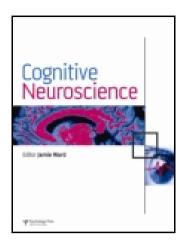
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Voluntary switching between identities in dissociative identity disorder: A functional MRI case study

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Patients who suffer from dissociative identity disorder present unique scientific and clinical challenges for psychology and psychiatry. We have been fortunate in working with a patient who—while undergoing functional MRI—can switch rapidly and voluntarily between her main personality (a middle-aged, high-functioning woman) and an alternate personality (a 4–6-year-old girl). A unique task was designed to isolate the processes occurring during the switches between these personalities. Data are from two imaging sessions, conducted months apart, each showing the same activated areas during switches between these personalities. The activated areas include the following: the primary sensory and motor cortex, likely associated with characteristic facial movements made during switching; the nucleus accumbens bilaterally, possibly associated with aspects of reward connected with switching; and prefrontal sites, presumably associated with the executive control involved in the switching of personalities.

Keywords: Dissociative identity disorder; Functional MRI; Switching personalities.

Patients who suffer from dissociative identity disorder (DID)—formerly called multiple personality disorder (MPD)—present unique scientific and clinical challenges (e.g., Chu, 1991). In the context of functional brain imaging, they also present unique opportunities, especially when the process of switching personalities can be predictably triggered. In that situation, it is possible to repeatedly image the subject's brain during distinct personality states, as well as during the transition process.

One of us (P.C.W.) has been working for more than 20 years with a DID patient, who will be referred to as "RV" (for "research volunteer"). Over the course of treatment, RV developed voluntary control over what had previously been involuntary switching between her main personality and two alternate personalities (conventionally called "alters"). In recent years, RV became interested in contributing to the scientific and experimental investigation of the processes associated with her DID, and indicated to P.C.W. her desire to be a subject for appropriately targeted experiments. Thus, we were fortunate to have a cooperative volunteer who can voluntarily switch between her main personality and two alternate personalities. Would she be able to do this in the noisy and distracting environment of functional MRI (fMRI)? Our preliminary studies demonstrated that she could.

RV's ability to switch in the fMRI environment makes a variety of studies possible. We decided to

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begin by investigating several aspects of the switching process itself. We have been able to confirm that RV's voluntarily controlled switching in her therapy sessions could be repeated during fMRI studies, and that this could be done with sufficiently limited head motion. We developed protocols to isolate the switching process precisely in time, and were thus able to identify brain regions selectively activated during switching.

METHODS

Subject

RV is a middle-aged woman suffering from DID (based on meeting all four of the diagnostic criteria of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*—DSM-IV). Her main personality will be called "A" (for adult). RV has two alternate personalities: a child of approximately 4–6 years of age ("C" for child) and a younger, pre-verbal personality ("B" for baby). Appropriate Institutional Review Board (IRB) approval for the procedures was obtained through McLean Hospital, with the condition that RV's therapist (P.C.W.) be present and act in a protective/therapeutic (rather than experimental) capacity during the imaging sessions.

Head movement

None of RV's personalities enjoyed the fMRI environment; and "B", the youngest, found various aspects of it particularly unpleasant. Nevertheless, RV was able to switch easily between all three personalities. Head movement data collected during preliminary studies indicated that the adult ("A") and child ("C") personalities could maintain a stable head position fairly well, but the same was not true for the baby ("B"). Therefore, we decided to use only A_to_C and C_to_A transitions in the present study. In all seven runs used for the final analysis, translation excursions in x, y, and z did not exceed 1 mm, rotational excursions did not exceed 0.015 radians, and there was no obvious stimulus-correlated movement. Rare time points with combined movement greater then ½ voxel were modeled out in the analysis.

Temporal precision of switching

Switching times between all three states were measured in preliminary fMRI studies. After a cue to switch was presented to her, RV pushed a button to indicate when she had switched. Average switch

time (and standard deviation) was 4 (± 1.4) s. (This switching speed is more rapid than was reported for another subject in the imaging literature (Tsai, 1999), whose average switching time was approximately 30 s; however, it is consistent with reports (Putnam, 1988) of more extensive reviews of timing of switching in DID.) While RV can switch quickly, this should not be interpreted to mean that she can switch *every* 4 s. Protocols in some preliminary studies required RV to switch every 20 s, soon causing fatigue and less control of switching. Therefore, in all runs of the present study, gaps of approximately 30 s separated switching cues.

Task paradigm

The goal was to make RV start to switch at a precise time, while isolating the switching process from general anticipatory or startle responses. Preliminary studies taught us that RV could switch in response to a variety of cues. Starting with audio-visual presentations of her therapist asking her to switch, we moved to increasingly abstract cues, ending with those described in the final paradigm. A background image was chosen based on its soothing qualities (as reported by all three personalities).

After viewing the background image (Figure 1a) for a variable amount of time (lasting at least 10 s), a sequence of preparatory images appeared, culminating in one of the four icons (Figure 1b) surrounded by a red rectangle, to indicate which action the subject should perform. Listed in order going clockwise from the upper left of Figure 1b, the choices were "NOACTION" (i.e., continued passive viewing of the background image); "C_to_A" (change from child to adult personality); "A_to_C" (change from adult to child personality); and "BUTTON" (push a button on the response box).

The timing for the preparatory and action cue sequence is shown in Figure 2. The four icons appear for 3 s; followed by an overlay of a bell shape in the middle (1 s on, 1 s off, 1 s on, 1 s off), and terminated by the action cue: a red box around one of the four pictures, for 3 s. The point of this sequence was to create a situation in which RV knows that a task is coming, and knows precisely when it is coming, but does not know which task will be required until the final cue—i.e., the red outline—appears.

In each run, there are 12 presentations of the red outline, with at least two instances of each switch type per run. The sequence is designed so that whenever the cue indicates that a personality switch should occur, RV is in the appropriate personality to make that switch.



Figure 1. Panel a shows the background image used throughout the experiment. (It is the image called "Aurora," a standard Apple Macintosh image that RV experienced as soothing.) Panel b shows the cueing image, with four different possible tasks indicated iconically. Starting in the upper left of panel b and going clockwise are the cues for push a button, switch from child to adult, switch from adult to child, and continue passive viewing of the background image.

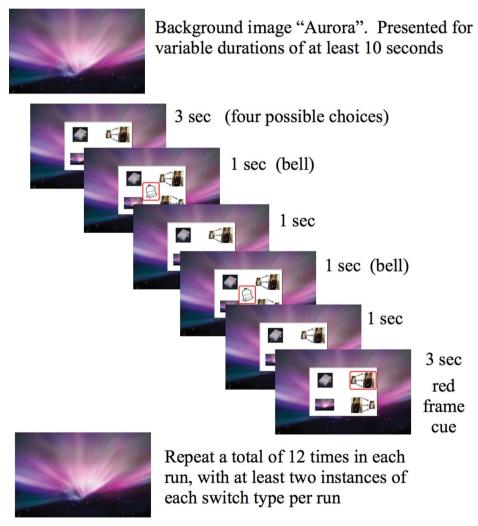


Figure 2. This is the timing sequence for presenting RV with a cue; e.g., as illustrated here, to switch from child to adult.

Image acquisition

All images were acquired on a 3 Tesla Siemens Trio MR scanner (Siemens Medical Systems, Malvern, PA, USA), using an eight-channel, phased-array,

receive-only head coil. After positioning and setup, RV underwent a (0:30) three-plane localizer scan for image prescription. A high-resolution anatomic image set was then acquired for later anatomic parcellation and coregistration of the functional data: T1-weighted

MPRAGE3D, resolution (RL, AP, SI) of $1.33 \times 1 \times 1$ mm (TI = 1100, TR/TE = 2100/2.74, $\alpha = 12^{\circ}$, FOV = $170 \times 256 \times 256$ mm, $128 \times 256 \times 256$ pixels, total imaging time 8:59. There followed a sequence of relatively brief (2–8 min during preliminary studies, 5:12 in the final protocol) functional runs using conventional BOLD-contrast T2*-weighted scans (single-shot gradient echo EPI, TR/TE = 3000/30 ms, 64×64 matrix, 220×220 mm FOV, 30 interleaved transverse slices 3.4 mm thick with no gap, 1 average, 104 repetitions).

Analysis

Preprocessing, statistical analysis, and visualization of the results were performed with routines from FSL (Oxford University's FMRIB Software Library; Smith et al., 2004; Woolrich et al., 2009) and FreeSurfer (Fischl et al., 2002).

Preprocessing

The following pre-statistics processing was applied: motion correction using MCFLIRT (Jenkinson, Bannister, Brad, & Smith, 2002); slice-timing correction using Fourier-space time-series phase-shifting; removal of non-brain portions of the images using BET (Smith, 2002); high-pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 25.0 s). To reduce motion-related variability, a program (based on Lemieux, Salek-Haddadi, Lund, Laufs, & Carmichael, 2007) was used to generate single point nuisance regressors to model out time points exhibiting motion >1.7 mm (½ voxel size).

Statistical analysis

Five regressors and their first derivatives were used to model the events during the functional runs. The BELL regressor represented the occurrences of the bell image cue, with each occurrence modeled as a single TR event convolved with a double gamma hemodynamic response function. Similarly, the other four regressors corresponded to the times for each of the rectangle cues A_to_C, C_to_A, BUTTON, and NOACTION. These regressors were designed to capture brain activity during the period of time immediately following the switch cue. Note that the stimuli prior to the presentation of the switch cue were the same for at least 18 s independent of the subsequent action condition. Six

confound regressors—corresponding to the motion parameters from MCFLIRT—were also used, plus any additional single point motion regressors. The primary contrast of interest was "A_to_C or C to A" versus NOACTION.

Visualization

Seven functional runs collected on different days (four on one day, three on the other) were used to generate the final activation maps, based on the primary contrast of interest. Data analyzed from each day individually showed similar results, so only the combined data are reported here. Cortical and subcortical activations were anatomically assigned by aligning the functional data with the high-resolution anatomic data sets parcellated in FreeSurfer 4.5.0. The direction of personality switching was also examined (i.e., A to C was also contrasted with C to A), but no consistent activation differences were observed in this contrast. Perhaps with more data on this subject, or with more subjects, some order-of-switching effects will be detectable, as has been suggested in other reviews of DID (Putnam. 1988).

RESULTS

The main contrast ("A_to_C + C_to_A" versus NOACTION) yielded bilateral activations in several cortical sites, as shown in Figure 3. The strongest activation is seen in primary sensory motor areas near the face representation and is probably due to characteristic facial gestures made by RV when she switches (Figure 3a). Her facial gestures include partial closing of her eyes, and this is reflected in the negative activations seen at the back of the head during switches (Figure 3b). The cortical activations in prefrontal cortex (Figure 3c) will be discussed in the General Discussion section.

The most striking non-cortical finding was consistent bilateral activation in the nucleus accumbens, as shown in Figure 4. Again, while it is premature to allow draw conclusions based on one subject, this activation is consistent with the idea that DID develops to allow escape from pain and consequently has reinforcing (rewarding) value. This notion is discussed in more detail elsewhere (Wolk, Frederick, & Savoy, 2012).

These results justify the claims at the end of our Introduction. RV could switch in response to simple iconic cues, and these switches were rapid, consistent, and not accompanied by excessive head movements. The task paradigm enabled us to isolate

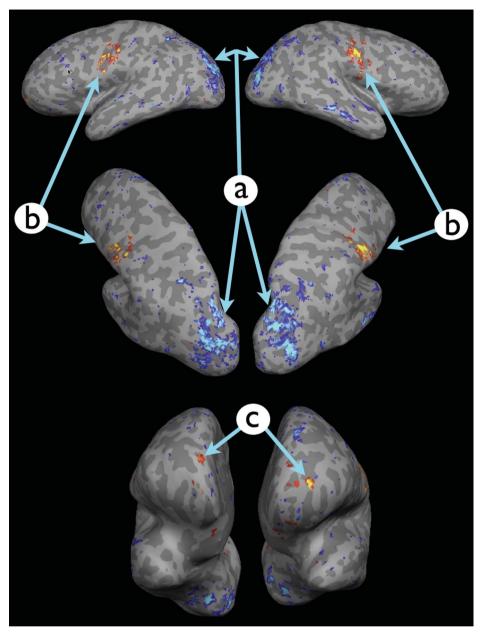


Figure 3. Cortical activations for "A=>C+C=>A" versus NOACTION (i.e., passive viewing of an image). Top: lateral views of inflated cortex for left and right hemispheres. Middle: views from the back of the head. Bottom: views from the front. The activations labeled "a", "b", and "c" are the visual cortex, sensory motor cortex, and frontal lobe areas activated by the task, as elaborated in the Results section. This figure shows the analysis of the combined data from two different days of imaging RV, but each day's data yielded similar pictures independently.

brain activations associated with personality switching, separate from the general cognitive preparation for an action. This enabled us to see the brain regions active during switching for this individual subject. Of course, it is unwise to speculate very much based on single-subject data. With this caveat in mind, we discuss possible interpretations of the three primary activations seen during switching.

GENERAL DISCUSSION

There have been other imaging studies of DID, including group studies using PET (Reinders et al., 2006) and SPECT (Sara, Unalb, & Ozturka, 2007), and a single subject using fMRI (Tsai, 1999). None of these had the luxury of being able to study multiple switches in a relatively short time. While there are obvious



Figure 4. This is a horizontal slice showing various subcortical areas, as created by FreeSurfer software based on our imaging data and the FSL statistical analysis described in the text. Note that the red areas are in the nucleus accumbens, bilaterally. This figure shows the analysis of the combined data from two different days of imaging RV, but each day's data yielded similar pictures.

limitations to studies based on a single subject, the history of neuropsychology, and even fMRI (Savoy, 2006), is replete with examples where single-subject investigations have been particularly revealing.

Some of the cortical activations seen in RV are easy to interpret. For example, both the activations near sensory motor cortex seen during switching, and the deactivation seen in visual cortex are presumably due to her tightening her facial musculature and partially closing her eyes during the switching process. This is actually consistent with behavioral reports from many DID patients studied during switching (Putnam, 1988).

The activations seen bilaterally in the nucleus accumbens are intriguing, and invite speculation (e.g., Wolk, Frederick, & Savoy, 2012). In this context, it is worth reflecting on the different notions of "reward." One form of reward is "escape from pain," based on terminating or avoiding a painful stimulus. (This is a different kind of "reward" from tactile pleasures or the feeling that results from accomplishing a goal.) The nucleus accumbens has been considered the reward nucleus as a result of research studies in rats (Damsma, Pfaus, Wenkstern, Phillips, & Fibiger, 1992; Koob, 1998) as well as investigative studies of human addictions (DiChara et al., 2004). Ikemoto and Panksepp (1999) noted that the nucleus accumbens, while well known for its role in reward mechanisms,

is also implicated in aversive contexts. For our subject (and other DID patients), we assume that "switching personalities" developed in an attempt to protect part of her psychological self from the consequences of physical assault, which would be consistent with the idea of an "escape nucleus." Clearly, the nucleus accumbens activation by itself warrants investigation with additional DID subjects.

The activations in various parts of the frontal cortex are, perhaps, the most intriguing, but they are also the most difficult to interpret precisely. The prefrontal activations are nominally in Brodmann's areas (BA) 9, 10, and 11. Keeping in mind that this is data from only one subject and awaits replication, a discussion of these areas—with their obvious possible connections to DID and switching—follows.

BA 9, also referred to as the dorsolateral prefrontal cortex (PFC), plays a critical role in dynamic adjustment of executive control, which allows for adaptive modulation of behavior in response to competition or conflict between behavioral options (Mansouri, Tanaka, & Buckley, 2009).

BA 10 overlaps to a great extent with the rostral PFC. One function of the rostral PFC is to enable multitasking, which is the ability to maintain multiple unrelated goals in mind while completing a given task (Burgess, 2000). Increased activation of the lateral

region of BA 10 is seen in multitasking that requires switching tasks voluntarily after a delay (Gilbert et al., 2006) and during tasks involving working memory (Gilbert et al., 2006). Additionally, the rostral PFC is involved in facilitating functioning during 'ill-structured' situations, in which the most preferable way to behave is not clearly defined: this requires individuals to contribute their own structural framework to the management of the situation (Goel & Grafman, 2000).

The lateral rostral PFC is implicated in "episodic retrieval" tasks that involve searching for and accessing information about past personal experiences from memory (Rugg, Fletcher, Chua, & Dolan, 1999; Simons et al., 2005). There is evidence that the rostral PFC is involved in recalling the feelings and thoughts triggered by events experienced in the past (Ramnani & Owen, 2004). Growing evidence suggests that the rostral PFC may be involved in "self-referential evaluation" as well as switching attention between external, perceptually derived information, and internal, self-generated stimuli (Dumontheil, Burgess, & Blakemore, 2008). The medial region of BA 10 has been linked to self-reflection (Passingham, Bengtsson, & Lau, 2010), and medial rostral PFC activation occurs during mentalization tasks that require individuals to contemplate their own mental states and the mental states of others (Amodio & Frith, 2006; Castelli, Happe, Frith, & Frith, 2000; Gilbert et al., 2006; Ochsner et al., 2004; Zysset, Huber, Samson, Ferstl, & von Cramon, 2003; Zysset, Muller, Lohmann, & von Cramon, 2001).

BA 11, known as the orbitofrontal cortex (OFC), is involved in integrating existing knowledge to generate actionable predictions and estimates of specific outcomes (Schoenbaum & Esber, 2010). This function likely underlies the region's apparent involvement in signaling related to complex phenomena such as regret (Camille et al., 2004), ambiguity/risk (Kepecs, Uchida, Zariwala, & Mainen, 2008; van Duuren et al., 2009; Venkatraman, Payne, Bettman, Luce, & Huettel 2009), willingness to pay (Plassmann, O'Doherty, & Rangel, 2007), and flexibility to switch behavior in the face of unexpected outcomes (Rushworth, Noonan, Boorman, Walton, & Behrens, 2011). The medial OFC, lateral OFC, ventromedial PFC, and anterior lateral PFC are components of a distributed neural circuit that underlies reward-guided learning and decision-making (Rushworth et al., 2011).

Given the collection of things that must be going on when a DID subject switches between personalities, it seems implausible that these prefrontal areas would not play an important role. However, it is very difficult to be more precise about connecting the activations seen in this particular subject with the general description of prefrontal tasks.

SUMMARY AND FUTURE WORK

This is a functional MRI case study of a person ("RV") with DID. Over the course of several imaging sessions, she demonstrated the ability to switch voluntarily and on cue, between her main personality and two alternate personalities. Our studies to date have focused on the switching process itself. These studies have revealed consistent cortical and subcortical activations during switching.

RV continues to be a cooperative and invested subject. We anticipate further work with her, including the examination of various network structures, including the default state network, while she is in steady-state engagement of her alternate personalities. And, if suitable psychological safeguards permit, we plan to examine the blockage of memories—both for neutral and traumatic events—between the various personalities. Of course, it will also be important to recruit additional DID subjects for these investigations, as the dangers of over-interpreting data for a single subject are well known.

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