國立臺灣大學理學院心理學研究所

博士論文

Graduate Institute of Psychology
College of Science
National Taiwan University

Doctoral Dissertation

健康與自閉症青少年之中文語意知識

Chinese Semantic Knowledge in Typically Developing Youths and Youths with Autism Spectrum Disorder

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中華民國 106 年 3 月

March, 2017

doi:10.6342/NTU201700744

國立台灣大學理學院心理學研究所

論文口試委員會審定書

翁巧涵 先生所提論文 健康與自閉症青少年之中文語意知識處理

經本委員會審議，符合博士學位標準，特此證明。

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中華民國105年 9月 12日

致謝

我畢業了！回顧這求學的這一路過程，心頭湧上許多回憶片段...數不清有多少個不眠的夜晚，天色微亮還是持續的敲著鍵盤、盯著螢幕、翻著論文，可能是為了研究結果非預期而重新檢查數據，可能是查找論文只為印象中看到的一段文字，可能是斟酌如何用字得以準確地描述研究論點...這樣辛苦與煎熬，想過乾脆兩手一攤轉身離開，但最終還是熬過來了，挺進到這一頁。

這一切要感謝所有不吝於提供指導與傳授知識的諸位教授們，此篇論文才得以完成。感謝我的兩位指導教授，周泰立教授與高淑芬教授。周教授悉心指導，不時地討論與耐心提點研究細節，幫助我釐清研究思路，注意邏輯。嚴謹求是，一絲不苟的研究態度，是身為學生、研究者的最佳榜樣。周教授也十分關心學生的日常生活與生活規劃，總會主動詢問近況或提供協助，令人覺得非常溫馨！感謝高教授讓不具臨床或醫療背景的我加入兒童與青少年醫學研究團隊，在研究上總不吝提供指導與給予精準建議，我很榮幸能加入這個優秀的研究團隊，並盡微薄之力提供些許的研究貢獻！感謝口試委員陳修元教授、陳欣進教授與龔俊嘉教授，對於論文的不足之處提出精闢的建議與修改方向，使得此篇論文得以更臻完善。也特別感謝陳修元教授，我的大學老師也是碩士論文指導教授，在當時肯定我的能力，並鼓勵我試著進入更高深的研究殿堂，在進入博士班後仍持續不斷的關心給予支持，謝謝陳教授從大學至今，十多年來亦師亦友的陪伴與照顧！

這段漫長的歲月裡，實驗室的學姊妹、學弟們已交疊更替了幾回，在成立了「阿立博士粉絲團」後，依舊互相協助與鼓勵！特別感謝學姊小 Ra，我們互相陪伴取暖度過無數夜晚，妳是我研究上的小老師，迷惘時為我解惑，妳對於研究的堅持，也讓我學習到做研究該有的態度；感謝學妹劉敏，有著相似背景的我們默契十足，妳的陪伴與傾聽，能讓人適時地紓解壓力，重拾動力。

對家人的感謝總是留到最後。謝謝你們支持我進入學術研究這個領域，讓我能無後顧之憂順利完成學業，取得博士學位。這份得來不易的成果，在此與我的家人們一同分享。

巧涵 謹誌於台北 106.03

doi:10.6342/NTU201700744

摘要

目的：瞭解語意處理的發展變化對於探討語意知識發展具有其重要性。過去關於健康青少年語意發展的研究，皆採用橫斷式取向觀察年齡變化的差異，而且沒有將語意關聯與類別語意關係對於語意處理的影響清楚區分。此外，神經發展障礙的自閉症疾病，其主要臨床症狀為溝通障礙與語意處理能力缺失，已被證實在進行語意處理時會伴隨著異常神經活動。然而，對於自閉症青少年與健康青少年在處理語意關係時，是否在神經機制上也有著異同表現的知識仍然缺乏。此論文藉由行為測量與功能性磁振造影（fMRI），檢驗健康青少年的語意關聯與類別語意關係的發展變化，並進一步地比較自閉症青少年處理語意關聯與類別語意關係時對應的神經活動表現。**方法：**實驗一採縱貫式取向，正交地操弄語意關聯（高、低）與類別語意關係（高、低）兩個變項，以檢驗 16 位 10 到 14 歲青少年參與者語意知識的發展。參與者在進入 fMRI 後，判斷依序出現的視覺中文字對是否具有意義關係，在間隔兩年後，再次進行相同作業。實驗一更進一步的檢驗第一次的行為表現是否能預測兩年後的神經活化變化。實驗二以 fMRI 檢驗 31 位自閉症青少年與 36 位年齡、性別、慣用手與智力配對的健康青少年在進行語意處理時相對應的神經活動表現，參與者需判斷視覺呈現的中文字是否具有語意關係。分析判斷結果時將語意相關字對，依照語意關聯與類別語意關係的評分視為一連續性的刺激（item-level）參數調節變項。**結果：**實驗一，在弱語意關聯字對的表現，第二次比第一次有較多的神經生理反應，顯現在左顳中回（middle temporal gyrus）與左額下回（inferior frontal gyrus）有較多的活化反應，而第一次的行為正確率表現也預測了第二次的左額下回活化反應。推論處理越精緻化的語意表徵時，需要更仔細的選擇適當的語意表徵。此外，高類別語意關係字對則是在左枕-顳葉皮質區（occipito-temporal cortex）與左楔前葉（precuneus）有較多的活化，而第一次的行為正確率表現則預測了第二次的左楔前葉活化反應。推論較為精緻

化的語意屬性能完整的整合語意訊息。實驗二，相較於健康青少年，自閉症青少年在進行語意關係判斷時，隨著語意關聯性減弱，在左楔狀葉（cuneus）有明顯的活化反應，而健康青少年則是在隨著語意關聯性減弱，在左額下回與左顳中回有較明顯的活化反應；隨著類別語意關係增加，在左楔前葉（precuneus）與左枕-顳葉皮質區（occipito-temporal cortex）有明顯的活化反應。根據結果推論自閉症青少年與健康青少年在處理語意關係時的神經生理反應層次不同。自閉症青少年仰賴使用較低層次的視覺處理來進行語意處理，而健康青少年有著較精緻化的語意表徵，以較高層次的提取能力選擇適當語意表徵，對於語意屬性的掌握也較為精熟，得以將類別知識進行整合。

關鍵詞：自閉症、類別語意關係、發展、語意關聯

Chinese Semantic Knowledge in Typically Developing Youths and Youths with Autism Spectrum Disorder

Ciao-Han Wong

Abstract

To understand the developmental changes of semantic processing in autism spectrum disorders (ASD) and typical development (TD) youths is crucial to know the nature of the organization of semantic knowledge. However, the distinction of semantic knowledge including association strength and categorical relatedness has not been made clear in the literature for these two groups. In Experiment 1, using a longitudinal approach for the TD group, I orthogonally manipulated association strength (strong, weak) and categorical relatedness (high, low) to examine the developmental changes in activation of sixteen 10- to 14-year-old children over a two-year interval. Moreover, I examined whether initial behavioral performance (Time 1) predicted brain activation changes (Time 2-Time 1). Experiment 2 used fMRI to examine the neural correlates of semantic processing in thirty-one male youths with ASD and thirty-six TD youths. The association strength and categorical relatedness were item-level parametric modulators as two continuous variables. In Experiment 1, for Time 2-Time 1, the

doi:10.6342/NTU201700744

weak versus strong association strength produced greater activation in the left middle temporal gurus (MTG, BA 21) and inferior frontal gyrus (IFG, BA 45) as well as accuracy (Time 1) predicted activation changes in the IFG, suggesting more elaborate semantic representations that require greater engagement of selection processes. Moreover, the high versus low categorical relatedness produced greater activation in the left occipito-temporal cortex (OTC, BA37) and precuneus (BA 30) as well as accuracy (Time 1) predicted activation changes in the precuneus, suggesting more elaborate features of categorical knowledge that allow complete integration. In Experiment 2, for group comparisons, the ASD group showed greater activation in the left cuneus (BA 7) for the weaker association strength. The TD group showed greater activation in the left IFG and MTG for the weaker association strength, and greater activation in the left precuneus and left OTC for the higher categorical relatedness as compared to the ASD group. The ASD group may use lower-level visual processing during semantic processing. The TD group showed higher-level controlled processes of more elaborate semantic representations for selection processes and more elaborate features of categorical knowledge for integration.

Keywords: Association strength, Autism spectrum disorders (ASD), Categorical relatedness, Development, Longitudinal

doi:10.6342/NTU201700744

Content

doi:10.6342/NTU201700744

Introduction

The developmental of semantic processing is characterized by increasing elaboration on the organization of semantic representations. In a behavioral study of semantic processing, Wong, Chen, and Chou (2014) showed that as age increase, learning experiences may enhance children to build more elaborate semantic representations and use more abstract manners to integrate the different categorical relationships. Moreover, the interaction of association strength and categorical relatedness suggests that semantic knowledge may be organized by both association strength and categorical relatedness. However, the underlying neural mechanism of developmental changes of semantic organization is unclear in typically developing (TD) youths. Further, the semantic impairment is prominent in Autism spectrum disorders (ASD), who is a pervasive neuro-developmental disorder characterized by impairments in social communication and semantic processing deficits. The organization of semantic knowledge has not been made clear in ASD. Established the knowledge about semantic processing in the TD youths to understand the pattern of communication impairment in youths with ASD. Therefore, in the current thesis, I applied two experiments to investigate the semantic processing in TD youths and youths with ASD. First, I used a longitudinal approach to investigate the roles of

doi:10.6342/NTU201700744

association strength and categorical relatedness in the developmental changes of semantic processing in TD youths. Afterwards, I examined the neural correlates of semantic processing to better understand the differential neural substrates of semantic processing between youths with ASD and TD youths.

doi:10.6342/NTU201700744

Chapter 1

Developmental changes of association strength and categorical relatedness on semantic processing in the brain

1-1 Introduction

Researchers have used different kinds of semantic relations to understand the organization of semantic knowledge. One of the semantic relations is association strength for stimulus pairs based on free association norms (Chou, Booth, Bitan, et al., 2006; Chou, Booth, Burman, et al., 2006; Chou, Chen, Fan, Chen, & Booth, 2009; Wong, Chen, Chou, & Lee, 2011). Another means to study semantic relations is categorical relatedness, which refers to stimulus pairs that have shared features or properties (Nation & Snowling, 1999; Wong et al., 2011). However, there are two shortcomings with previous developmental studies. First, association strength has not been distinguished from categorical relatedness, which causes potential confounds in interpreting developmental differences in semantic processing (McRae & Boisvert, 1998). Second, these studies used cross-sectional designs that may not be able to accurately characterize age-related differences in semantic processing. Therefore, we systematically manipulated association strength and categorical relatedness to

doi:10.6342/NTU201700744

investigate the developmental changes of semantic processing using a longitudinal approach.

A cross-sectional design may overestimate the magnitude of a true age change due to cohort-related influences in cognitive test performance observed at a single point (Rönnlund, Nyberg, Bäckman, & Nilsson, 2005). We used a longitudinal design in the current study because it distinguishes changes from differences among people in their baseline by allowing an examination over time within individuals (Diggle, Heagerty, Liang, & Zeger, 2002). Longitudinal designs can more accurately characterize age-related trajectories (Salthouse, 2000; Schaie, 1990, 1994) and they additionally allow prediction over time (Gabrieli, Ghosh, & Whitfield-Gabrieli, 2015). Previous work in semantic development examining similar effects has found contradictory results using cross-sectional and longitudinal designs. For example, Lucariello, Kyratzis, and Nelson (1992) conducted a word association task to explore the organization of semantic knowledge in children. Their results showed that 7-year-olds provided more taxonomic responses than thematic responses, while 4-year-olds provided more thematic responses than taxonomic responses. In contrast, other researchers found that 5-, 8-, and 10-year-old children all produced more thematic responses than taxonomic responses (Borghi & Caramelli, 2003). These

doi:10.6342/NTU201700744

inconsistent results demonstrate the potential advantage of using a longitudinal design to examine the developmental changes in semantic processing.

Association strength has most often been defined by free association norms (Hung, Lee, Chen, & Chou, 2010; Lee, Chen, & Chou, 2009; Moss, Ostrin, Tyler, & Marslen-Wilson, 1995; Nation & Snowling, 1999; Wong et al., 2011). Several previous studies have found higher accuracy on stronger than weaker association items (Hung et al., 2010; Lee et al., 2009; Wong et al., 2011). However, these studies have not distinguished categorical relatedness from association strength, and this distinction is important on theoretical grounds. Modeling studies based on distributed networks have shown that associative relations and categorical relations have different impacts on semantic processing (McClelland & Rogers, 2003; Plaut, 1995). Word association norms can contain a miscellaneous variety of relations, such as synonyms, antonyms, or same categories (Hue, Gao, & Lo, 2005). Indeed, Hutchison (2003) classified each stimulus and its primary associate from norms into 1 or more of 14 possible relations, showing that stimuli may fall into more than one classification. Thus, it is necessary to separate categorical relatedness from association strength to examine semantic processing in children.

Categorical relatedness refers to character pairs that entail membership in a category on the basis of shared features (Estes, Golonka, & Jones, 2011; Hampton,

doi:10.6342/NTU201700744

2006). Computational models suggest that related concepts are represented by similar patterns such that the similarity between two concepts depends on the degree of feature overlap (Plaut, 1995). For example, cows and sheep share many features, such as being warm-blooded, and belong to the category of mammals. Members of the same category are all related to one another by their shared properties (Estes et al., 2011). As compared with low categorical pairs, high categorical pairs produce a greater priming effect, suggesting that the high categorical relatedness should produce greater activation of the memory representation of the category (Hines, Czerwinski, Sawyer, & Dwyer, 1986). Similarly, modeling findings demonstrate greater semantic priming for high categorical pairs with more overlapping features as compared to low categorical pairs with fewer overlapping features (Plaut, 1995). A neuro-cognitive account also proposes that categorical information with many features is represented and processed in the occipito-temporal cortex (Taylor, Devereux, & Tyler, 2011).

The neuroimaging evidence of association strength shows that two major brain regions exhibit greater activation for weak association pairs as compared to strong association pairs. One critical region is the left inferior frontal gyrus (IFG). The greater activation in the IFG is related to on-line searching during semantic processing in adults (Binder, Desai, Graves, & Conant, 2009; Fletcher, Shallice, & Dolan, 2000), particularly when there are increased demands on retrieval or selection of semantic

doi:10.6342/NTU201700744

knowledge (Badre & Wagner, 2007; Zhu et al., 2009). Child studies using association strength have found greater activation for weaker association pairs in the IFG (Chou, Booth, Bitan, et al., 2006; Chou, Booth, Burman, et al., 2006; Chou et al., 2009; Lee, Booth, Chen, & Chou, 2011), suggesting difficulty of on-line searching of semantic information for these pairs (Fletcher et al., 2000). Another critical region implicated in the processing of weak association pairs is the left middle temporal gyrus (MTG). Greater activation in this region in adults is thought to be related to the storage of lexical representations (Binder et al., 2009; Lau, Phillips, & Poeppel, 2008) and the representation of conceptual contents (Fairhall & Caramazza, 2013). Child studies using association strength have found greater activation for weaker association pairs in the MTG, indicating more elaborate semantic representations in older children (Chou, Booth, Bitan, et al., 2006; Chou, Booth, Burman, et al., 2006).

Regarding the neural substrates of processing categorical relatedness, Sachs, Weis, Krings, Huber, and Kircher (2008) examined semantic relations with a category construction task in which participants selected among two options that best went with a target (e.g., car). Their results showed that choosing an option with categorical relatedness (e.g., bus) was associated with increased activation of the left precuneus. When participants processed categorical pairs in a lexical decision task, greater activation was also found in the precuneus (Sachs, Weis, Zellagui, et al., 2008).

Furthermore, an age-related increase in precuneus activation is related to feature extraction for semantic categorization in a visual working memory task (Ciesielski, Lesnik, Savoy, Grant, & Ahlfors, 2006). Another region implicated in the processing of categorical relatedness is the left occipito-temporal cortex. This region plays a critical role in storing visual-perceptual features contributing to category-specific semantic memory (Binder et al., 2009) and greater activation in this region is related to difficulty of access of visual-perceptual features in the processing of object knowledge (Grossman et al., 2013). Greater activation in this region is thought to reflect the storage of many features of a general-level category rather than a few features of a specific-level category (Taylor et al., 2011). Thus, processing high categorical pairs with more overlapping features is hypothesized to be related to the storage of visual features in the occipito-temporal cortex that are integrated in the precuneus. Taken together, previous research suggests that we should focus on the roles of the left IFG and MTG in association strength as well as the precuneus and occipito-temporal cortex in categorical relatedness when we examine developmental changes in semantic processing.

In the present study, we used a semantic judgment task to investigate the underlying mechanisms of developmental changes of association strength and categorical relatedness in 10- to 14-year-old children. We chose this age range

doi:10.6342/NTU201700744

because categorical knowledge is gradually learned during this time (Borghi & Caramelli, 2003; Nation & Snowling, 1999). The first goal of the present study was to examine the neural correlates of semantic processing by orthogonally manipulating association strength and categorical relatedness between character pairs. According to previous studies, we expected that weak association pairs should produce greater activation in the left IFG and MTG, and high categorical pairs should produce greater activation in the left precuneus and left occipito-temporal cortex. Second, we examined developmental changes of children over a two-year interval using a longitudinal approach. We hypothesized an age-related increase in activation in the IFG and MTG for processing weak association pairs as well as in the precuneus and occipito-temporal cortex for processing high categorical pairs, and that this would be related to behavioral performance. This would be consistent with the hypothesis that as children age they have more elaborated semantic representations in the left MTG that require greater engagement of selection processes in the left IFG, and that they have more elaborate features of categorical knowledge in the occipito-temporal cortex that are integrated in the precuneus.

1-2 Methods

Participants. Sixteen native speakers of Chinese (in Time 1, age range = 10-14, mean age = 12.1, standard deviation = 1.4, 5 females) participated in this longitudinal study.

doi:10.6342/NTU201700744

The children received the functional magnetic resonance (fMRI) scans twice over a two-year interval. They were recruited from the Taipei city metropolitan area and their parents were given an informal interview to ensure that their children met the following inclusionary criteria: (1) right-handedness, (2) normal hearing and normal or corrected-to-normal vision, (3) free of neurological disease or psychiatric disorders, (4) no history of intelligence, reading, or oral-language deficits, (5) not taking medication affecting the central nervous system, and (6) no learning disability or attention deficit hyperactivity disorder (ADHD). After the administration of the interview, informed consent was obtained. The informed consent procedures were approved by the Institutional Review Board at the National Taiwan University Hospital. Standardized intelligence testing was then administered, using the Wechsler Intelligence Scale for Children (WISC-III) Chinese version. Participants' standard scores (mean ± *SD*) were 112.0 ± 12.5 on the verbal scale and 111.1 ± 12.3 on the full scale.

Functional activation tasks. The children were given two practice sessions, one outside the scanner and the other in the scanner, to make sure that they understood the task. The practice items were different stimuli from those used in fMRI sessions. Forty-eight character pairs were divided into 2 association strength (strong and weak) by 2 categorical relatedness (high and low) pairs, each condition having 12 pairs (see

doi:10.6342/NTU201700744

Appendix A). Association strength was defined by free association values (mean = 0.14, *SD* = 0.13, ranging from 0.73 to 0.01) (Chou et al., 2009; Hue et al., 2005). Categorical relatedness was defined by rating scores from teachers (fifth to seventh-grade) who were asked to determine categorical relationship including artifacts (e.g., dish-plate) and natural kinds (e.g., dog-cat) by using a 7-point rating scale on each pair (Moss et al., 1995; Sachs, Weis, Krings, et al., 2008; Wong, Chen, & Chou, 2014; Wong et al., 2011). Thus, there were four semantically related conditions including strong association strength–high categorical relatedness, strong association strength–low categorical relatedness, weak association strength–high categorical relatedness, and weak association strength–low categorical relatedness. In addition, twenty-four character pairs were semantically unrelated, with zero association values and no categorical relatedness.

In the semantic judgment task, two Chinese characters were visually presented sequentially and the participants had to determine whether the character pair was related in meaning. Trials lasted 4500 ms and consisted of a solid square (500 ms), followed by the first character (800 ms), a 200-ms blank interval, and the second character for 3000 ms. The participants were instructed to make a response during the presentation of the second word. They were instructed to quickly and accurately press with their right hand the yes button to the related pairs and the no button to the

doi:10.6342/NTU201700744

unrelated pairs. The perceptual control condition had 24 pairs of non-characters. Non-characters were created by replacing radicals of real characters with other radicals that did not form real Chinese characters. Non-characters were larger (50 point font size) than real characters (40 point font size) in order to encourage participants to perform the task based on recognizing a low level of visual similarity and not on the extraction of semantic information (Chou et al., 2009). Trials consisted of a solid square (500 ms), followed by the first non-character (800 ms), a 200 ms blank interval, and the second non-character for 3000 ms. Participants determined whether the pair of stimuli was identical or not by pressing a yes or no button with their right hand. There were also 24 baseline events as “null” trials so that we could better deconvolve the response to the lexical and perceptual trials. The participant was instructed to press a button when a solid square (1300 ms) at the center of the visual field turned to a hollow square (3000 ms) after a blank interval (200 ms).

Stimulus characteristics. Several lexical variables were controlled across the related and unrelated conditions (Table 1-1). First, all characters were monosyllabic. Second, the first and second character did not share radicals (Lee, Booth, & Chou, 2015). Third, the first and second character together did not form a word (Sinica Corpus, 1998; Wu & Liu, 1987). Fourth, characters were matched for visual complexity (in terms of strokes per character) across the related conditions. Fifth, characters were

doi:10.6342/NTU201700744

matched for written frequency for adults (Wu & Liu, 1987) and written familiarity for children across the related conditions. Familiarity scores were obtained from pre-tests in which all the characters were rated on a 7-point scale by thirty age-matched children. The correlation of the character familiarity measure was not significant, with association values or categorical ratings, indicating that association or categorical effects should not be due to familiarity differences. Sixth, imageability was matched across the related conditions. Imageability scores were rated for individual characters on a 7-point scale by ten age-matched children who did not participant this study. A 2 (association strength) by 2 (categorical relatedness) ANOVA on imageability scores was not significant for the main effects or interaction (*ps* > .05). Seventh, concreteness based on a Chinese psycholinguistic norms (Liu, Shu, & Li, 2007) was matched across the related conditions. A 2 (association strength) by 2 (categorical relatedness) ANOVA on concreteness scores was not significant for the main effects or interaction (*ps* > .05). It should be noted that not every character had a concreteness rating on the norms. The missing values were 4% (strong association strength–high categorical relatedness), 16% (strong association strength–low categorical relatedness), 16% (weak association strength–high categorical relatedness), and 29% (weak association strength–low categorical relatedness).

doi:10.6342/NTU201700744

MRI data acquisition. Participants lay in the scanner with their head position secured by a specially designed vacuum pillow. An optical response box was placed in the participants' right hand. The head coil was positioned over the participants' head. Participants viewed visual stimuli projected onto a screen via a mirror attached to the inside of the head coil. This study adopted an event-related design.

All images were acquired using a 3 Tesla Siemens Trio scanner. Gradient-echo localizer images were acquired to determine the placement of the functional slices. For the functional imaging studies, a susceptibility-weighted single-shot EPI (echo planar imaging) method with BOLD (blood oxygenation level-dependent) was used. Functional images were interleaved from bottom to top collected parallel to the AC-PC plane. The scanning parameters were the following: repetition time (TR) = 2000 ms; echo time (TE) = 24 ms; flip angle = 90º; matrix size = 64 × 64; field of view = 25.6 cm; slice thickness = 3 mm; number of slices = 34. Each participant performed two 4.5-min functional runs with 136 image volumes. A high-resolution, T1-weighted three dimensional image was also acquired (Magnetization Prepared Rapid Gradient Echo, MP-RAGE; TR = 1560 ms; TE = 3.68 ms; flip angle = 15º; matrix size = 256×256; field of view = 25.6 cm; slice thickness = 1 mm, number of slices = 192). Orientation of the 3D image was identical to the functional slices. The task was administered in a pseudorandom order for all participants, in which the order

doi:10.6342/NTU201700744

of conditions was optimized for event-related design (Burock, Buckner, Woldorff, Rosen, & Dale, 1998).

fMRI analysis. Data analysis was performed using SPM2 (Statistical Parametric Mapping 2). The functional images were corrected for differences in slice-acquisition time to the middle volume and were realigned to the first volume in the scanning session using affine transformations. No participant had more than 3 mm of movement in any plane. Co-registered images were normalized to the MNI (Montreal Neurological Institute) average template (12 linear affine parameters for brain size and position, 8 non-linear iterations and 2 x 2 x 2 nonlinear basis functions). Statistical analyses were calculated on the smoothed data (10 mm isotropic Gaussian kernel), with a high pass filter (128 seconds cutoff period) in order to remove low frequency artifacts.

Data from each participant was entered into a general linear model using an event-related analysis procedure (Josephs & Henson, 1999). Character pairs were treated as individual events for analysis and modeled using a canonical HRF (Hemodynamic Response Function). There were seven event types: strong association strength–high categorical relatedness, strong association strength–low categorical relatedness, weak association strength–high categorical relatedness, weak association strength–low categorical relatedness, unrelated, perceptual, and baseline. Parameter

doi:10.6342/NTU201700744

estimates from contrasts of the canonical HRF in single subject models were entered into random-effects analysis using one-sample t-tests across all participants to determine whether activation during a contrast was significant (i.e., parameter estimates were reliably greater than 0). The incorrect trials were included for the following analyses, considering that the statistical power should be equal between conditions with different accuracies for fMRI analyses (Bitan et al., 2007; Chen, Gau, Lee, & Chou, 2016).

We conducted bi-directional comparisons between the strong and the weak association strength in Time 1 and Time 2 separately, and bi-directional comparisons between the high and the low categorical relatedness for Time 1 and Time 2 separately ($p < .001$ uncorrected at the voxel level). A mask was formed by combining these 4 maps with a logical "OR" operation. In order to examine developmental changes within this mask, we compared Time 2 with Time 1 using $p < .05$ corrected for FDR (false discovery rate) at the voxel level with a cluster size greater than 10 voxels. In addition, reported areas of activation for developmental changes in the left MTG (-58, -42, -1) and occipito-temporal cortex (-48, -66, 6) were $p < .05$ corrected for multiple comparisons at the voxel level with a sphere of 6 mm radius from a study of semantic development (Chou et al., 2009) and from a study of categorical knowledge (Grossman et al., 2013), respectively.

doi:10.6342/NTU201700744

Regression analyses. The relationship between behavior at Time 1 and brain activation change from Time 1 to Time 2 was examined using a simple regression model. In order to determine whether behavioral performance was predictive of increased regional activity during semantic judgments, the accuracy for the weak minus the strong association strength at Time 1 was used as a regressor of interest, with the change in beta values for the left IFG (BA 45) and MTG (BA 21) from Time 1 to Time 2 as the dependent variable. Moreover, the accuracy for the high minus the low categorical relatedness at Time 1 was used as a regressor of interest, with the change in beta values for the left precuneus (BA 30) and occipito-temporal cortex (BA 37) from Time 1 to Time 2 as the dependent variable.

1-3 Results

Behavioral performance: accuracy. Accuracy (mean ± *SD*) for the strong association strength–high categorical relatedness, strong association strength–low categorical relatedness, weak association strength–high categorical relatedness, and weak association strength–low categorical relatedness conditions were 88 ± 12%, 84 ± 14%, 82 ± 17%, and 72 ± 12% in Time 1, and 95 ± 5%, 88 ± 16%, 90 ± 12%, and 85 ± 14% in Time 2, respectively. A 2 association strength (strong, weak) by 2 categorical relatedness (high, low) by 2 age (Time 1, Time 2) ANOVA on accuracy was performed. The main effect of association strength was significant, *F*(1, 15) =

doi:10.6342/NTU201700744

15.37, $p < .05$, $\eta^2 = .51$, reflecting higher accuracy for the strong relative to the weak association strength. The main effect of categorical relatedness was significant, $F(1, 15) = 12.44$, $p < .05$, $\eta^2 = .45$, reflecting higher accuracy for the high relative to the low categorical relatedness. The main effect of age was significant, $F(1, 15) = 8.01$, $p < .05$, $\eta^2 = .35$, reflecting higher accuracy for Time 2 relative to Time 1. All interactions were not significant, *ps* > .05.

Behavioral performance: reaction times. Reaction times (mean ± *SD*) for the strong association strength–high categorical relatedness, strong association strength–low categorical relatedness, weak association strength–high categorical relatedness, and weak association strength–low categorical relatedness conditions were 962 ± 223 ms, 1077 ± 212 ms, 1050 ± 210 ms, and 1164 ± 182 ms in Time 1, and 801 ± 179 ms, 934 ± 241 ms, 898 ± 202 ms, and 971 ± 201 ms in Time 2, respectively. A 2 association strength (strong, weak) by 2 categorical relatedness (high, low) by 2 age (Time 1, Time 2) ANOVA on reaction times was performed. The main effect of association strength was significant, $F(1, 15) = 31.43$, $\eta^2 = .68$, $p < .05$, reflecting faster reaction times for the strong relative to the weak association strength. The main effect of categorical relatedness was significant, $F(1, 15) = 31.70$, $p < .05$, $\eta^2 = .68$, reflecting faster reaction times for the high relative to the low categorical relatedness. The main effect of age was significant, $F(1, 15) = 28.53$, $p < .05$, $\eta^2 = .66$, reflecting faster

doi:10.6342/NTU201700744

reaction times for Time 2 relative to Time 1. All interactions were not significant *ps* > .05.

Brain activation patterns. Table 1-2 summarizes brain regions for the bi-directional comparisons between the strong and the weak association strength in Time 1 and Time 2 separately, and for the bi-directional comparisons between the high and the low categorical relatedness in Time 1 and Time 2 separately. The weak versus the strong association strength produced greater activation in the left precentral gyrus (BA 1) and left putamen for Time 1, and in the bilateral IFG (BA 45), left supplementary motor area (BA 6), left precentral gyrus (BA 4), left MTG (BA 21), and left inferior parietal lobule (BA 40) for Time 2, respectively (Figure 1-1A). The strong versus the weak association strength was not significant for Time 1, and produced greater activation in the right superior frontal gyrus (BA 10) for Time 2. Moreover, the high versus the low categorical relatedness produced greater activation in the right cuneus (BA 19) for Time 1, and in the left occipito-temporal cortex (BA 37) and left precuneus (BA 30) for Time 2, respectively (Figure 1-1C). The low versus high categorical relatedness produced greater activation in the bilateral anterior cingulate cortices (BA 32/33), left cingulate gyrus, and bilateral middle frontal gyri (BA 8/46) for Time 1, and was not significant for Time 2.

The developmental changes of semantic processing are shown in Table 1-2. The contrast of the weak versus the strong association strength produced greater activation in the left IFG (BA 45) and MTG (BA 21) (Figure 1-1B) for Time 2 compared to Time 1. The contrast of the high versus the low categorical relatedness elicited greater activation in the left precuneus (BA 30) and occipito-temporal cortex (BA 37) (Figure 1-1D) for Time 2 compared to Time 1.

To further unpack the developmental changes in IFG activation, we plotted Time 1 and Time 2 activation separately for the weak and strong association items. There was a greater difference in IFG activation at Time 2 compared to Time 1 (Figure 1-2A). To further unpack the developmental changes in precuneus activation, we plotted the Time 1 and Time 2 activation separately for the high and low categorical items. There was a greater difference in precuneus activation at Time 2 compared to Time 1 (Figure 1-2B).

Regression analysis. A simple regression model was used to determine whether behavioral performance at Time 1 was predictive of Time 2 minus Time 1 brain activity in significant brain regions. For the contrast of the weak versus the strong association strength, we performed a simple regression analysis using the Time 2 minus Time 1 beta values of the left IFG (BA 45) as the dependent variable, and overall accuracy of the weak minus strong association strength at Time 1 was entered as a predictor. The model was significant, *F(*1, 14) = 22.92, *p* < .05 (Figure 1-3A). The regression analysis of association strength was not significant for the left MTG (BA 21). Moreover, for the contrast of the high versus the low categorical relatedness, we performed a simple regression analysis using the Time 2 minus Time 1 beta values of the left precuneus (BA 30) as the dependent variable, and overall accuracy of the high minus low categorical relatedness at Time 1 was entered as a predictor. The model was significant, *F*(1, 14) = 6.59, *p* < .05 (Figure 1-3B). The regression analysis of categorical relatedness was not significant for the left occipito-temporal cortex (BA 37).

1-4 Discussion

To understand the distinction of association strength and categorical relatedness in children is important due to the fact that these two factors appear to play different roles in semantic development but previous research has not teased these factors apart (Hue, Gao, & Lo, 2005; Hutchison, 2003; Moss, Ostrin, Tyler, & Marslen-Wilson, 1995; Scheuner, Bonthoux, Cannard, & Blaye, 2004). The present study used a longitudinal design to examine the developmental changes in neural correlates of association strength and categorical relatedness in children. In summary, we found developmental increases in the left IFG for association strength that were correlated with skill, and developmental increases in the precuneus for categorical relatedness

doi:10.6342/NTU201700744

that were correlated with skill. The developmental increase in the left IFG may be related to more elaborate semantic representations that require greater engagement of selection processes, whereas the developmental increase in the left precuneus might be associated with more elaborate features of categorical knowledge that allow complete integration.

Weak association strength produced greater activation in the left IFG as compared to the strong association strength. This is consistent with child studies using a cross-sectional approach in Chinese (Chou, Chen, Fan, Chen, & Booth, 2009; Lee, Booth, Chen, & Chou, 2011) and in English (Chou, Booth, Bitan, et al., 2006). Greater activation in this region is thought to be related to access to semantic representations that require greater engagement of selection processes for weak association pairs. Therefore, the children may need effortful semantic search for distantly related stimuli, particularly when there were increased demands on the process of selecting relevant semantic knowledge as for low association pairs (See also Blumenfeld, Booth, & Burman, 2006).

There was a developmental increase in left IFG activation for the weak versus the strong association strength in Time 2 relative to Time 1. In the region of interest analyses, there was also a developmental increase in left MTG activation for the weak versus the strong association strength in Time 2 relative to Time 1. The

doi:10.6342/NTU201700744

developmental change in the MTG may reflect the elaboration of semantic knowledge with increasing numbers of lexical associations (McGregor & Appel, 2002; McGregor, Friedman, Reilly, & Newman, 2002). Altogether, age-related increases in activation suggest that there may be a greater number of potential lexical associates with age in the left MTG and these associates may increase selection demands for the weak association strength in the left IFG. Older children may have more elaborate semantic representations in the temporal cortex that require greater engagement of selection processes for the weak association strength in the frontal cortex.

For the association strength variable, the regression analyses indicated that behavioral performance at Time 1 was predictive of activation change in the left IFG from Time 1 to Time 2. Specifically, the difference in accuracy of the weak association minus accuracy of the strong association at Time 1 was predictive of activation change in left IFG activation of Time 2 minus Time 1 for the contrast of weak association minus strong association. Accuracy for the weak association was overall lower than accuracy for the strong association, and activation for the weak association was overall greater than the strong association, so it is reasonable that the regression analysis shows that this relationship is negative. More generally, this analysis suggests that lower accuracy for the weak association early in development is associated with greater activation changes over time potentially because semantic

doi:10.6342/NTU201700744

connections for these items are later acquired (Hung, Lee, Chen, & Chou, 2010; McGregor & Appel, 2002). Behavioral data in our study shows larger developmental changes for the weak compared to the strong association items. Strong association items are earlier acquired so they are less likely to show large individual differences earlier in development, and be less predictive of later changes.

High categorical relatedness elicited greater activation in the left precuneus as compared to the low categorical relatedness. The left precuneus has been proposed to be involved in elaborating highly integrated information (Cavanna & Trimble, 2006) and in the conceptual representation of semantic knowledge (Fairhall & Caramazza, 2013). In order to perform a relatedness judgment, children need to compare the overlapping semantic features for stimulus pairs (Nation & Snowling, 1999). The high categorical relatedness may allow for greater integration of features due to many overlapping semantic features between characters (Plaut, 1995). Greater activation in the left precuneus may reflect that many similar or overlapping features are activated and integrated during processing the high categorical relatedness.

We found greater activation in the left precuneus for the high versus low categorical relatedness in Time 2 compared to Time 1. In a region of interest analyses, we also found greater activation in the left occipito-temporal cortex for the high versus low categorical relatedness in Time 2 compared to Time 1. The developmental

doi:10.6342/NTU201700744

increase in the occipito-temporal cortex may reflect the elaboration of features with increasing connections among relevant features for high categorical pairs (McClelland & Rogers, 2003). Taken together, the age-related increases might be due to more elaborate features of categorical knowledge in the occipito-temporal cortex that allow more complete integration of the overlapping features for the high categorical relatedness in the precuneus for older children as compared to younger children. The developmental increase in activation for high categorical relations might also be related to educational experiences (Hashimoto, McGregor, & Graham, 2007; Wong et al., 2014). With two years of exposure to formal schooling and training in analytical skills, character pairs have more complete hierarchical relations and shared semantic features, such that categorical concepts are getting more robust (Wong et al., 2014). Older children have learned that features are not equally important and some features with little significance must be ignored when establishing a categorical relationship. Therefore, the ability to compare overlapping features allows older children to more completely integrate highly categorical pairs.

For the categorical relatedness variable, the regression analyses indicated that behavioral performance at Time 1 was predictive of activation change in the left precuneus from Time 1 to Time 2. Specifically, the difference in accuracy of the high categorical relatedness minus accuracy of the low categorical relatedness at Time 1

doi:10.6342/NTU201700744

was predictive of activation change in left precuneus activation of Time 2 minus Time 1 for the contrast of high categorical minus low categorical relatedness. Accuracy for the high categorical relatedness was overall higher than accuracy for the low categorical relatedness, and activation for the high categorical relatedness was overall greater than low categorical relatedness, so it is reasonable that the regression analysis shows that this relationship is positive. The behavioral data shows that the high categorical relatedness shows comparable behavioral changes over development to those of the low categorical relatedness, but this condition also shows greater activation changes over development, so these two effects are dissociated. However, our behavioral data are consistent with those reported by previous studies (Nation & Snowling, 1999; Wong et al., 2014), suggesting that children over age 10 produce robust priming effects on both high and low categorical relatedness over time.

The present study used a semantic judgment task to investigate the developmental changes in semantic knowledge. To accomplish the task, children need to fully understand the meanings of two characters to decide if character pairs are related in meaning. That is, the semantic judgment task emphasizes voluntary and explicit semantic processing. In contrast, previous studies have used the lexical decision task that requires participants to indicate whether the target is a word after seeing a semantically related or unrelated prime (Moss et al., 1995; Nation &

doi:10.6342/NTU201700744

Snowling, 1999). The lexical decision task involves automatic and implicit access to semantic representations because participants are not instructed to pay attention to the relation between prime and target (McNorgan, Chabal, O'Young, Lukic, & Booth, 2015; Moss & Tyler, 1995). In the present study, the semantic judgments task may place more weight on semantic relations as compared to primed lexical decisions (Wong et al., 2014). The explicit task may increase demands on retrieving/selecting semantic knowledge or processing features of categorical knowledge (Sauzéon, Lestage, Raboutet, N'Kaoua, & Claverie, 2004). Thus, our children may rely more on the inferior frontal gyrus for searching on-line semantic information or on the precuneus for integrating overlapping features during semantic judgments. This may explain the comparatively stronger effects in these regions.

In conclusion, we found an age-related increase in activation within the left MTG and left IFG, suggesting more elaborate semantic representations that require greater engagement of selection processes in weak association pairs over age. In addition, we found a developmental increase in activation in the left occipito-temporal cortex and precuneus for the high categorical relatedness, suggesting that older children may have more elaborate semantic features that allow complete integration.

doi:10.6342/NTU201700744

Chapter 2

Association strength and categorical relatedness of semantic processing in youth with autism spectrum disorder

2-1 Introduction

In Experiment 1, different semantic relations induced different neural activity in the TD children. Based on these findings, I compared youths with ASD and TD youths while doing semantic judgment task in Experiment 2 to further examine whether there is different neural mechanism between these two groups.

Autism spectrum disorders (ASD) is a pervasive neuro-developmental disorder characterized by impairments in social communication and social reciprocity, as well as restricted and repetitive behaviors, interests or activities (American Psychiatric Association, 2013). Individuals with ASD often present impairment across different domains of language, including pragmatic, prosody, syntax, morphology, phonology, and semantic (Bartolucci, Pierce, & Streiner, 1980; Bishop et al., 2004; Capps, Losh, & Thurber, 2000; Kjelgaard & Tager-Flusberg, 2001; Roberts, Rice, & Tager-Flusberg, 2004; Shriberg et al., 2001). Among language impairments in children with ASD, semantic and pragmatic functions that tie closely with cognitive

doi:10.6342/NTU201700744

and social development are prominently deficient (Tager-Flusberg, 1981). However, the organization of semantic knowledge has not been made clear in previous studies of semantic processing.

Researchers have explored two kinds of semantic relations to understand semantic knowledge. One of the semantic relations is association strength for stimulus pairs based on free association norms (Booth et al., 2002; Chou, Booth, Bitan, et al., 2006; Chou, Booth, Burman, et al., 2006; Chou et al., 2009; Hung et al., 2010; Lee, Chen, & Chou, 2009; Wong, Chen, Chou, & Lee, 2011). The other way to study semantic relations is categorical relatedness that is referred to stimulus pairs based on semantic category that entails membership in a category on the basis of shared features or properties (Estes, Golonka, & Jones, 2011; Lin & Murphy, 2001; Moss et al., 1995; Nation & Snowling, 1999; Wong et al., 2011). Processing categorical relatedness allows individuals to organize information into conceptual groupings and then make inferences about new information based on previously formed concepts (Klinger & Dawson, 2001).

As to the neural correlates of semantic processing, studies using functional magnetic resonance imaging (fMRI) have shown abnormal neural activity in ASD, for instance, decreased activation in left inferior frontal gyrus (IFG) for adults with ASD relative to control participants, and increased activation in the left middle temporal

doi:10.6342/NTU201700744

gyrus (MTG) (Gaffrey et al., 2007; Groen et al., 2010; Harris et al., 2006; Just, Cherkassky, Keller, & Minshew, 2004; Kana, Keller, Cherkassky, Minshew, & Just, 2006). Furthermore, the activation in the visual area has been observed in ASD during semantic processing. Kana et al. (2006) found that adults with ASD produced less activation in the IFG but additional recruitment of visual areas during sentence comprehension. Similarly, adults with ASD elicited decreased activation in the left IFG but greater activation in extrastriate visual cortices bilaterally relative to the TD group in a semantic task, suggesting an immature brain mechanism associated with semantic processing in adults with ASD (Gaffrey et al., 2007). A recent study also showed that boys with ASD produced less activation in the left IFG and greater activation in the cuneus during semantic judgment task (Chen, Gau, Lee, & Chou, 2016). Greater activation in the IFG and MTG have to be found for weak association pairs as compared to strong association pairs in TD youths. Greater IFG activation has been proposed to play an important role in on-line searching during semantic processing (Fletcher, Shallice, & Dolan, 2000; Gaillard et al., 2003; Schlaggar et al., 2002), including controlled access to stored representations and selection process (Badre & Wagner, 2007). Child studies using association strength have found greater activation for weaker association pairs in the IFG, suggesting the difficulty of on-line searching of semantic information these pairs (Fletcher et al., 2000). Moreover,

doi:10.6342/NTU201700744

greater MTG activation is thought to be associated with the storage of lexical representations (Binder, Desai, Graves, & Conant, 2009; Lau, Phillips, & Poeppel, 2008) and the representation of conceptual contents (Fairhall & Caramazza, 2013). Child studies using association strength have found greater activation for weaker association pairs in the MTG (Chou et al., 2009). These two regions play an inter-connection role during semantic processing. A study investigated the effective connectivity among brain regions during semantic judgment task suggested that there is a modulatory effect form the left IFG to the left MTG for retrieving semantic representations (Fan, Lee, & Chou, 2010). A review by Lai, Lombardo, and Baron-Cohen (2014) suggests that individuals with ASD often have a local perception-based preference with recruitment of primary sensory cortices, in contrast to individuals without ASD focusing on top-down control processing with recruitment of frontal cortices to deal with global language/communication context.

Specifically, with regard to the cognitive mechanisms of categorical relatedness, previous ASD studies found that they performed poorly than the TD group on pre-symbolic object concept (Sigman & Ungerer, 1984), sorting task (Shulman, Yirmiya, & Greenbaum, 1995), concept formation (Johnson & Rakison, 2006; Klinger & Dawson, 2001), and category verification (Gastgeb, Strauss, & Minshew, 2006). Individuals with ASD have difficulty categorizing new information by forming

doi:10.6342/NTU201700744

prototypes and tend to rely on a rule-based approach for learning (Klinger & Dawson, 2001). For instance, Klinger and Dawson (2001) showed that the ASD group was able to group geometric figures correctly on a rule defined category membership; however, they were unable to do so when successful categorization required the formation of prototypes. These studies suggested an impairment of abstract reasoning in ASD (Klinger & Dawson, 2001; Minshew, Meyer, & Goldstein, 2002; Minshew, Muenz, Goldstein, & Payton, 1992; Sigman & Ungerer, 1984). Individuals with ASD may use a rule-based style rather than an abstract or prototype form of concept processing to organize information around conceptual themes (Minshew et al., 2002).

Regarding the neural correlates of categorical relatedness, previous studies indicated that the precuneus was engaged during categorical relatedness processing (Kotz, Cappa, von Cramon, & Friederici, 2002; Sachs, Weis, Krings, Huber, & Kircher, 2008; Sachs, Weis, Zellagui, et al., 2008). Sachs, Weis, Krings, et al. (2008) used a category construction task in which participants were presented with a target word (e.g., car) followed by the presentation of two match words (e.g., garage and bus). They had to select one match word that went best with the target word. Greater precuneus activation was found for the participants to link the match and target words with a categorical relation (e.g. car-bus). In a lexical decision task, processing categorical condition also produced greater activation in the precuneus (Sachs, Weis,

doi:10.6342/NTU201700744

Zellagui, et al., 2008) Furthermore, the precuneus is related to feature extraction for semantic categorization on a visual working memory task (Ciesielski, Lesnik, Savoy, Grant, & Ahlfors, 2006). This region may, therefore, respond to process the categorical relatedness which entails membership in the same category due to shared semantic features between the members. Another region implicated in the processing of categorical relatedness is the left occipito-temporal cortex. This region plays a critical role in storing visual-perceptual features contributing to category-specific semantic memory (Binder et al., 2009) and greater activation in this region is related to the difficulty of access to visual-perceptual features in the processing of object knowledge (Grossman et al., 2013). Greater activation in this region is thought to reflect the storage of many features of a general-level category rather than a few features of a specific-level category (Taylor, Devereux, & Tyler, 2011). Therefore, processing high categorical pairs with more overlapping features in hypothesized to be related to the storage of visual features in the occipito-temporal cortex that are integrated in the precuneus.

In the current study, I systematically manipulated association strength and categorical relatedness to better understand the differential neural substrates of semantic processing between ASD and TD youths. According to the aforementioned studies, these following regions were chosen as hypothesis-driven regions to explore

doi:10.6342/NTU201700744

semantic processing, including the left IFG, left MTG, left precuneus, and left occipito-temporal cortex. I hypothesized that youths with ASD would present atypical patterns of neural activation in response to a semantic judgment task when compared to the TD group. That is, for weaker association pairs, the TD group should produce greater activation in the left IFG and MTG as compared to the ASD group. Moreover, for higher categorical pairs, the TD group should produce greater activation in the left precuneus and occipito-temporal cortex than the ASD group.

2-2 Methods

Participants. We recruited thirty-one male youths with clinical diagnosis of ASD according to the DSM-IV diagnostic criteria (mean age = 12.1 years, SD = 1.5) and thirty-six age-, sex-, full intelligence quotient (FIQ) and handedness-matched typically developing (TD) youths (mean age = 11.9 years, SD = 1.0) in this study (Table 2-1). Participants and their parents were interviewed to ensure that the participants met the following inclusion criteria: (1) native Mandarin-Chinese speakers, (2) normal hearing and normal or corrected-to-normal vision, and (3) no clinical diagnosis of learning disability, attention deficit hyperactivity disorder, mood disorders, schizophrenia, schizoaffective disorder, or organic psychosis.

The ASD group was recruited from the Department of Psychiatry, National Taiwan University Hospital. They were diagnosed by the full-time board-certificated

doi:10.6342/NTU201700744

child psychiatrists of this hospital according to the DSM-IV, and ICD-10 diagnostic criteria. The clinical diagnosis was further confirmed by interviewing the parents using the Chinese version of the Autism Diagnostic Interview-Revised (ADI-R) by Professor Gau SS (Gau et al., 2011; Rutter & Lord, 2003).

The TD group was recruited from similar school districts of the ASD group by teachers' referral rather than advertisement. All the participants were clinically assessed and their parents were interviewed by using the Chinese Kiddie epidemiologic version of the Schedule for Affective Disorders and Schizophrenia (K-SADS-E) (Gau, Chong, Chen, & Cheng, 2005) by Professor Gau SS to ensure that they were free of any neuropsychiatric disorders, not taking medication affecting the central nervous system, no history of attention, reading, or verbal-language deficits, and no learning disability. All participants were also right handed according to Edinburgh Handedness Inventory (Oldfield, 1971). This study was approved by the Ethics Research Committee at the National Taiwan University Hospital before implementation (IRB ID, 9561709027, 200807036R; ClinicalTrials.gov number, NCT00494754, NCT00755430). All the participants and their parents provided written informed consents.

Functional activation tasks. The participants were given two practice sessions, one outside the scanner and the other in the scanner, to make sure that they understood the

doi:10.6342/NTU201700744

task. The practice items were different stimuli from those used in fMRI sessions. In fMRI sessions, forty-eight character pairs were arranged in a continuous variable according to free association values or categorical rating scores. Association strength was defined by free association values (mean = 0.14, *SD* = 0.13, ranging from 0.73 to 0.01) (Chou et al., 2009; Hue et al., 2005). Categorical relatedness were defined by rating scores form teachers (fifth to seventh-grade) who were asked to determine categorical relationship including artifacts (e.g., dish-plate) and natural kings (e.g., dog-cat) by using a 7-point rating scale on each pair (Moss et al., 1995; Wong et al., 2014; Wong et al., 2011). Therefore, 48 character pairs were semantically related conditions that included stronger association strength pairs with higher free association values and weaker association strength pairs with lower free association values. Also, the 48 semantically related pairs included higher categorical relatedness with higher rating scores and lower categorical relatedness with lower rating scores. In addition, 24 character pairs were semantically unrelated, with zero free association values and no categorical relatedness.

In the semantic judgment task, two visual Chinese characters (mono-morphemic words) were presented sequentially and the participant had to determine whether the character pair was related in meaning. Trials lasted 4500 ms and consisted of a solid square (500 ms), followed by the first character (800 ms), a 200-ms blank interval, and the second character for 3000 ms. The participants were instructed to make a response during the presentation of the second word. They were instructed to quickly and accurately press with their right hand the yes button to the related pairs and the no button to the unrelated pairs.

The perceptual control condition had 24 pairs of non-characters. Non-characters were created by replacing radicals of real characters with other radicals that did not form real Chinese characters. Non-characters were larger (50 font size) than real characters (40 font size) in order to encourage participants to perform the task based on the recognition of low level visual similarity and not on the extraction of semantic information (Chou et al., 2009). Trials consisted of a solid square (500 ms), followed by the first non-character (800 ms), a 200 ms blank interval, and the second non-character for 3000 ms. Participants determined whether the pair of stimuli was identical or not by pressing a yes or no button with their right hand. There were also 24 baseline events as “null” trials so that we could better deconvolve the response to the lexical and perceptual trials. The participant was instructed to press a button when a solid square (1300 ms) at the center of the visual field turned to a hollow square (3000 ms) after a blank interval (200 ms).

Stimulus characteristics. Several lexical variables were controlled across the related and unrelated conditions (Table 2-2). First, all characters were monosyllabic. Second,

doi:10.6342/NTU201700744

the first and second character did not share radicals. Third, the first and second character together did not form a compound word (Sinica Corpus, 1998; Wu & Liu, 1987). Fourth, characters were matched for visual complexity (in terms of strokes per character) across the related and unrelated conditions. Fifth, characters were matched for written frequency for adults (Wu & Liu, 1987) and written familiarity for children across the related conditions. Familiarity scores were obtained from pre-tests in which all the characters were rated on a 7-point scale by thirty age-matched children. The instruction for written familiarity asked the children how often they saw the character in books, newspaper, and magazines. The correlations of the character familiarity measures were not significant, with free association values or categorical rating scores, indicating that association or categorical effects should not be due to familiarity differences.

MRI data acquisition. Participants lay in the scanner with their head position secured. An optical response box was placed in the participants' right hand. The head coil was positioned over the participants' head. Participants viewed visual stimuli projected onto a screen via a mirror attached to the inside of the head coil. This study adopted an event-related design. Each participant performed two functional runs. Each run took 4.7 minutes.

All images were acquired using a 3 Tesla Siemens Trio scanner. Gradient-echo

doi:10.6342/NTU201700744

localizer images were acquired to determine the placement of the functional slices. For the functional imaging studies, a susceptibility weighted signal-shot EPI (echo planar imaging) method with BOLD (blood oxygenation level-dependent) was used. Functional images were interleaved from bottom to top collected parallel to the AC-PC plane. The scanning parameters were the following: repetition time (TR) = 2000 ms; echo time (TE) = 24 ms; flip angle = 90º; matrix size = 64 × 64; field of view = 25.6cm; slice thickness = 3 mm; number of slices = 34. Each participant performed 4.5-min functional runs. Each functional run had 136 image volumes. A high-resolution, T1-weighted three dimensional image was also acquired (Magnetization Prepared Rapid Gradient Echo, MP-RAGE; TR = 1560 ms; TE = 3.68 ms; flip angle = 15º; matrix size = 256×256; field of view = 25.6 cm; slice thickness = 1 mm, number of slices = 192). The orientation of the 3D image was identical to the functional slices. The task was administered in a pseudorandom order for all participants, in which the order of conditions was optimized for event-related design (Burock, Buckner, Woldorff, Rosen, & Dale, 1998).

fMRI analysis. Data analysis was performed using SPM8 (Statistical Parametric Mapping). The functional images were corrected for differences in slice-acquisition time to the middle volume and were realigned to the first volume in the scanning session using affine transformations. No participant had more than 3 mm of

doi:10.6342/NTU201700744

movement in any plane. Co-registered images were normalized to the MNI (Montreal Neurological Institute) average template (12 linear affine parameters for brain size and position, 8 non-linear iterations and 2 x 2 x 2 nonlinear basis functions). Statistical analyses were calculated on the smoothed data (10 mm isotropic Gaussian kernel), with a high pass filter (128 seconds cutoff period) in order to remove low frequency artifacts.

Data from each participant was entered into a general linear model using an event-related analysis procedure (Josephs & Henson, 1999). Character pairs were treated as individual events for analysis and modeled using a canonical HRF (Hemodynamic Response Function). There were five event types: association strength, categorical relatedness, unrelated, perceptual, and baseline. For semantically related pairs, we entered free association values and categorical rating as two continuous variables to determine if brain activation was systematically correlated with these variables. The values of association strength and categorical rating were implemented for character pairs as item-level parametric modulators in a first-level (within-subject) statistical model. The resulting model coefficients for individual subjects were entered into subsequent second-order random effects analyses for group effects in a whole brain analysis. Random effects analysis using one-sample t-test across all participants to determine whether activation during a contrast was significant (i.e., parameter

doi:10.6342/NTU201700744

estimates were reliably greater than 0). The incorrect trials were included for the following analyses, considering that the statistical power should be equal between conditions with different accuracies for fMRI analyses (Bitan et al., 2007; Chen et al., 2016).

In order to determine the effects of association strength and categorical relatedness within group and between groups, we examined the effect of these two continuous variables with signal intensity for the related pairs. Positive effects indicated progressively greater activation for character pairs with stronger association strength or higher categorical relatedness, whereas negative effects indicated progressively greater activation for character pairs with weaker association strength or lower categorical relatedness. For within-group analysis, we examined the stronger association strength and weaker association strength in the ASD group and in the TD group, and higher categorical relatedness and lower categorical relatedness in the ASD group and in the TD group, respectively ($p < .001$ uncorrected at the voxel level with cluster greater than 0 voxels). Moreover, for between-groups analysis, three hypothesis-driven regions of interest (ROIs) were chosen for the weaker association strength and, including the left IFG (-51,27,10), the left MTG (-57,-48,3) (Chou et al., 2009) with a radius 10 mm centered at peak voxels of brain regions, and the left cuneus using the WFU Pickatlas (Maldjian, Laurienti, Kraft, & Burdette, 2003), as

doi:10.6342/NTU201700744

well as two hypothesis-driven ROIs with a radius of 6 mm centered at peak voxels of brain regions for the higher categorical relatedness, including the left occipito-temporal cortex (-45,-66,6) (Grossman et al., 2013) and the left precuneus (-3,-51,18) (Sachs, Weis, Krings, et al., 2008; Sachs, Weis, Zellagui, et al., 2008). All reported areas of activation were significant using $p < .05$ FWE (family-wise error) corrected at the voxel level with the use of ROIs. In addition, to explore the role of cuneus in visual processing, I extracted the signal intensity for the weaker association strength in the left cuneus for the ASD group and then computed correlation with the scores of Perceptual Organization Index of WISC-III associated with visual perception.

2-3 Results

Behavioral performance. The analysis of accuracy (mean ± SD) for the ASD and the TD group was 73 ± 22% and 79 ± 17%, respectively. In a two-sample t-test, two groups were not significantly different in accuracy, $t(65) = 0.27$, $p > .05$. The analysis of reaction time (mean ± SD) for the ASD and the TD group was 1194 ± 242 ms and 1133 ± 216 ms, respectively. In a two-sample t-test, there was no significant difference in reaction time between the ASD and TD groups, $t(65) = 0.28$, $p > .05$.

Brain activation patterns. The effects of association strength and categorical relatedness on signal intensity for related pairs are shown in Table 2-3.

doi:10.6342/NTU201700744

Association strength. For within-group analysis, the ASD group showed greater activation in the left superior occipital gyrus (BA 31) and the right cuneus (BA 7) for the weaker association strength. The TD group showed greater activation in the left IFG (BA 45), left MTG (BA 21), left inferior parietal lobule (BA 40), left fusiform (BA 37), and right insula (BA 13) and right middle cingulate gyrus (BA 8) for the weaker association strength. For between-groups analysis, the ASD group showed greater activation in the cuneus (Figure 2-1A) as compared to the TD group, and the TD group showed greater activation in the left IFG (BA 45) and left MTG (BA 21) for the weaker association strength (Figure 2-1B).

Categorical relatedness. For within-group analysis, the ASD group showed greater activation in the left anterior cingulate cortex, right caudate, right hippocampus and right middle frontal gyrus (BA 10) for the higher categorical relatedness. The TD group produced greater activation in the left precuneus (BA 30) and right meddle temporal gyrus (BA 22) for the higher categorical relatedness. For between-groups analysis, as compared to the ASD group, the TD group showed greater activation in the left precuneus (BA 30) and left occipito-temporal cortex (BA 37) for the higher categorical relatedness (Figure 2-1C).

Correlation analysis. I correlated the left cuneus activation for the weaker association strength with the scores of the sub-scores of Perceptual Organization

doi:10.6342/NTU201700744

Index of WISC-III which is associated with visual perception. The left cuneus activation was positively correlated with the score of picture completion, $r = .45$, $p < .05$.

2-4 Discussion

In the present study, the main goal was to examine the neural correlates of association strength and categorical relatedness between the ASD and the TD group. We manipulated the association values of association strength and the scores of categorical relatedness for the related pairs. For the ASD group, the weaker association strength produced greater activation in the left superior occipital gyrus and right cuneus, and the higher categorical relatedness produced greater activation in the left anterior cingulate cortex, right caudate, right hippocampus and the right middle frontal gyrus For the TD group, the weaker semantic association produced greater activation in the left IFG and left MTG, and the higher categorical relatedness produced greater activation in the right precuneus and right MTG. Moreover, as compared to TD group, the ASD group elicited greater activation in the left cuneus for the weaker association strength, and the cuneus activation also positively correlated with the picture completion. The TD group showed greater activation in the left IFG and left MTG for the weaker association strength, and greater activation in

doi:10.6342/NTU201700744

the left precuneus and left occipito-temporal cortex for the higher categorical relatedness as compared to the ASD group.

The first major finding in this study was the left cuneus activation in ASD for the weaker association strength The ASD group showed greater activation in the left cuneus in contrast to the greater left MTG and left IFG activation in the TD group. This finding is in agreement with the studies of atypical reliance on the visual cortex in individuals with ASD (Chen et al., 2016; Kana et al., 2006). Youths with ASD may tend to use visuo–spatial regions to compensate the dysfunction of higher-order frontal regions (Koshino et al., 2005). Also, atypical involvement of extrastriate regions might be related to impaired functions in the prefrontal cortex during semantic judgments (Gaffrey et al., 2007; Shen et al., 2012). Moreover, a connectivity study demonstrated that atypically increased connectivity between frontal and extrastriate regions, along with greater activity within the extrastriate cortex, could suggest compensatory mechanisms in ASD (Shen et al., 2012). Thus, the greater activation in the left cuneus in the ASD group might suggest that youth with ASD tend to include primary visual cortex for semantic processing and to rely more on lower-level visual processing in order to compensate the deficits of higher-level semantic processing.

The second major findings is that the TD group showed additional activation in the left MTG and left IFG as compared to the ASD group for the weaker association strength. The left MTG has often been suggested to be responsible for the storage of lexical representations (Binder et al., 2009; Lau et al., 2008) and the representation of conceptual contents (Fairhall & Caramazza, 2013). Participants may need extensive search of semantic representations in order to identify distant relationships. The left IFG is typically associated with lexical retrieval of semantic knowledge (Bookheimer, 2002). Many studies have also shown increased activation in the left IFG as the task difficulty increases, implying greater processing demands (Binder et al., 2009; Chou et al., 2009; Lee et al., 2011). In this study, greater activation in the left IFG for the weaker semantic association could be attributed to increased demands on the retrieval or selection of appropriate semantic knowledge between character pairs. Our result is consistent with a top-down control processing with the recruitment of frontal cortices in the TD group (Fan et al., 2010; Lai et al., 2014). Fan et al. (2010) examined the effective connectivity between brain regions involved in semantic judgment, showing that there is a modulatory effect from the left IFG to the left MTG to suggest top-down influences of the frontal cortex.

The third major finding is that the TD group showed greater activation in the left precuneus and left occipito-temporal cortex for the higher categorical relatedness as compared to the ASD group. The left precuneus has been linked with elaborating highly integrated information (Cavanna & Trimble, 2006) and in the conceptual

doi:10.6342/NTU201700744

representation of semantic knowledge (Fairhall & Caramazza, 2013). In order to perform a semantic relatedness judgment, children need to compare the overlapping semantic features for stimulus pairs (Nation & Snowling, 1999). The higher categorical relatedness may allow for greater integration for features due to many overlapping semantic features between characters (Plaut, 1995). Greater activation in the left precuneus may reflect that many similar or overlapping features are activated and integrated during processing the higher categorical relatedness. In this study, the participants had to retrieve the conceptual knowledge about each of the characters and compare the similarity between those semantic features that would help to decide whether the pairs were related in meaning. The higher categorical pairs have more shared perceptual features between stimulus pairs (Estes et al., 2011; Hampton, 2006), thus producing greater activation in the left precuneus. Furthermore, the TD group also showed greater activation in the occipito-temporal cortex for the higher categorical relatedness as compared to the ASD group. Greater activation in the occipito-temporal cortex is thought to reflect the storage of many features of a general-level category (Taylor et al., 2011), reflecting the elaboration of features with increasing connections among relevant features for higher categorical pairs (McClelland & Rogers, 2003). Therefore, greater activation in the left precuneus and left occipito-temporal cortex might be related to more elaborate features of categorical

doi:10.6342/NTU201700744

knowledge in the occipito-temporal cortex that allow a complete integration of the overlapping features for the higher categorical relatedness.

In conclusion, our findings suggest a differential neural mechanism during semantic processing between youths with ASD and TD youths. The ASD group may rely more on the lower-level visual processing to support the semantic processing. In contrast to youths with ASD, the TD youths showed higher-level controlled processes of more elaborate semantic representations for selection processes and more elaborate features of categorical knowledge for integration.

doi:10.6342/NTU201700744

Chapter 3

General Discussion

These two experiments were attempt to (1) understand the developmental changes of semantic processing and (2) to examine the differential neural substrates of semantic processing between TD youths and youths with ASD.

In this thesis, for the TD children, I used a longitudinal approach to solve the defect of previous studies that used cross-sectional approaches to examine developmental changes. Moreover, I orthogonally manipulated association strength and categorical relatedness to investigate the role of different semantic relation during semantic processing. Afterward, I systematically manipulated the association strength and categorical relatedness with entered free association values and categorical ratings as two continuous variables to determine if brain activation was systematically correlated with these variables to better understand the neural correlated of semantic processing between youths with ASD and TD youths.

The main findings of this thesis showed that, for the TD children, (1) developmental increases in the left IFG and left MTG for association strength, it may be related to more elaborate semantic representations that require greater engagement of selection processes, and (2) developmental increases in the left precuneus and OTC

doi:10.6342/NTU201700744

for categorical relatedness, it may be associated with more elaborate features of categorical knowledge that allow complete integration. In contrast to the TD youths, (3) youths with ASD showed greater activation in the left cuneus for the weaker association strength, it may suggest that youth with ASD tend to include primary visual cortex and rely more on lower-level visual processing in order to compensate the impairment of higher-level semantic processing. (4) The TD youths showed greater activation in the left MTG and left IFG for the weaker association strength and greater activation in the precuensu and left OTC for the higher categorical relatedness as compared to the youths with ASD, suggesting TD youths have more elaborate semantic representations for selection processes and more elaborate features of categorical knowledge for integration. These findings provide further evidence of the developmental of semantic knowledge in the TD children, and show that youths with ASD may more rely on visualization to support semantic processing.

doi:10.6342/NTU201700744

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Tables

Table 1-1

Stimulus Characteristics of Association Strength and Categorical Relatedness.

	Free association value		**Categorical relationship** [1]	
	High categorical	Low categorical	High categorical	Low categorical
Strong association	24.7(16.9)	20.4(9.6)	6.3(0.4)	3.9(1.0)
Weak association	7.3(2.5)	3.8(3.0)	6.0(0.3)	4.6(1.0)

	Stroke		**Frequency**	
	High categorical	Low categorical	High categorical	Low categorical
Strong association	9.7(4.5)	11.8(3.3)	317.7(472.2)	242.0(251.0)
Weak association	10.3(3.5)	12.2(4.0)	475.9(807.0)	222.5(340.9)

	Familiarity		**Semantic relatedness**	
	High categorical	Low categorical		
Strong association	6.3(0.3)	6.2(0.3)	Free association value	.29[2]
Weak association	6.2(0.4)	6.2(0.2)		

	Imageability		**Concreteness**	
	High categorical	Low categorical	High categorical	Low categorical
Strong association	5.1(0.9)	5.3(0.9)	5.3.(0.9)	5.9(0.6)
Weak association	4.9(1.2)	4.6(0.9)	5.1(0.8)	5.2(0.8)

Note. 1. Mean score of categorical relationship, 2. Correlation of semantic relatedness and free association value ($p < .05$). (Standard deviations in parentheses)

Table 1-2

Greater Activation for Time 1, Time 2, and Time 2-Time 1 for Association Strength and Categorical Relatedness in Experiment 1

Condition	Regions	BA	*z*- test	Voxels	*x*	*y*	*z*
Strong - Weak							
association strength							
Time 1	n.s						
Time 2	R Superior frontal gyrus	10	3.17	12	24	54	3
Time 2 - Time 1	n.s						
Weak - Strong							
association strength							
Time 1	L Precentral gyrus	1	3.15	1	-42	3	18
	L Putamen		3.12	1	-24	12	12
Time 2	L Inferior frontal gyrus	45	4.28	280	-57	21	6
	R Inferior frontal gyrus	45	3.43	1	60	27	6
	L Supplementary motor area	6	3.38	9	-6	3	72
	L Precentral gyrus	4	3.36	5	-45	-12	57
	L Middle temporal gyrus	21	3.33	3	-54	-42	6
	L Inferior parietal lobule	40	3.10	2	-45	-45	48
Time 2 - Time 1	L Inferior frontal gyrus[a]	45	3.56	134	-57	12	24
	L Middle temporal gyrus[a]	21	2.25	37	-54	-39	3

(continued)

Table 1-2

Greater Activation for Time 1, Time 2, and Time 2-Time 1 for Association Strength and Categorical Relatedness in Experiment 1

Condition	Regions	BA	*z*- test	Voxels	*x*	*y*	*z*
High - Low categorical relatedness							
Time 1	R Cuneus	19	3.25	5	9	-96	21
Time 2	L Precuneus	30	3.16	9	-3	-51	15
	L Occipito-temporal cortex	37	3.15	2	-51	-60	3
Time 2 - Time 1	L Precuneus[a]	30	2.84	61	-3	-51	18
	L Occipito-temporal cortex[a]	37	2.25	37	-45	-66	6
Low - High categorical relatedness							
Time 1	R Anterior cingulate	32	3.22	51	12	33	21
	L Anterior cingulate	33	3.20	51	-3	9	27
	L Cingulate gyrus	9	3.58	74	-3	36	33
	R Medial frontal gyrus	8	3.24	74	3	36	48
	L Middle frontal gyrus	46	3.39	68	-39	45	9
Time 2	n.s						
Time 2 - Time 1	n.s						

Note. n.s: no significant activation; L: left; R: right; BA: Brodmann's area; Coordinates of activation peak(s) within a region based on a z-test are given in the MNI stereotactic space (x, y, z). Voxels: number of voxels. [a]$p < .05$ corrected for multiple comparisons at the voxel level with a cluster size greater than 10 voxels with the use of functional masks.

Table 2-1

Demographic Characteristics of Youths with Autism Spectrum Disorder (ASD) and Typically Developing Youths (TD) in Experiment 2

	ASD (*n* = 31)	TD (*n* = 35)	*P value* (ASD vs. TD)
	Mean (*SD*)	Mean (*SD*)	
Handedness : Right	31	36	
Age (years)	12.1 (1.2)	11.9 (1.0)	.38
Verbal intelligence quotient	106.1 (12.9)	113.3 (11.1)	.02*
Performance intelligence quotient	106.8 (12.9)	110.6 (14.6)	.27
Full intelligence quotient	106.8 (12.5)	112.8 (12.5)	.06

Note. Independent sample t-test was used for test statistics. Handedness was assessed by using Edinburgh Handedness Inventory. Verbal intelligence quotient, performance intelligence quotient and full intelligence quotient were measured by using Wechsler Intelligence Scale for Children, 3rd version.

**P* value < .05.

doi:10.6342/NTU201700744

Table 2-2

Stimuli Characteristics of the First (1st) and Second (2nd) Characters in the Related and Unrelated Pairs.

		Related	Unrelated
Stroke	1st character	10 (3)	11 (3)
	2nd character	11 (4)	10 (3)
Frequency	1st character	167 (295)	37 (267)
	2nd character	462 (751)	201 (174)
Familiarity^{a}	1st character	6.0 (0.5)	6.1 (0.4)
	2nd character	6.4 (0.3)	6.2 (0.4)
Correlation	Association value^{b}	1st character	-.08
		2nd character	.24
	Categorical rating^{c}	1st character	-.01
		2nd character	.1
	Association value and Categorical rating^{d}		.29

Note. ^{a}Mean score of characters; Correlation: ^{b}correlation of association value and familiarity. ^{c}correlation of categorical rating and familiarity. ^{d}correlation of association value and categorical rating ($p > .05$). (Standard deviations in parentheses)

Table 2-3

Areas of activation for the association strength and categorical relatedness for the ASD and TD groups in Experiment 2

Cortical regions	H	BA	voxels	Z test	MNI coordinates		
					X	Y	Z
Stronger association strength							
ASD group[a]							
Superior frontal gyrus	L	10	21	3.02	-18	59	31
Superior medial frontal gyrus	L	6	13	2.71	-9	32	61
TD group[b]							
Middle cingulate gyrus	L	31	210	3.88	0	-46	34
Middle occipital gyrus	R	39	53	3.79	48	-70	28
Superior medial frontal gyrus	L	9	47	3.74	0	50	31
TD>ASD[b]							
Middle cingulate gyrus	L	31	1	3.12	0	-46	34
ASD>TD							
-							
Weaker association strength							
ASD group[b]							
Superior occipital gyrus	L	31	71	3.84	-15	-70	28
Cuneus	R	7	16	3.41	12	-70	34
TD group[b]							
Inferior frontal gyrus	L	45	483	4.05	-39	29	22
Inferior parietal lobule	L	40	95	3.46	-33	-46	43

(continued)

Table 2-3

Areas of activation for the association strength and categorical relatedness for the ASD and TD groups in Experiment 2

Cortical regions	H	BA	voxels	Z test	MNI coordinates		
					X	Y	Z
Middle temporal gyrus	L	21	22	3.54	-54	-55	-2
Insula	R	13	56	3.28	36	17	13
Middle cingulate gyrus	R	8	11	3.40	12	17	43
Supra Marginal	L	40	3	3.18	-54	-34	31
Fusiform	L	37	2	3.12	-36	-52	-17
TD>ASD^c							
Inferior frontal gyrus	L	45	5	2.77	-54	29	4
Middle temporal gyrus	L	21	1	2.77	-54	-55	-2
ASD>TD^c							
Cuneus	L	7	25	3.36	-9	-73	34
Higher categorical relatedness							
ASD group^a							
Anterior cingulate cortex	L	-	331	2.90	-9	26	-2
Caudate	R	-		2.88	15	23	-5
Hippocampus	R	-	29	2.28	42	-19	-17
Middle frontal gyrus	R	10	22	2.78	6	47	-8
TD group^b							
Precuneus	L	30	171	4.44	9	-52	19
Middle temporal gyrus	R	22	192	3.99	42	-55	13

(continued)

doi:10.6342/NTU201700744

Table 2-3

Areas of activation for the association strength and categorical relatedness for the ASD and TD groups in Experiment 2

Cortical regions	H	BA	voxels	Z test	MNI coordinates		
					X	Y	Z
TD>ASD[c]							
Precuneus	L	30	52	3.03	-3	-49	13
Occipito-temporal cortex	L	37	15	2.74	-48	-61	10
ASD>TD[b]							
Middle orbital frontal gyrus	R	10	1	3.13	24	53	-8
Lower categorical relatedness							
ASD group[b]							
Superior medial frontal gyrus	L	8	27	3.43	0	26	46
TD group[b]							
Middle frontal gyrus	L	8	51	3.88	-36	11	55
Supplementary motor area	R	8	89	3.74	0	20	55
Angular gyrus	L	40	5	3.23	-42	-61	46
TD>ASD[b]							
Superior orbital frontal gyrus	R	10	1	3.11	24	53	-8
ASD>TD[b]							
Inferior temporal gyrus	L	19	3	3.26	-48	-61	-11

Note. ASD: autism spectrum disorders; TD: typically developing; H: hemisphere; L: left; R: right; BA: Brodmann's area; Voxels: number of voxels in cluster at [a] $p < .01$ uncorrected with clusters greater than 10 in a whole brain analysis. [b] $p < .001$ uncorrected with clusters greater than 0 in a whole brain analysis. [c] $p < .05$ FWE corrected with the use of masks; Coordinates of activation peak(s) within a region based on a z test are given in the MNI stereotactic space (x, y, z).

Figures

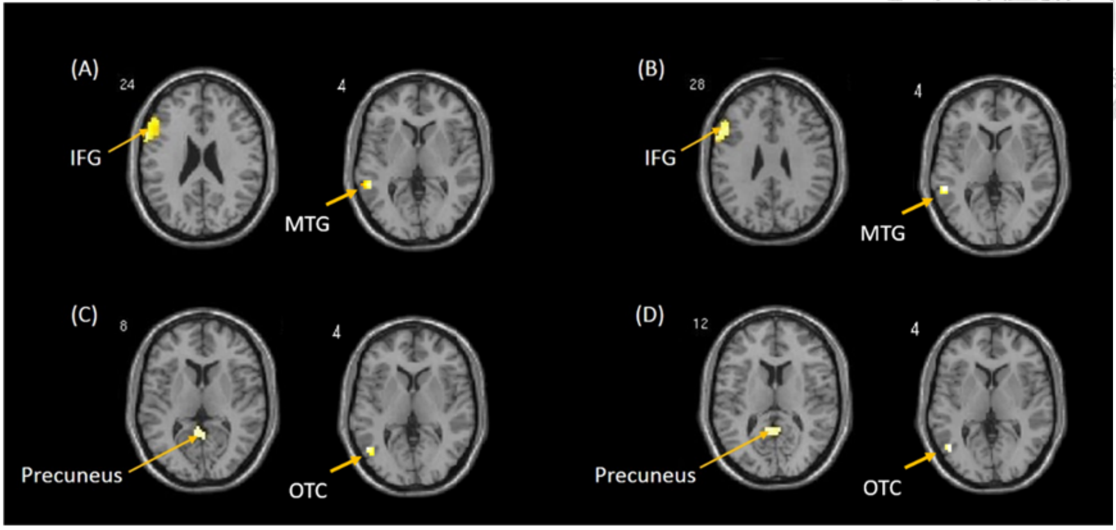
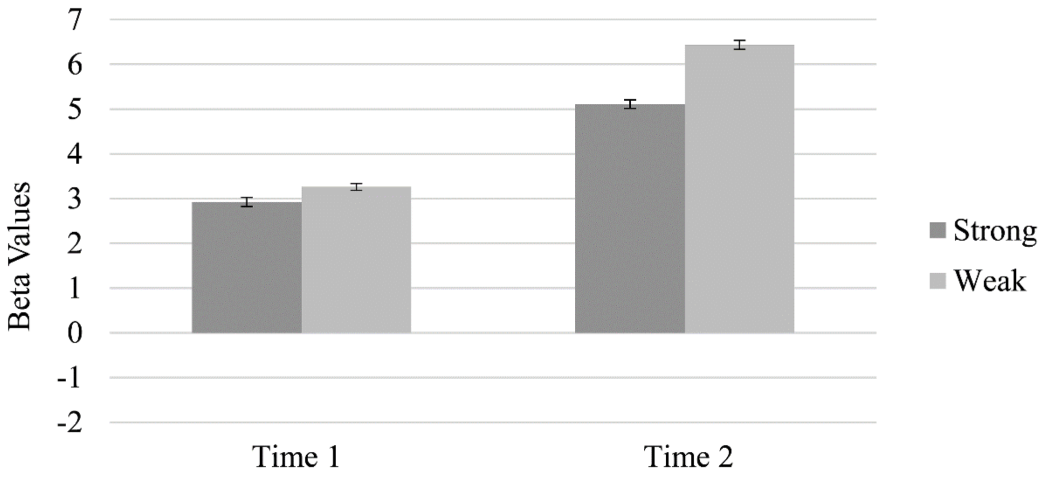


Figure 1-1. Greater activation for (A) the contrast of the weak versus the strong association strength produced greater activation in the left inferior frontal gyrus (IFG, BA 45) and left middle temporal gyrus (MTG, BA21) for time 2, (B) the developmental changes of semantic processing for the contrast of the weak versus the strong association strength produced greater activation in the left IFG (BA 45) and left middle temporal gyrus (MTG, BA21) for Time 2 compared to Time 1, (C) the contrast of the high versus the low categorical relatedness elicited greater activation in the left precuneus (BA 30) and left occitipo-temporal gyrus (OTC, BA37) for Time 2, and (D) the developmental changes of semantic processing for the contrast of the high versus the low categorical relatedness elicited greater activation in the left precuneus (BA 30) and left occitipo-temporal gyrus (OTC, BA37) for Time 2 compared to Time 1.

(A) IFG: association strength



(B) Precuneus: categorical relatedness

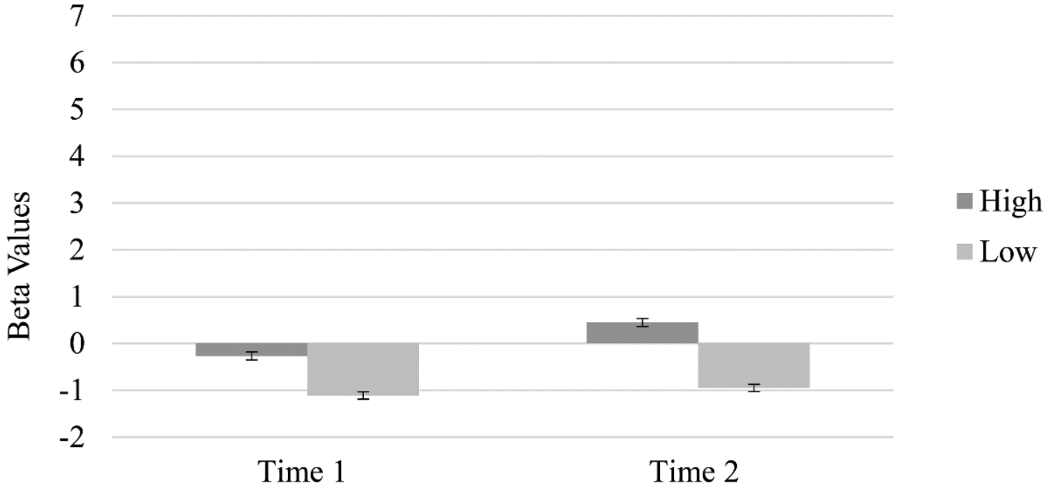
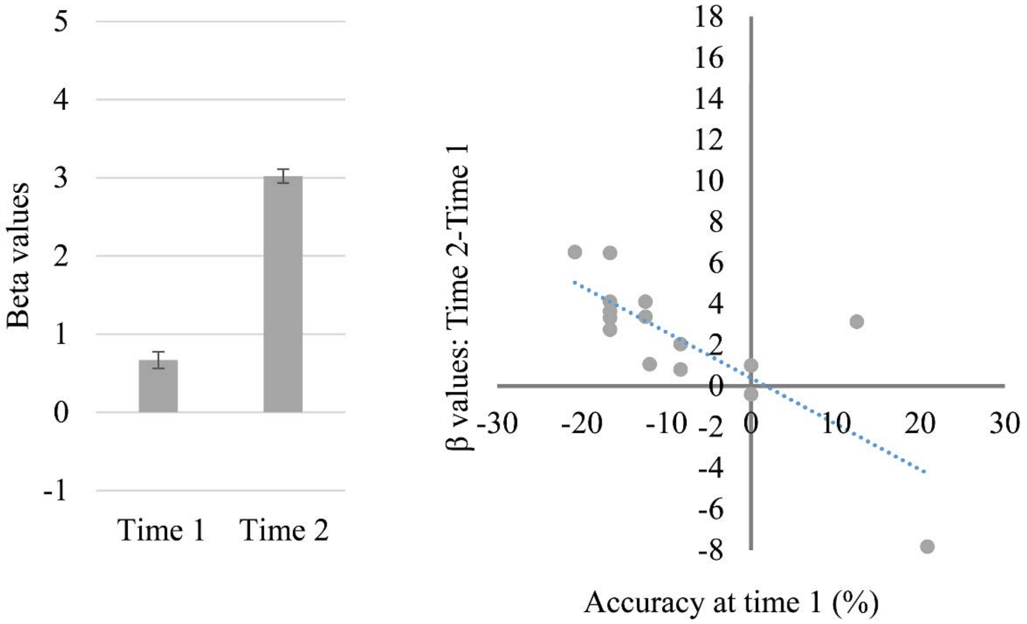


Figure 1-2. Developmental changes in brain activation (beta values). (A) For the weak versus strong association strength, a greater difference in IFG activation at Time 2 compared to Time 1 is driven by an increase for the weak association. (B) For the high versus low categorical relatedness, a greater difference in precuneus activation at Time 2 compared to Time 1 is driven by an increase for the high categorical relatedness.

doi:10.6342/NTU201700744

(A) Weak versus Strong association strength: IFG



(B) High versus Low categorical relatedness: Precuneus

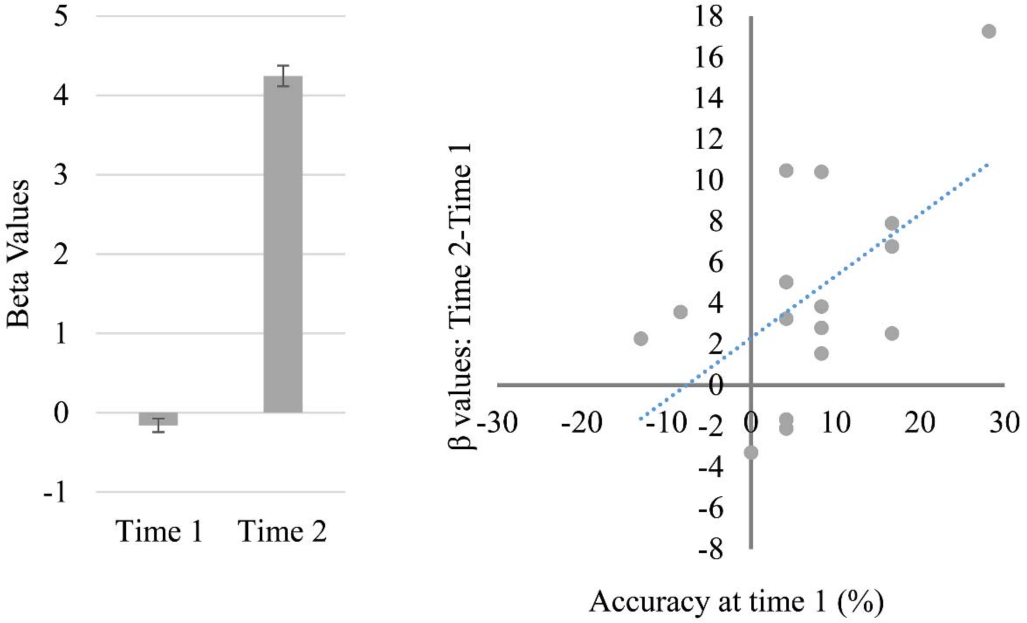


Figure 1-3. (A) For the weak versus strong association strength, the beta values at Time 2 were higher than Time 1 for the left inferior frontal gyrus (IFG) in the left panel. The negative correlation between accuracy (percentage of the weak association minus percentage of the strong association) at Time 1 and the signal change (beta

values of the weak association minus beta values of the strong association) of the IFG for Time 2 vs. Time 1 in the right panel. (B) For the high versus low categorical relatedness, the beta values at Time 2 were higher than Time 1 for the left precuneus in the left panel. The positive correlation between accuracy (percentage of the high categorical minus percentage of the low categorical relatedness) at Time 1 and the signal change (beta values of the high categorical minus beta values of the low categorical relatedness) of the left precuneus for Time 2 vs. Time 1 in the right panel.

doi:10.6342/NTU201700744

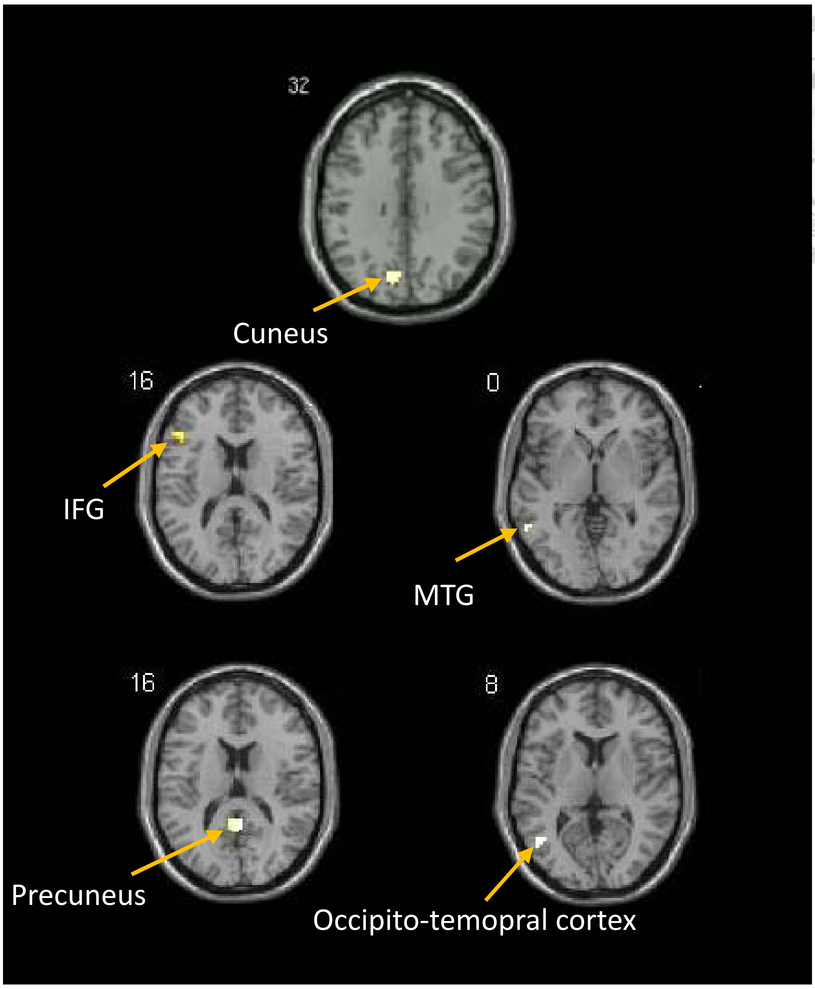


Figure 2-1. For group comparisons, (A) the ASD group showed greater activation in the left cuneus (BA 7) for the weaker association strength as compared to the TD group. (B) The TD group showed greater activation in the left IFG (BA 45) and MTG (BA 21) for the weaker association strength, and (C) greater activation in the left precuneus (BA 30) and left occipito-temporal cortex (BA 37) for the higher categorical relatedness as compared to the ASD group.

doi:10.6342/NTU201700744

Appendix

The forty-eight character pairs in a 2 (strong, weak association) by 2 (high, low categorical relatedness) matrix for the semantic related condition.

	高類別語意關係		低類別語意關係	
高語意關聯	卒	兵	禪	佛
	劍	刀	線	針
	扔	丟	笑	哭
	面	臉	嫂	兄
	優	好	鼠	貓
	畏	怕	站	坐
	乏	少	噸	重
	郎	男	磅	重
	持	拿	棉	軟
	按	壓	稅	錢
	憨	笨	枕	睡
	暑	熱	燈	亮
低語意關聯	劣	差	組	群
	劈	砍	群	黨
	殃	禍	季	年
	堂	室	賤	貴
	叩	敲	橫	直
	逛	走	屑	粉
	頂	上	折	彎
	乾	濕	餅	糧
	陡	斜	垃	廢
	宜	好	港	船
	最	極	匠	雕
	花	樹	晒	陽

Curriculum Vitae

Education

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Teacher’s Certificate of Elementary School

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doi:10.6342/NTU201700744

Research Experience

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2010-present. Attended Professor Tai-Li Chou's lab (National Taiwan University, Taipei, Taiwan) using fMRI to study the neural correlates of semantic processing in children.

2007-present. Attended Professor Shiou-Yuan Chen's lab (Department of Early Childhood Education, University of Taipei, Taiwan) using longitudinal approach collecting the association norms of Taiwanese young readers

Teaching/Mentoring Experience

2016/9-2017/1 Teaching Assistant in Introduction to Functional Magnetic Resonance Imaging

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Publications

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Manuscript submitted for publication

Chou, T. L., **Wong, C. H.**, Chen, S. Y., Fan, L. Y., & Booth, J. R. Developmental changes of association strength and categorical relatedness on semantic processing in the brain.

Manuscript in preparation

Wong, C. H, Gau, S. S. F, & Chou, T. L. Neural correlates of processing categorical relatedness in youths with autism spectrum disorder.

Conference Posters

Wong, C. H, Gau, S. S. F, & Chou, T. L, (2016).Neural correlates of processing categorical relatedness in youths with autism spectrum disorder. The 18th

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doi:10.6342/NTU201700744