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Exploring the neural correlates of self-related names in healthy subjects

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Abstract

Objectives: This study aimed to clarify the neural correlates and underlying mechanisms of the subject's own name (SON) and the unique name derived from the SON (SDN).

Methods: A name that was most familiar to the subject (SFN) was added as a self-related reference. We used 4 auditory stimuli—pure tone (1000 Hz), SON, SDN, and SFN—to evaluate the corresponding activated brain areas in 19 healthy subjects by using functional magnetic resonance imaging.

Results: Our results demonstrated that pure tone activated the fewest brain regions. Although SFN was a very strong self-related stimulus, it failed to activate many midline structures. The brain regions activated by SON and SDN were very similar. SFN as a self-related stimulus was less self-related compared with SDN. What's more, the additionally activated fusiform gyrus and parahippocampal gyrus of SDN might revealed its processing path.

Conclusions: SDN, which has created by us, is a new and self-related stimulus similar to SON. They might provide a useful reference for consciousness assessment with SON and SDN.

Abbreviations: DoC patients = disorders of consciousness patients, fMRI = functional magnetic resonance imaging, SDN = the unique name derived from the subject's own name, SFN = a name that was most familiar to the subject, SON = subject's own name.

Keywords: a name derived from the subject's own name, auditory stimuli, functional magnetic resonance imaging, neuroimaging, subject's own name

1. Introduction

Although we tried to distinguish disorders of consciousness patients (DoC patients) with the subject's own name (SON) and the unique name derived from the SON (SDN), the neural correlates and underlying mechanisms were unclear.

Monti et al also verified that not all unconscious patients were suitable for the active tasks.[1] The automatic lexical processing with passive stimuli was observed not only in minimally conscious states, but also in vegetative states.[2] SON was a special word. Di Haibo et al verified the effectiveness of SON in 66 DoC patients. Vegetative state traumatic patients with higher levels of activation patterns recovered well, whereas non-traumatic patients with lower levels of activation patterns recovered poorly.[3,4] However, another study indicated that the sensitivity and specificity of SON was low in minimally conscious patients.[5] Based on the above context, we innovatively created SDN which were composed of the same Chinese characters with SON. Distinguishing SDN from SON required a longer latency.[6] Accordingly, patients who could distinguish SDN from SON would wake up soon after.[7] To know more about their neural correlates and underlying mechanisms after getting this inspiring phenomenon, we did the functional magnetic resonance imaging (fMRI) study.

Generally, patients who can fulfill a difficult task may represent more residual awareness and faster recovery speed. In our auditory task, we used a powerful stimulus—SON. SON had the highest self-correlation and was easier to attract the subject's attention no matter with conscious or unconscious perception.[8] It was reported that hearing one's own name could enhance the vigilant attention and improve the performance during a monotonous task.[9,10] It has been replicated in many experiments whether the subjects are normal adults or DoC patients.[11,12] Next, to facilitate a difficult task, we used a unique stimulus—SDN. Coch et al observed that both a real word ("dark") and a pronounceable pseudoword ("darl") exhibited a similar quality.[13] Moreover, in Chinese, we can obtain a derived pseudoword by changing the constituent order of a real word. For example, if "Bei jing" was a real word, "Jing bei" was a derived pseudoword. Accordingly, we created SDN such as "Ran Li", which was generated by reversing the constituent order of the SON such as "Li Ran". Then, the similarity certainly reduced the differences between SON and SDN. It must be difficult to discriminate synonyms. It was

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inferred that the brain activations of SON and SDN were highly overlapping.

In order to add a reference name, a name that was most familiar to the subject (SFN) was introduced. SFN was the name of their most familiar person. The person could be their partner, their best friend, their father, their mother, their best friend and so on. Kempny et al considered SON and other familiar names to be the most similar.[14] Another study even found that amplitudes of P200, N250, and P300 did not differ between visually presented one's own and close other's name.[15] So SFN and SON were personally relevant and familiar. SFN was a very strong self-related stimulus. By comparing the brain activations of SON-SDN and SON-SFN, we could infer the relationship of SON and SDN.

The aim of this study was to preliminarily clarify the neural correlates and underlying mechanisms of SON and SDN with healthy subjects. We assumed that if SDN had a stronger self-correlation, then the self-related brain activity differences of SON-SDN would be smaller than that of SON-SFN.

2. Methods

2.1. Participants

Healthy volunteers (10 males, 9 females) aged 21 to 58 years participated in this study. The median (IQR) was 27 (27, 40.5). All participants had normal hearing and were right-handed. Written informed consent was obtained. The participants were excluded if they had a history of neurological or psychiatric disorders, claustrophobia, or metal implants; had taken sedatives 24 hours before the fMRI; or had a history of smoking and alcohol consumption and had not stopped at least 1 month before the functional magnetic resonance imaging.

All procedures were performed in compliance with relevant laws and institutional guidelines. The ethics committee of our hospital approved the study. Informed consent was obtained for experimentation with every participant. The privacy rights of human subjects must always be observed.

2.2. Stimuli preparation

Our stimuli consisted of a 1000 Hz tone lasting for 100 ms, SON, SDN, and SFN. The tone was generated by Adobe Audition software (version 3.0, Adobe Systems Incorporated, San Jose, CA). All participants' names were composed of 2 characters. SON/SDN was called by their most familiar person such as their partner or best friend. SFN was the name of their most familiar person and called by the most familiar person himself/herself. The average duration of SON, SDN, and SFN was 532 ms ± 70 ms, 548 ms ± 50 ms, and 568 ms ± 35 ms, respectively, and exhibited no statistical differences. The stimulus intensity was 80 dB.

2.3. The fMRI paradigm

Using a block-designed paradigm with a Latin square fashion, 4 stimuli were presented as follows: tone - SON - SDN - SFN - SON - SDN - SFN - tone. Each participant underwent fMRI twice while receiving each active stimulus. There were 8 active blocks and 8 baseline blocks in total. Each active block lasted 24 seconds during which the stimulus was presented 24 times. Each baseline block lasted 20 seconds with only the attenuated machine noise.

2.4. The fMRI data acquisition

The functional and structural images were acquired with a 3 Tesla Siemens MRI system which had standard 8-channel head coils. The metal implants in vivo and metal carriers were excluded before going into the examination room. Participants lied in the scanner with MRI-compatible headphones to decrease the noise. Cushions were placed between the head and the scanner to minimize head movements. All participants received the auditory stimuli passively and consciously with eyes closed throughout the scan.

(1) fMRI scanning in task state: repetition time = 2000 ms, echo time = 30 ms, field of view = 200 mm, flip angle = 90°, slice thickness = 4 mm, slices (n = 33), voxel size = 3.1 × 3.1 × 4.0 mm, base resolution = 64 × 64, and scans (n = 181). The entire session lasted for 362 seconds (6 minutes and 2 seconds).
(2) T1-weighted structural scanning: repetition time = 2530 ms, echo time = 3.39 ms, field of view = 256 mm, flip angle = 7°, slice thickness = 1.33 mm, slices (n = 33), voxel size = 1.3 × 1.0 × 1.3 mm, base resolution = 256 × 256. The entire session lasted for 487 seconds (8 minutes and 7 seconds).

2.5. The fMRI data analysis

Data preprocessing was performed with Analysis of Functional Neuro Images software. A 3-dimensional image was reconstructed on the basis of each slice alignment and whole brain alignment to correct for head motion. The image was smoothed at 6 mm full width at half maximum. To correct the heat noise of the machine, we considered the de-linear drift. Thereafter, we identified stimuli that induced blood oxygen level-dependent signal changes, and we normalized the raw data.

Statistical analysis was performed using Analysis of Functional Neuro Images software. With a general linear model, the regression coefficient of each voxel (β value) was acquired. The β value was then superimposed on the 3-dimensional whole brain structural image. The random effect model was used in the group analysis. First, we obtained the activation maps of tone, SON, SDN, and SFN. Second, the semantic activation regions were obtained by subtracting the tone activation result from SON, SDN, and SFN activation results. Third, to verify the familiarity of SDN and the similarity of SON - SDN, we subtracted SDN and SFN from SON. AlphaSim was used in the multiple comparison correction. Each voxel in each cluster had a significant threshold of $P < .01$ and $t > 2.20$, cluster volume $> 864\ mm^3$ ($P < .05$ after correction).

3. Results

3.1. Tone-Induced activation

The tone task evoked significant activations only in the bilateral superior temporal gyrus (BA41, 22) (Fig. 1, Table 1). There was no activation over the frontal lobe or parietal lobe. No activation was found in the cerebellum.

3.2. SON/SDN/SFN-induced activation

In the SON task, we found activations as follows:

(1) in the bilateral superior temporal gyrus (BA22);

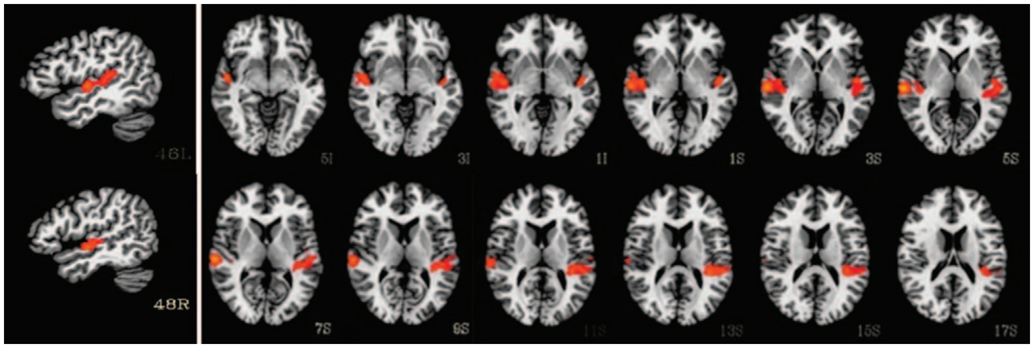

Figure 1. Group analysis of tone-induced brain activation. The main anatomical localizations were bilateral superior temporal gyrus (Voxel level threshold was set at P<.01 and t>2.20, cluster level threshold was set at P<.05 corrected).

Table 1

Significant clusters and their peak coordinates for tone and subject's various names.

		Anatomic location		BA	Volume (mm^3)	Peak t-score	Peak coordinates (MNI) x	y	z
TONE	1	Superior temporal gyrus	L	41	260	5.278	−34.5	−34.5	11.5
	2	Superior temporal gyrus	R	22	223	7.142	58.5	−22.5	5.5
SON	1	Superior temporal gyrus	L	22	878	8.791	−49.5	−16.5	5.5
	2	Superior temporal gyrus	R	22	726	9.189	49.5	−4.5	−9.5
	3	Cerebellum	L		420	9.545	−31.5	−70.5	−42.5
	4	Cerebellum	R		293	5.464	22.5	−61.5	−51.5
	5	Pallidum	R		155	4.739	22.5	4.5	2.5
	6	Middle frontal gyrus	L	48	124	4.783	−28.5	10.5	20.5
	7	Caudate	L		111	5.181	−22.5	40.5	14.5
	8	Precentral gyrus	R	6	108	4.863	49.5	−1.5	41.5
	9	Angular gyrus	L	39	89	5.715	−43.5	−58.5	26.5
	10	Inferior frontal gyrus	R	47	41	4.562	34.5	40.5	−3.5
	11	inferior parietal lobule	L	7	41	4.336	−31.5	−70.5	44.5
	12	Inferior frontal gyrus	L	47	37	4.213	−37.5	40.5	−12.5
SDN	1	Superior temporal gyrus	L	22	945	10	−46.5	−19.5	5.5
	2	Superior temporal gyrus	R	22	794	9.599	49.5	−10.5	−6.5
	3	Angular gyrus	L	39	166	6.651	−43.5	−58.5	29.5
	4	Medial frontal gyrus	L	32	94	5.972	−4.5	31.5	35.5
	5	Middle frontal gyrus	R	47	60	4.779	28.5	49.5	−0.5
	6	Middle frontal gyrus	L	46	55	4.075	−43.5	49.5	−6.5
	7	Inferior frontal gyrus	L	44	50	4.872	−46.5	10.5	38.5
	8	Cerebellum	R		46	4.498	28.5	−64.5	−39.5
	9	Middle frontal gyrus	R	48	43	5.154	43.5	−1.5	17.5
	10	Inferior frontal gyrus	R	45	42	4.083	40.5	34.5	17.5
SFN	1	Superior temporal gyrus	L	48	727	10.297	−46.5	−22.5	8.5
	2	Superior temporal gyrus	R	48	676	7.973	52.5	−13.5	2.5
	3	Inferior frontal gyrus	R	47	291	5.714	49.5	13.5	−14.5
	4	Inferior frontal gyrus	L	44	186	5.12	−49.5	10.5	35.5
	5	Cerebellum	R		129	5.561	16.5	−61.5	−30.5
	6	Supramarginal gyrus	L	40	104	5.087	−55.5	−43.5	32.5
	7	Medial frontal gyrus	L	9	64	5.476	−4.5	37.5	38.5
	8	Cerebellum	L		46	4.165	−19.5	−58.5	−30.5
	9	Inferior frontal gyrus	L	47	39	4.552	−52.5	28.5	−3.5
SON>SDN	1	Cerebellum	L		34	4.457	−31.5	−73.5	−39.5
SON>SFN	1	Periventricular area	L		152	5.126	−25.5	7.5	20.5
	2	Inferior frontal gyrus	R	47	116	5.083	25.5	31.5	−3.5
SDN>SON	1	Fusiform	R	37	74	4.598	40.5	−46.5	−12.5
	2	Parahippocampal gyrus	R	36	38	4.145	25.5	−16.5	−24.5

BA=Brodmann area, L=left, MNI=Montreal Neurological Institute, R=right, SDN=the unique name derived from the subject's own name, SFN=a name that was most familiar to the subject, SON=subject's own name, x, y, z=coordinates in Talairach space.

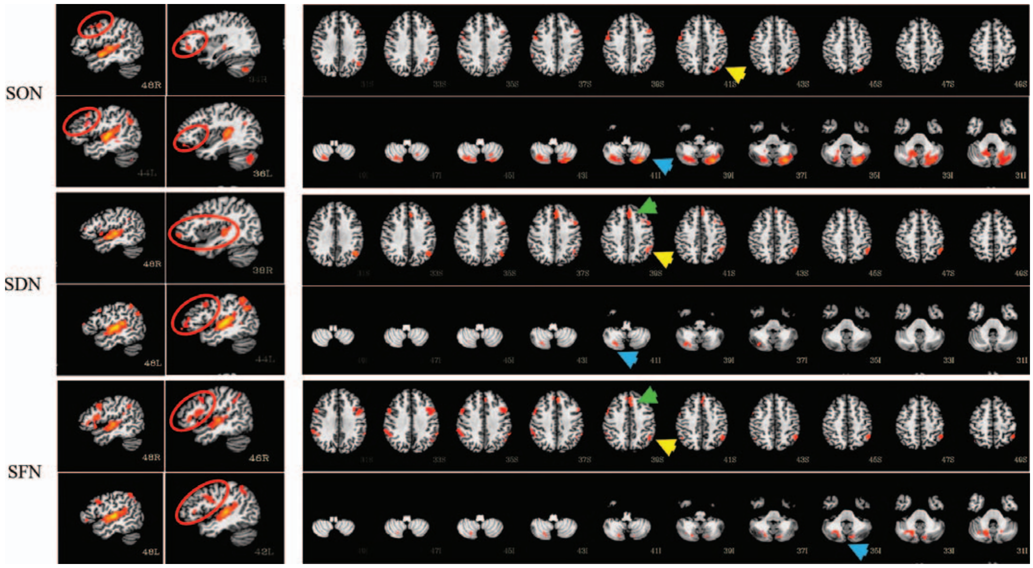

Figure 2. Group analysis of brain areas that were activated by subject's own name (SON), the unique name derived from the SON, and a name that was most familiar to the subject. SON, the unique name derived from the SON, and a name that was most familiar to the subject all activated a large part of temporal gyrus. Red circles indicate the activated frontal gyrus. Yellow arrows indicate the activated parietal gyrus. Blue arrows indicate the activated cerebellum. Green arrows indicate the activated medial frontal gyrus (Voxel level threshold was set at $P<.01$ and $t>2.20$, cluster level threshold was set at $P<.05$ corrected).

(2) in the left middle frontal gyrus (BA48) and inferior frontal gyrus (BA47), in the right precentral gyrus (BA6) and inferior frontal gyrus (BA47);
(3) in the left angular gyrus (BA39) and inferior parietal lobule (BA7);
(4) in the bilateral cerebellum, left caudate nucleus and right pallidum (Fig. 2, Table 1).

In the SDN task, we found activations as follows:

(1) in the bilateral superior temporal gyrus (BA22);
(2) in the left middle frontal gyrus (BA46) and inferior frontal gyrus (BA44), in the right middle frontal gyrus (BA47, BA48) and inferior frontal gyrus (BA45);
(3) in the left angular gyrus (BA39);
(4) in the left medial frontal gyrus (BA32) and right cerebellum (Fig. 2, Table 1).

In the SFN task, we found activations as follows:

(1) in the bilateral superior temporal gyrus (BA22);
(2) in the right inferior frontal gyrus (BA47), in the left inferior frontal gyrus (BA44,47);
(3) in the left supramarginal gyrus (BA40);
(4) in the left medial frontal gyrus (BA9) and bilateral cerebellum (Fig. 2, Table 1).

3.3. The similarity of SON and SDN

To clarify the similarity of SON and SDN, we observed the different brain areas of the SON task minus the SDN task or the SFN task.

(1) SON only activated more left cerebellum than SDN. But the BOLD signals were very strong during the SON task compared with the SFN task. The dominant activations were in the periventricular area (the left caudate, cingulate gyrus, medial frontal gyrus, middle frontal gyrus, inferior frontal gyrus) and the right inferior frontal gyrus (BA47);
(2) Surprisingly, there were significantly greater activations in the SDN task than in the SON task. They were observed in the right fusiform gyrus (BA37) and para-hippocampal gyrus (BA36) (Fig. 3, Table 1).

According to the above results, we postulated that SON and SDN were very similar. The differences between them were mainly observed at the left cerebellum. However, the differences between SON and SFN were many areas near the midline. What's more, our brain had its special processing for SDN through the right fusiform gyrus and para-hippocampal gyrus.

4. Discussion

In our study, according to the neural correlates of the auditory stimuli, we preliminarily clarified that SFN as a self-related stimulus was not more familiar than SDN. The unique SDN was very similar to SON but had its unique processing path. Our findings also seemed to disclose the associated mechanisms behind our previous studies.

4.1. Tone-Induced brain activation

In our study, the 1000 Hz tone activated the bilateral superior temporal gyrus. This result is consistent with those of previous studies.[16] What's more, 500 Hz, 1000 Hz, and 2000 Hz tones activated temporal and frontal regions, with higher intensity tones activating more frontal areas.[17] Therefore, it is reasonable that our moderate intensity 1000 Hz tone activated the temporal region.

4.2. Brain activation induced by SON, SDN, and SFN

SON, SDN, and SFN exhibited similarities.

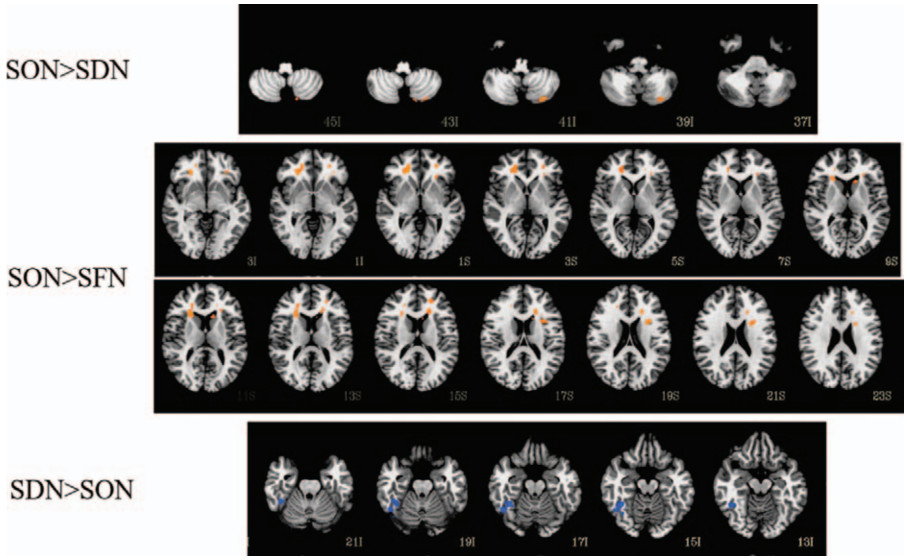

Figure 3. The comparison of brain activation by subject's own name (SON), the unique name derived from the SON, and a name that was most familiar to the subject. SON minus the unique name derived from the SON showed a negative activation (a); SON failed to activate the fusiform gyrus and para-hippocampal gyrus. SON minus a name that was most familiar to the subject showed a positive activation (b); SON activated many midline structures (Voxel level threshold was set at $P < .01$ and $t > 2.20$, cluster level threshold was set at $P < .05$ corrected).

(1) They all activated the basic bilateral superior temporal gyrus. That meant they exhibited the basic characteristics of auditory stimulation.
(2) The parietal processing of SON, SDN, and SFN was focused on the temporo-parietal junction areas. It was found that the left angular gyrus was recruited when hearing the forward narrative compared with the backward narrative.[18] But in our study, both SON and SDN activated the left angular gyrus. According to Wu, the angular gyrus could convert visual stimuli to linguistic stimuli.[19] We presumed that the auditorily presented SDN was automatically converted to visual Chinese characters in a certain area, and turned into auditory stimuli again after getting relevant semantic processing at the angular gyrus. What's more, SON also activated the left inferior parietal lobule and SFN activated the left supramarginal gyrus. Both SON and SFN clearly activated the bilateral cerebellum while SDN activated little cerebellum. The supra- marginal gyrus belongs to the dorsal stream of the language network, participating in the auditory-motor integration of language.[20] We inferred the subjects might subconsciously make a response to SON, or called SFN. As to SDN, they just made a series of special processing silently.
(3) SON, SDN, and SFN activated bilateral middle and inferior frontal gyrus, right precentral gyrus. Usually the left hemisphere is thought to be dominant when it comes to language processing. Wu et al summarized previous findings and found that the left inferior frontal gyrus participates in semantic retrieval, categorization, and other associated conditions. If the stimulus was a Chinese character, the functional area extended to the middle frontal gyrus.[19] About the right hemisphere, there are evidences implicating the role of it in language processing in recent decades. Qiu et al found that normal participants had activations in the right hemisphere region that mirrored Broca area when doing the picture-naming task, although its intensity was weaker than that in the left hemisphere. Broca area covers not only the opercularis inferior frontal gyrus, but also the middle frontal and precentral gyrus.[21] The right middle and inferior frontal gyrus, precentral gyrus was really activated in our study. What's more, the right inferior frontal gyrus was crucial in the processing of emotional information and semantic integration.[22] Thus, we concluded that the SON, SDN, and SFN were emotion related words and needed semantic processing.
(4) SDN and SFN clearly activated the left medial frontal gyrus. SON activated left caudate nucleus and right pallidum. These midline structures were thought to be closely related to self-related stimulus processing, especially the medial frontal gyrus.[18,23] This confirmed our original hypothesis that our newly created SDN were closely related to one's self.

4.3. The similarity of SON and SDN

In order to verify the similarity of SON and SDN, we observed the brain activations of SON minus SDN and SON minus SFN.

Compared with SON, SFN failed to activate many midline structures such as the left caudate, cingulate gyrus, medial frontal gyrus, middle frontal gyrus, inferior frontal gyrus. According to previous studies, there were overlaps between midline structures and self-related information processing.[24–25] Odinak et al found that awareness of oneself depended on midline structures such as the posterior cingulate gyrus, precuneus, medial frontal lobe, and temporoparietal junctions; while awareness of the environment depended on the lateral parts of the frontal and the parietal lobes.[26] SFN activated fewer midline structures compared with SON, indicating that SFN is a less self-related stimulus. What's more, compared with SFN, SON also activated more right inferior frontal gyrus which was associated with emotional information processing. It showed that SFN had less emotional element.

On the contrary, SDN only activated less left cerebellum compared with SON, indicating that SDN is more self-related compared with SFN. Accordingly, differentiating SON and SDN must need a high-order cortical information processing ability. The effect of SON and SDN stimuli was also verified in other studies of our research group. Minimally conscious state patients who could process the names better would have a significant improvement after transcranial direct current stimulation treatment.[27]

4.4. The quality of SDN

Before we did this study, what had puzzled us was whether SDN represented a meaningful name or a meaningless pseudoword. It was believed that the processing duration of meaningless pseudowords was greater than of meaningful words and that this most likely activated the left inferior frontal gyrus, left superior temporal gyrus, and right superior frontal gyrus.[28] According to our results, there was no extra SDN activations at these areas compared with SON, indicating that SDN might represent a meaningful name. Although SDN seemed to be a meaningless pseudoword, it was actually a meaningful name through the special processing of our brain.

SDN additionally activated the right fusiform gyrus and parahippocampal gyrus compared with SON. The fusiform gyrus is usually considered to be related to visual computations such as reading, object recognition, and face perception.[29] Qiu et al also found that when doing visual processing of an object, the occipital lobe and fusiform were engaged.[21] Therefore, the processing of SDN must involve the transformation from auditory to visual form at the fusiform gyrus. Because we had no actual auditory stimulus, the occipital lobe had no activation.

Combined with the above results, we postulated the possible processing path of SDN. Upon hearing SDN, subjects did preliminary auditory processing at bilateral superior temporal gyrus. Then, further processing took place in the adjacent fusiform. Subjects transformed SDN into visual characters and did visual word form processing at the fusiform gyrus. After reversing the Chinese character order, the visual input was transformed to linguistic representation again at the angular gyrus. Further integration was done at the bilateral frontal cortices.

4.5. Limitations

We found SON and SDN had similar brain activations with a relatively small sample size. Moreover, because of the common intracranial metal implants such as the ventriculoperitoneal shunt and the titanium alloy after a cranioplasty, we are unable to obtain the neural correlates of DoC patients with fMRI. In the future, we will try to complete it with positron emission tomography.

5. Conclusions

SDN was first proposed by our research group when SON and SFN was widely used in the assessment and prognosis prediction of DoC patients. SFN as a self-related stimulus was similar to SON; however, SDN was more self-related and more similar to SON. And tone-SON-SDN could be really used as an effective assessment tool in our previous study. In this study, the underlying mechanism was further revealed based on the brain activation areas. The possible processing path of SDN was clarified preliminarily. It laid the foundation for the use of tone-SON-SDN pattern to detect the residual consciousness and predict the prognosis of DoC patients in the future.

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Methodology: Ran Li, Weiqun Song.
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Supervision: Weiqun Song.
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Writing – review & editing: Weiqun Song.

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