dynamics of reorganization of conceptual tool knowledge in association with the evolution of apraxic symptoms between acute and chronic stage of stroke represent a promising avenue of research.

The aim of this project is to explore the pattern of recovery of action tool and semantic tool knowledge between acute and chronic stage of the stroke. Several tasks already described in the present manuscript at different time points will be proposed to LBD patients. We will also test whether the evolution of each of these representations can predict the performance in tool use tasks and for some other functional outcomes (e.g., Barthel index). We will test the main prediction of the hierarchical hypothesis: if mechanical knowledge is critical for using tools, thus patients improving their tool use performance, should also improve their performance in tasks assessing mechanical knowledge. If not, which representations can compensate, at least in part, a loss of mechanical knowledge? This project will start at the end of September 2022, LBD patients will be included in the Neurovascular Unit of the CHU of Besançon and will be tested twice, a first time at the acute stage of the stroke and a second time in the chronic stage of the stroke. Several Master students will work on this project during the two next years.

Of course, this work should have clinical outcomes, by building a predictive model of long-term recovery, based on several predictors (e.g., cognitive dimensions, location of the brain lesion, etc.), using machine learning algorithms (Rehme et al., 2015). Predicting individual long-term recovery pattern in brain damaged patients may allow early clinical indications and may improve the development of more efficient therapies.

5.2.5. Do the LOTC potentiate action understanding through social features?

In this work, we found that the LOTC has a particular role in action understanding/producing. The LOTC is part of the Action Observation Network (AON), a brain network involved when observing other's actions (for reviews see Caspers, Zilles, Laird, & Eickhoff, 2010; Grosbras, Beaton, & Eickhoff, 2012). In the present work, we showed that the left LOTC was sensitive to several kinds of representations (i.e., hand-tool but not tool-object relationships) and was involved in several tasks assessing action and semantic tool tasks (i.e., manipulation, function, and associative compatibility tasks). Other recent studies showed that the LOTC was able to represent actions from low to higher level of abstractedness (Wurm et al., 2016, 2017; Wurm & Lingnau, 2015), with posterior part of the LOTC encoding perceptual features of actions and anterior part of the LOTC processing abstract concepts (for a review see Wurm & Caramazza, 2022). Moreover, the LOTC contains also social representations about object-related actions (Wurm et al., 2017). The LOTC contains information about interacting versus non interacting agents (Walbrin, Downing, & Koldewyn, 2018), directedness of actions toward different target and the presence of another person in the scene (Wurm & Caramazza, 2019). In a neurodevelopmental study (not published yet), we found that adults and adolescents showed higher decoding accuracies for social and transitive actions at both low and high level of abstraction in the LOTC compared to IPS/SPL and PMv (**Figure 37**). We also found that adolescents had lower decoding accuracies for sociality compared to adults whereas there was no difference for transitivity, suggesting that the ability to decode sociality in the LOTC was still maturing in adolescence.

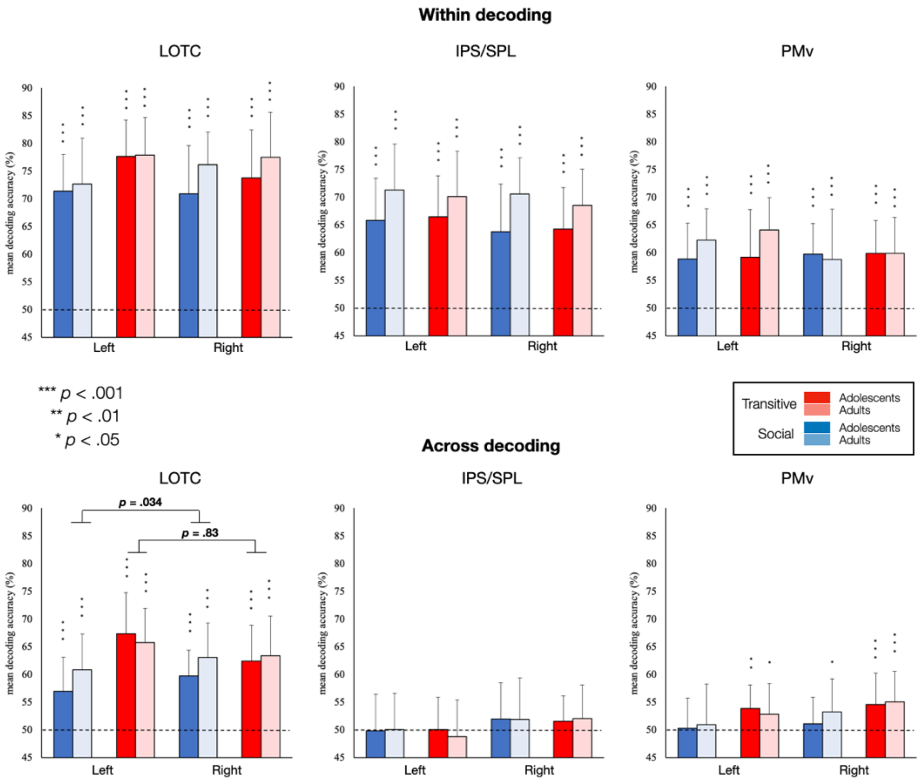

Figure 37. fMRI ROI MVPA results of a study where adults and adolescents saw social transitive, social intransitive, non-social transitive and non-social intransitive videos. Bar graphs shows group averaged decoding accuracies for within (top) and across (bottom) decoding for social versus non-social actions (blue) and transitive versus intransitive actions (red) for both groups of subjects (adolescents = dark and adults = light). Error bars indicate Standard Deviation (SD). Asterisk represents statistical significance (FDR-corrected for the number of tests). Dotted line indicates decoding accuracy at chance-level (50%). *** $p < .001$, ** $p < .01$, * $p < .05$. Adapted from Lesourd, Afyouni, Geringswald, et al. (under review in *Journal of Neuroscience*).

These data suggest that the LOTC participates in the understanding of object-related actions through social features. One may hypothesis that these social features may potentiate the learning/retrieving of abstract concepts by observing other's actions. This hypothesis will be tested in a project funded by the ANR (ANR TECHNITION), and a PhD student (Maximilien Métaireau) will start to work on this project at the end of the year (October-November 2022).

Conclusion

In this HDR manuscript, I presented a part of my research that took place during the last decade (2013-2021), and which was the result of an important collaborative work. I am fully aware that this manuscript is humble and did not handle a lot of theoretical questions which are still pending at the last page of this manuscript. One of the main purposes of this work was to test the predictions of two different theories of tool use, and how they can explain the actual use of tools. The main hypothesis was that mechanical knowledge is critical for using tools and is involved whatever the context of use. This hypothesis was generally verified. If the reasoning-based approach is an interesting framework, we also found that it cannot explain several results observed in the present work, such as the fact that hand-tool relationships are supported by the temporal lobe (i.e., LOTC/pMTG). Consequently, the existence of manipulation knowledge cannot be excluded. Thus, we proposed in the last part, the possibility that mechanical and manipulation knowledge can neurocognitively coexist. I think that several studies already assess both manipulation knowledge and mechanical knowledge with recognition of tool manipulation and mechanical problem-solving tasks, therefore assuming that both forms of representations co-exist. Even in the attempt to propose a new operational definition of apraxia, manipulation and mechanical knowledge are considered as core representations of praxis system, which in case of impairment, would cause an *idiopathic* apraxia in contrast to *symptomatic* apraxia (Baumard & Le Gall, 2021).

It is time to go beyond the current debate and to propose a neurocognitive hypothesis, in which tool-object and hand-tool relationships may both explain the actual use of tools. We proposed to test this hypothesis within the framework of the 4-pathway model, in which mechanical knowledge occupies a critical role, followed by semantic and manipulation knowledge (hierarchical hypothesis). It is of first importance to propose a theoretical framework that may guide new rehabilitation therapies. Bridging the gap between theoretical debates and clinical reality should be the main interest of researchers in the field of apraxia for the next decade. Indeed, the concepts that is currently developed in the research framework meet great difficulties to be transferred in the clinical setting, which lead the clinicians to still use the old traditional dichotomy between ideomotor and ideational apraxia.

This is the objective that I will pursue in the next decade, i.e., testing this model in the rehabilitation setting, without forgetting that the possibility to recover from apraxic deficits does not depend solely on motor and cognitive functions, but may be also supported by the living context of each patient. For instance, Goldenberg and Hagmann (2001) reported that the involvement of caregivers could modulate the recurrence of apraxic symptoms in post-stroke patients. To date, we have the mathematical tools (machine learning algorithms) to propose robust models, that are not just explaining but go one step further by predicting (for a discussion see Yarkoni & Westfall, 2017) the possibility for a particular patient to recover from apraxic deficits, and therefore proposing as early as possible the most appropriate therapy. This project will necessarily have to be carried by several research teams disseminated in different countries.

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Curriculum Vitae

1. État civil

Nom :	Lesourd
Prénom :	Mathieu
Date de naissance :	10/08/1981 (42 ans)
Nationalité :	Française
Situation familiale :	Marié, 2 enfants
Adresse professionnelle :	Laboratoire de recherches Intégratives en Neurosciences et psychologie Cognitive (UMR INSERM 1322) 19 rue Ambroise Paré 25030 Besançon Cedex Département de Psychologie Université de Franche-Comté 30-32 rue Mégevand 25000 Besançon mathieu.lesourd@univ-fcomte.fr

2. Diplômes

Habilitation à Diriger des Recherches (Université de Lille)

Titre :	*How action tool and semantic tool representations shape object-related actions: a neurocognitive approach*
Soutenance :	27 septembre 2022
Membre du jury :	Angela Bartolo, Université Lille Solène Kalénine, Université Lille Michael Andrès, Université Catholique de Louvain, Belgique Yan Coello, Université Lille Peter Weiss-Blankenhorn, Institute of Neuroscience and Medicine, Jeulich, Germany Guy Vingerhoets, Université de Gent, Belgique

Doctorat de Sciences Cognitives mention psychologie (Université Lyon 2)

Titre :	*Les interactions et intégrations multi-sensorielles sous l'angle d'un modèle de mémoire à traces multiples*
Soutenance :	22 septembre 2011
Mention :	Très honorable avec félicitations
Directeur de thèse :	Pr. Rémy Versace (Université Lyon 2)
Membres du jury :	Pr. Olivier Koenig (Université Lyon 2), Président Micah M. Murray (CHU Vaudois, Lausanne, Suisse), Rapporteur Pr. Denis Brouillet (Université Montpellier 3), Rapporteur

Stéphane Rousset (Université Grenoble 2), Rapporteur

Master 2 professionnel Neuropsychologie clinique, Évaluation péri-chirurgicale et Réhabilitation cognitive (Université Lille 3)

Obtenu en septembre 2011
Mention Assez Bien

Master 1 Psychologie Cognitive et Neuropsychologie (Université Lyon 2)

Obtenu en juillet 2010
Mention Bien

Licence 3 Psychologie (Université Lyon 2)

Obtenu en juillet 2009
Mention Bien

Master 2 recherche Sciences Cognitives (Université Lyon 2)

Obtenu en juillet 2007
Mention Bien

Maîtrise de Sciences Cognitives (Université Nancy 2)

Obtenu en juillet 2004
Mention Bien

Licence de Sciences Cognitives (Université Nancy 2)

Obtenu en juillet 2003
Mention Bien

DEUG Psychologie (Université Nancy 2)

Obtenu en juillet 2002
Mention Bien

3. Expériences universitaires

Maître de conférences en Neuropsychologie et Psychologie cognitive, Université de Franche-Comté *(2019 à maintenant)*

Laboratoire de rattachement

2021 à *maintenant* : Laboratoire de recherches intégratives en neurosciences et psychologie cognitive (UMR INSERM 1322 LINC), dirigé par E. Haffen (PU PH)

2019 à 2020 : Laboratoire de Psychologie (EA 3188)

Département de rattachement

2019 à *maintenant* : Département de psychologie

Post-doctorat au Laboratoire de Neurosciences Cognitives (CNRS UMR 7291), Université Aix-Marseille *(2017-2019)*

Équipe : Neuro-développement de la cognition motrice et sociale dirigé par C. Assaïante (DR CNRS)

Thème : Étude en IRMf du développement du réseau cérébral d'observation de l'action entre l'adolescence et l'âge adulte, sous la direction de M.-H. Grosbras (DR CNRS)

Attaché Temporaire d'Éducation et de Recherche (ATER), Université Lyon 2 (2015-2017)

Laboratoire de rattachement : Laboratoire d'Étude des Mécanismes Cognitifs (EMC, EA 3082)

Post-doctorat au laboratoire d'Étude des mécanismes Cognitifs (EMC, EA 3082), Université Lyon 2 *(2012-2015)*

Équipe : Cognition Outils Systèmes (COSy) dirigé par F. Osiurak (PU)

Thème : Étude des troubles apraxiques dans la maladie d'Alzheimer, la démence sémantique et la dégénérescence cortico-basale, sous la direction de F. Osiurak (PU)

4. Expériences cliniques

Psychologue neuropsychologue à la consultation de l'Hôpital de jour Cognition et Cancer (Dr. Virginie Desestret), Hôpital neurologique Pierre Wertheimer, Lyon *(sept.-nov. 2017)*

Mission : Réalisation d'évaluations neuropsychologiques de patients traités par chimiothérapie dans le cadre d'un cancer (*chemobrain*)

Psychologue neuropsychologue (25%) dans le service d'Epileptologie et de neurologie fonctionnelle (Pr. Sylvain Rheims) à l'hôpital Neurologique Pierre Wertheimer, Lyon *(2013-2017)*

Mission : Réalisation de bilans pré- et post-opératoires de patients candidats à une chirurgie de l'épilepsie

Psychologue neuropsychologue stagiaire dans le service de neuropsychologie (Dr. Bernard Croisile) à l'Hôpital Neurologique Pierre Wertheimer, Lyon *(2010-2011)*

Mission : Réalisation d'évaluations neuropsychologiques dans le cadre de pathologies neurodégénératives (Maladie d'Alzheimer, Démence sémantique, ACP, DCB, etc.), Soutien aux aidants, Animation d'atelier de stimulation cognitive

5. Activités d'encadrement

5.1. Doctorant

Maximilien Métaireau (début 2022 ; taux encadrement 70%)
Chloé Bryche (début 2022 ; taux encadrement 50%)

5.2. Master 2 Recherche Neuropsychologie et psychologie cognitive

Axel Ricaud (2023-2024)
Margaux de Bergen (2021-2022)

5.3. Master 2 Professionnel de Neuropsychologie

13 étudiants (2009-2023) répartis entre l'université de Lyon 2 (*n* = 2, 2009-2011) et l'université de Franche-Comté (*n* = 11, 2020-2023), dans le cadre de leur mémoire professionnel.

5.4. Master 1 Psychologie

15 étudiants (2008-2023) répartis entre l'université Lyon 2 (*n* = 10, 2008-2017) et l'université de Franche-Comté (*n* = 5, 2020-2023), dans le cadre de leur Travail d'Étude et de Recherche (TER).

5.5. Master 1 Neurosciences

2 étudiants (2017-2019) à l'université d'Aix-Marseille sur le thème *« Exploration visuelle d'actions sociales dans une perspective développementale ».*

5.6. Master d'Orthophonie

2 étudiants (2012-2014) à l'Institut des Sciences et Techniques de Réadaptation (ISTR) de Lyon dans le cadre de leur mémoire de fin d'étude *« Détection des troubles sémantiques chez le patient MCI de haut niveau socio-culturel : validation d'une batterie et étude de groupe »*

6. Activités scientifiques

6.1. Synthese de la production scientifique

	International		National		Total
	1er/dernier	2nd auteur	1er/dernier	2nd auteur	
Articles publiés	18	13	3	0	34*
Chapitre d'ouvrage	1	0	1	0	2
Présentation orale	8	0	5	0	13
Posters	7	0	1	0	8

* Ce nombre s'élève à 54 lorsque l'on considère l'ensemble des publications (voir dans le document joint)

6.2. Programmes de recherche

- **Partenaire** d'un projet ANR « *On the neurocognitive origins of cumulative technological culture* » (TECHNITION)
  Coordinateur : F. OSIURAK
  Début du projet : Mars 2022
  Durée du projet 48 mois
  Financement de l'ANR : 490 551€
  Financement alloué au laboratoire LINC (UR481) : 127 680€
- **Coordinateur** d'un projet Région Bourgogne Franche-Comté (dispositif : AMORCAGE) « Étude des bases neurocognitives de la représentation d'actions chez le sujet sain et chez le patient cérébrolésé » (REPRESACT)
  Partenaires : Service de neurologie vasculaire (Pr. T. MOULIN), CHU Besançon & MSHE Ledoux
  Début du projet : Septembre 2021
  Durée du projet 36 mois
  Financement alloué : 13 947€
- **Coordinateur** d'un projet Université de Franche-Comté (dispositif : CHRYSALIDE Nouveaux arrivants)
  Début du projet : Janvier 2021
  Durée du projet 12 mois
  Financement alloué : 4 991€
- **Coordinateur** d'un projet Université de Franche-Comté (dispositif : CHRYSALIDE Nouveaux arrivants)

Début du projet : Janvier 2020
Durée du projet 12 mois
Financement alloué : 4 987€

- **Membre** d'un projet ANR « Développement du couplage perception sociale et contrôle de l'action dans le cerveau adolescent » (ADOBRAIN)
  Coordinateur : M.-H. GROSBRAS
  Début du projet : Juin 2015
  Durée du projet 48 mois
  Financement de l'ANR : 549 995€

- **Membre** d'un projet ANR (MALZ 006 03) « Démence et utilisation d'outils (DUO)
  Coordinateur : D. LE GALL
  Début du projet : Décembre 2011
  Durée du projet 48 mois
  Financement de l'ANR : 293 900€

6.3. Expertise scientifique

Expertise pour différentes revues :
- Journal of Alzheimer's disease (*n* = 1),
- Journal of Geriatric Psychiatry and Neurology (*n* = 1),
- Frontiers in Psychology (*n* = 2),
- Frontiers in Neuroscience (*n* = 1)
- Journal of Neuropsychology (*n* = 1),
- Cortex (*n* = 3),
- Biological Psychology (*n* = 1),
- Brain and Cognition (*n* = 1),
- Topics in Cognitive Science (*n* = 1),
- International Journal of Geriatric Psychiatry (*n* = 1),
- Neuropsychologia (*n* = 2),
- NeuroImage (*n* = 1),
- Cerebral Cortex (*n* = 1),
- Brain Structure and Function (*n* = 1)

6.4. Participation a des comites de selection de MCF

2020	Université Paris Nanterre, Dysco	MCF « Neuropsychologie »
2021	Université Rouen Normandie, CRFDP	MCF « Neuropsychologie, Neurosciences cognitives »
2022	Université Rouen Normandie, CRFDP	MCF « Psychologie cognitive, Neuropsychologie, Neurosciences cognitives »
2024	Université de Bourgogne, LEAD	MCF « Psychologie cognitive et ergonomie cognitive »

6.5. Participation a des jurys de these

2023	Rapporteur	Fabrizzia Gallo (SCALab; Université de Lille)

Study of the relationship between gestures and socio-emotional processes using fMRI and physiological measurements

6.6. Participation a des societe savantes

Depuis 2021 Membre de l'alliance FondaMental

Depuis 2021 Membre senior de la Société de Neuropsychologie de Langue Française (SNLF)

6.7. Organisation de colloques/seminaires

2023 Organisation de la journée annuelle de neuropsychologie de Franche-Comté sur les troubles du neuro-développement, 24 novembre

Organisation de séminaires dans le thème « Individu dans son milieu : puissances et vulnérabilités » porté par la MSHE de Besançon

Amandine Rey : Sommeil et fonctionnement cognitif chez l'enfant et l'adolescent : De l'étude des marqueurs électrophysiologiques de la consolidation mnésique à l'éducation au sommeil

2016 Membre du comité scientifique pour le colloque des Journées Internationales de Neuropsychologie : « Apraxie et action » à Angers

2013 Membre du comité d'organisation pour le congrès de la Société Française de Psychologie (SFP) à Lyon

2008 Membre du comité d'organisation pour le colloque de l'Association pour la Recherche cognitive (ARCo) à Lyon

6.8. Conferences *« invite »*

- *« The neural bases of action semantics system : new insights from fMRI and neuropsychological data",* Réunion Mensuelle de Neuroimagerie (RMN), Aix-Marseille Université, 14 septembre 2023, Marseille
- *« Récupération des troubles cognitivo-moteurs post-AVC : quelle perspective ? »,* Journées de Neurologie Psychiatrie et Neurosciences, 29-30 juin 2023, Paris.
- *"Brain activity during transitive and social action observation in adults and adolescent"*, Annual scientific fMRI day, Timone Institute of Neurosciences, September 2019, Marseille.
- *« Bases neurocognitives de l'utilisation d'outils : apport du fonctionnement normal et pathologique »* au laboratoire TIMC-IMAG (CNRS) à l'université de Grenoble-Alpes (UGA), laboratoire Vision Action Cognition (VAC) à l'université Paris V, laboratoire de Psychologie Cognitive (LPC) à l'université d'Aix-Marseille (AMU), mars-avril 2017

6.9. Activites de vulgarisation et de diffusion scientifique

- *« Les Neuromythes » et « Les biais cognitifs »*, Conférences décalées à l'Institut Régional de l'Administration (IRA) de Lyon, Novembre 2023, Avril et Mai 2024
- Participation au dispositif *DECLICS* : Dialogues entre chercheurs et lycéens pour les intéresser à la construction des savoirs, 19 décembre 2023 au Lycée Victor Hugo de Besançon

7. Responsabilités pédagogiques et administratives

7.1. Synthese des enseignements realises

Discipline	Niveau	Description
Neuropsychologie et neurosciences cognitives (767h)	L1	Initiation à la neuropsychologie dans une perspective historique, Neuromythes
	L2	Méthodes en neuropsychologie (étude de groupe, étude de cas)
	L3	Introduction à la neuropsychologie cognitive (étude de cas, principe des dissociations) et à la neuropsychologie expérimentale Présentation des méthodes de neuroimagerie (IRMf, EEG, etc.) et leur application dans le domaine de la cognition
	M1	Outils pour psychologues (conduite du bilan neuropsychologique, anamnèse, rédaction, etc.), Bases anatomo-fonctionnelles
	M2	Epilepsie, Troubles cognitivo-moteurs (apraxie)
Supervision clinique (118h)	M1	Supervision d'un groupe d'étudiants dans le cadre de l'analyse de la pratique clinique
Psychologie cognitive et expérimentale (589h)	L1	Introduction à la méthode expérimentale
	L2	Introduction aux grandes fonctions cognitives (mémoire, langage, attention, etc.)
	L3	Modèles de la cognition
Statistiques (91h)	L1	Statistiques descriptives, loi normale, corrélations
	L2	Statistiques inférentielles (paramétriques et non paramétriques)
	L3	Analyse de variance et de covariance
	M1	Statistiques avancées et programmation sur le logiciel R
Outils de conception d'expérience (292h)	L1	Introduction à la programmation avec Python
	L2	Programmation avancée en Python, découverte de la bibliothèque Psychopy pour programmer des expériences de psychologie expérimentale sur ordinateur
	M1	Programmation avancée avec Psychopy
TICE (21h)	L1	Initiation à la bureautique à la découverte de l'environnement informatique et multimédia

Total = 1878h

7.2. Responsabilites d'Unites d'Enseignement (UE) au sein du departement de psychologie de l'UFC

U.E. Neuropsychologie

Date de prise de responsabilité : Septembre 2019

Niveau et cursus : Licence 3 Psychologie

Thématique : Dans cet enseignement, les grands concepts et courants de la neuropsychologie sont présentés : les dissociations

(simples et doubles), les études de cas vs les études de groupe, et des notions de statistiques du cas unique.
Nous abordons également les fondements de la neuropsychologie cognitive (modularité, transparence, universalité, fractionnement) et la méthodologie expérimentale (VI, VD, variable contrôle, plan expérimentaux, effets principaux et interactions) appliquée à la neuropsychologie et à l'étude des patients.

U.E. Outils pour psychologues

Date de prise de responsabilité :	Septembre 2019
Niveau et cursus :	Master 1 Psychologie cognitive et neuropsychologie
Thématique :	Cet enseignement a pour but de donner aux étudiants les différents outils nécessaires à la bonne conduite du bilan neuropsychologique : conduite de l'anamnèse, l'examen neuropsychologique de base rédaction du dompte rendu, et la méthode statistique pour l'évaluation de cas.

U.E. Perception et motricité

Date de prise de responsabilité :	Septembre 2019
Niveau et cursus :	Master 2 Psychologie cognitive et neuropsychologie
Thématique :	Cet enseignement s'intéresse principalement à la perception visuelle et la gestualité intentionnelle. Il est présenté les grands troubles qui touchent ces fonctions : l'agnosie et l'apraxie. Les étudiants découvrent les outils permettant d'évaluer ces fonctions tout en se référant aux modèles cognitifs existants. Les troubles intéressant le développement (e.g., dyspraxie) sont également abordés.

7.3. Responsabilites au sein de l'Universite de Bourgogne Franche-Comte (UBFC) et de l'Universite de Franche-Comte (UFC)

Président du Comité d'Éthique pour le Recherche au sein de l'Université Bourgogne Franche-Comté (CER UBFC)	Mai 2023 – présent
Vice-président du Comité d'Éthique pour le Recherche au sein de l'Université Bourgogne Franche-Comté (CER UBFC)	Septembre 2022 – Mai 2023
Membre du comité de direction de la MSHE Ledoux de Besançon et co-responsable du thème *« L'individu dans son milieu : puissances et vulnérabilités »*	Septembre 2022 – présent
Membre du Comité d'Éthique pour le Recherche au sein de l'Université Bourgogne Franche-Comté (CER UBFC)	Depuis 2021
Responsable du Master de Psychologie Cognitive et Neuropsychologie (PCN)	Depuis 2021
Membre du conseil de département de Psychologie de l'UFC	Depuis 2019

Membre de la commission Parcoursup au sein du département de psychologie à l'UFC	2021 - 2023

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